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Este livro reúne os artigos científicos dos membros da nossa Academia, que gentilmente nos encaminham para publicação no nosso site. A lista segue uma ordem cronológica decrescente.

No site, temos também uma tabela com todos estes artigos com critérios de pesquisa por palavra-chave (data, autor, título, etc).

Produção: Renato Reis





AGRADECIMENTOS aos nossos parceiros e apoiadores:



Diabetic Bone Disease: A Comprehensive Narrative Review of Pathophysiology, Diagnosis, and Evidence-Based Management

- João Protásio Netto
- Vagner Camargo Pires
- Mariana Garcia Martins Castro

Publicação: 11 de Novembro de 2025
Veículo: MDPI- Diabetology

Pesquisa completa aqui!



diabetology



Review

Diabetic Bone Disease: A Comprehensive Narrative Review of Pathophysiology, Diagnosis, and Evidence-Based Management

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Abstract

Background: Diabetic bone disease affects over 537 million people with diabetes worldwide, characterized by increased fracture risk despite paradoxically normal or elevated bone mineral density (BMD) in Type 2 diabetes. This narrative review synthesizes current evidence on pathophysiology, diagnostic approaches, and management strategies.

Methods: We performed a comprehensive literature search of the PubMed, Embase, and Cochrane databases (2007–2025), prioritizing systematic reviews, meta-analyses, large-scale population studies, and clinical trials examining bone health in diabetes, including bone density, quality, fracture risk, imaging techniques, biomarkers, and therapeutic interventions. **Results:** Advanced glycation end products fundamentally alter bone metabolism through mechanisms distinct from traditional osteoporosis. Type 1 and Type 2 diabetes produce contrasting skeletal phenotypes requiring tailored management. Recent umbrella reviews of 71 meta-analyses demonstrated skeletal benefits of metformin and GLP-1 receptor agonists, while confirming thiazolidinedione risks. Trabecular bone score enhances fracture prediction when DXA appears normal. Large-scale studies revealed heterogeneous risk patterns, with specific subgroups showing substantially elevated fracture risk. Advanced imaging revealed distinct microarchitectural changes between diabetes types. Diabetic patients experienced doubled healing complications, necessitating specialized peri-operative protocols. **Conclusions:** Diabetic bone disease represents a distinct clinical entity requiring enhanced diagnostic strategies beyond traditional densitometry, evidence-based treatment selection considering skeletal and metabolic effects, and specialized management protocols extending beyond conventional osteoporosis care.

Keywords: diabetes mellitus; bone quality; fracture risk; advanced glycation end products; trabecular bone score; diabetic osteopathy

1. Introduction

Diabetic bone disease has emerged as a significant complication affecting the rapidly expanding global diabetes population. The International Diabetes Federation estimates 537 million adults currently live with diabetes worldwide, with projections reaching 783 million by 2045 [1]. This growing prevalence makes understanding diabetes-bone interactions increasingly critical for clinical practice.



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Diabetology 2025, 6, 140.

<https://doi.org/10.3390/diabetology6110140>

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Pulsed magnetic field in the treatment of fractures in the elderly: Unraveling mechanisms and optimizing clinical practice

- Palmerindo Antônio Tavares de Mendonça Néto
- Mayara Magda Dantas Tavares de Mendonça
- Carlos Eduardo Miranda
- Dirceu Moraes Junior
- Carlos Stéfano Hoffmann Brito
- Daniel Ramos Gonçalves Lopes
- André Cândia de Oliveira Amorim
- Paulo Cezar Schutz

Publicação: 30 de Outubro de 2025

Veículo: WJARR– World Journal of Advanced Research and Reviews

Pesquisa completa aqui!



Pulsed magnetic field in the treatment of fractures in the elderly: Unraveling mechanisms and optimizing clinical practice

Palmerindo Antônio Tavares de Mendonça Néto ^{1,*}, Mayara Magda Dantas Tavares de Mendonça ², Carlos Eduardo Miranda ³, Dirceu Moraes Junior ⁴, Carlos Stéfano Hoffmann Brito ⁵, Daniel Ramos Gonçalves Lopes ⁶, André Cândia de Oliveira Amorim ⁷ and Paulo Cezar Schutz ⁸

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Abstract

This scientific paper explores the use of Pulsed Magnetic Field (PEMF) as a therapeutic modality in the treatment of fractures, with a special focus on its application in elderly patients. It addresses the growing incidence of fractures in the geriatric population, the risk factors that may contraindicate traditional surgical interventions, and the complex physical and biological mechanisms by which PEMF acts to promote bone healing. The detailed analysis of the scientific evidence aims to provide an in-depth understanding of the potential of PEMF as a safe and effective alternative, contributing to the optimization of treatment strategies and improvement of patients' quality of life.

Keywords: Fractures; Elderly; Osteoporosis; Pulsed Magnetic Field (PEMF); Alternative Therapies; Quality of Life.

1. Introduction

The treatment of bone fractures represents a constantly evolving field in medicine, with the aim of accelerating healing, reducing pain – minimizing the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and opioid analgesics –, reducing postoperative complications, and improving patients' functional outcomes. With the accelerated aging of the world's population, it is estimated that by 2050 there will be more than two billion people aged 60 or over, 426 million of whom will be 80 years of age or older, which implies a significant increase in the incidence of fractures, especially in the elderly. [1,2]

Fractures in this age group are often associated with osteoporosis, sarcopenia, chronic comorbidities, and a higher risk of falls, making the rehabilitation process more complex and prolonged [3]. The loss of functional independence and the increase in post-fracture mortality reinforce the need for less invasive and more effective therapeutic approaches. In this context, non-invasive therapies that favor bone healing and reduce the need for aggressive surgical interventions have gained prominence.

Among these, the Pulsed Electromagnetic Field (PEMF) has emerged as a promising modality, approved by the Food and Drug Administration (FDA) of the United States and recognized by European agencies such as the European Medicines Agency (EMA), through CE certification, for the treatment of fractures with nonunions [4]. Despite the clinical

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Precision Medicine in Orthobiologics: A Paradigm Shift in Regenerative Therapies

- Annu Navani
- Madhan Jeyaraman
- Naveen Jeyaraman
- Arulkumar Nallakumarasamy
- Gabriel Azzini
- Swaminathan Ramasubramanian
- José Fábio Lana

Publicação: 24 de Agosto de 2025
Veículo: MDPI – Bioengineering

Pesquisa completa aqui!



Review

Precision Medicine in Orthobiologics: A Paradigm Shift in Regenerative Therapies

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Abstract

The evolving paradigm of precision medicine is redefining the landscape of orthobiologic therapies by moving beyond traditional diagnosis-driven approaches toward biologically tailored interventions. This review synthesizes current evidence supporting precision orthobiologics, emphasizing the significance of individualized treatment strategies in musculoskeletal regenerative medicine. This narrative review synthesized literature from PubMed, Embase, and Web of Science databases (January 2015–December 2024) using search terms, including ‘precision medicine,’ ‘orthobiologics,’ ‘regenerative medicine,’ ‘biomarkers,’ and ‘artificial intelligence.’ Biological heterogeneity among patients with ostensibly similar clinical diagnoses—reflected in diverse inflammatory states, genetic backgrounds, and tissue degeneration patterns—necessitates patient stratification informed by molecular, genetic, and multi-omics biomarkers. These biomarkers not only enhance diagnostic accuracy but also improve prognostication and monitoring of therapeutic responses. Advanced imaging modalities such as T2 mapping, DTL, DCE-MRI, and molecular PET offer non-invasive quantification of tissue health and regenerative dynamics, further refining patient selection and treatment evaluation. Simultaneously, bioengineered delivery systems, including hydrogels, nanoparticles, and scaffolds, enable precise and sustained release of orthobiologic agents, optimizing therapeutic efficacy. Artificial intelligence and machine learning approaches are increasingly employed to integrate high-dimensional clinical, imaging, and omics datasets, facilitating predictive modeling and personalized treatment planning. Despite these advances, significant challenges persist—ranging from assay variability and lack of standardization to regulatory and economic barriers. Future progress requires large-scale multicenter validation studies, harmonization of protocols, and cross-disciplinary collaboration. By addressing these limitations, precision orthobiologics has the potential to deliver safer, more effective, and individualized care. This shift from generalized to patient-specific interventions holds promise for improving outcomes in degenerative and traumatic musculoskeletal disorders through a truly integrative, data-informed therapeutic framework.



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Not All Platelets Are Created Equal: A Review on Platelet Aging and Functional Quality in Regenerative Medicine

- Fábio Ramos Costa
- Joseph Purita
- Rubens Martins
- Bruno Costa
- Lucas Villasboas de Oliveira
- Stephany Cares Huber
- Gabriel Silva Santos
- Luyddy Pires
- Gabriel Azzini
- André Kruel
- José Fábio Lana

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Veículo: MDPI – Cells

Pesquisa completa aqui!



A Transcutaneous Randomized Pulsed Radiofrequency Application for Spine Pain Conditions: A Case Series

- Daniel de Moraes Ferreira Jorge
- Olav Rohof
- Melina Brigato Ferreira Jorge
- Alexandre Teixeira
- Cezar Augusto de Oliveira
- Pablo Sobreiro
- Douglas Freitas Dos Santos
- Stephany Cares Huber
- José Fábio Lana

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Veículo: MDPI – Journal of Functional Morphology and Kinesiology

Pesquisa completa aqui!



Integrative review of the gut microbiome's role in pain management for orthopaedic conditions

- Naveen Jeyaraman
- Madhan Jeyaraman
- Priya Dhanpal
- Swaminathan Ramasubramanian
- Arulkumar Nallakumarasamy
- Sathish Muthu
- Gabriel Silva Santos
- Lucas Furtado da Fonseca
- José Fábio Lana

Publicação: 20 de Junho de 2025
Veículo: WJEM – World Journal of Experimental Medicine

Pesquisa completa aqui!



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Integrative review of the gut microbiome's role in pain management for orthopaedic conditions

Naveen Jeyaraman, Madhan Jeyaraman, Priya Dhanpal, Swaminathan Ramasubramanian, Arulkumar Nallakumarasamy, Sathish Muthu, Gabriel Silva Santos, Lucas Furtado da Fonseca, José Fábio Lana

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Abstract

The gut microbiome, a complex ecosystem of microorganisms, has a significant role in modulating pain, particularly within orthopaedic conditions. Its impact on immune and neurological functions is underscored by the gut-brain axis, which influences inflammation, pain perception, and systemic immune responses. This integrative review examines current research on how gut dysbiosis is associated with various pain pathways, notably nociceptive and neuroinflammatory mechanisms linked to central sensitization. We highlight advancements in metabolomics technologies, such as metagenomics and metaproteomics, which deepen our understanding of microbiome-host interactions and their implications in pain. Recent studies emphasize that gut-derived short-chain fatty acids and microbial



A Breakthrough for Regenerative Medicine! Standardized Low-Cost Platelet-Rich Plasma Preparation in a Closed System (PRP-LCCS)

- Palmerindo Antônio Tavares de Mendonça Néto
- Mayara Magda Dantas Tavares de Mendonça
- Dirceu Moraes Junior
- Carlos Stéfano Hoffmann Brito
- Leonardo Lemos Rebouças
- Radanezi Potengy Junior
- Gustavo Costa Rios
- Joel Dourado Franco
- Daniel Ramos Gonçalves Lopes

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Veículo: WJARR– World Journal of Advanced Research and Reviews

Pesquisa completa aqui!



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Volume 1, Issue 2 (June) 2025
Research Article

A Breakthrough for Regenerative Medicine! Standardized Low-Cost Platelet-Rich Plasma Preparation in a Closed System (PRP-LCCS)

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ABSTRACT
 Resume

The clinical use of platelet-rich plasma (PRP) has gained prominence in orthopedic regenerative medicine due to its autologous nature and bioactive potential. However, the lack of standardization in preparation techniques, the excessive costs of commercial kits and the requirement for environments with microbiological control remain important limitations, especially in low-resource contexts. This study describes a closed, vacuum-based, low-cost system for PRP processing, which maintains high platelet concentration and good reproducibility. The protocol compared platelet yields from three operators using standardized tubes with specific anticoagulant dimensions and formulations. The centrifugation parameters were optimized to enhance platelet recovery while reducing leukocyte contamination and mechanical activation. The approach is scalable, economically feasible and suitable for implementation in public health systems.

Keywords: Regenerative medicine, Platelet rich plasma (PRP), Closed system, Low cost, Standardization, Public health

1. Introduction

Musculoskeletal diseases represent one of the leading causes of disability in the world, affecting millions of people annually¹. According to the World Health Organization, musculoskeletal

injuries are responsible for approximately 4.37 million deaths per year². In addition, these conditions rank first among the causes of morbidity and mortality in individuals aged 0 to 39 years, resulting in about 150,000 deaths annually. The prevalence of

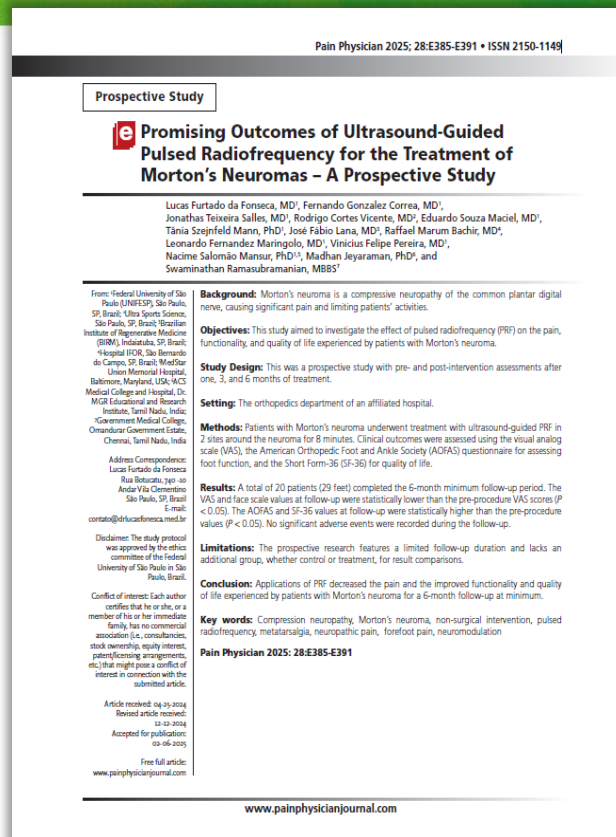


Promising Outcomes of Ultrasound-Guided Pulsed Radiofrequency for the Treatment of Morton's Neuromas – A Prospective Study

- Lucas Furtado da Fonseca
- Fernando Gonzalez Correa
- Jonathas Teixeira Salles
- Rodrigo Cortes Vicente
- Eduardo Souza Maciel
- Tânia Szejnfeld Mann
- José Fábio Lana
- Raffael Marum Bachir
- Leonardo Fernandez Maringolo
- Vinicius Felipe Pereira
- Nacime Salomão Mansur
- Madhan Jeyaraman
- Swaminathan Ramasubramania

Publicação: 02 de Junho de 2025
Veículo: Pain Physician Journal

Pesquisa completa aqui!



The Potential of Red Blood Cells in Regenerative Medicine: A Paradigm Shift in Cellular Therapy

- Fábio Ramos Costa
- Joseph Purita
- Ansar Mahmood
- Rubens Martins
- Bruno Costa
- Bruno Lima Rodrigues
- Stephany Cares Huber
- Gabriel Silva Santos
- Luyddy Pires
- Gabriel Azzini
- André Kruei
- José Fábio Lana

Publicação: 29 de Maio de 2025
Veículo: MDPI – Cells

Pesquisa completa aqui!



Review

The Potential of Red Blood Cells in Regenerative Medicine: A Paradigm Shift in Cellular Therapy

Fábio Ramos Costa ^{1,*}, Joseph Purita ², Ansar Mahmood ³, Rubens Martins ^{4,5}, Bruno Costa ⁵, Bruno Lima Rodrigues ^{6,7}, Stephany Cares Huber ^{6,7}, Gabriel Silva Santos ^{6,7,*}, Luyddy Pires ^{6,7}, Gabriel Azzini ^{6,7}, André Kruei ^{6,7} and José Fábio Lana ^{6,7,8,9,10}

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Abstract: Red blood cells (RBCs) have traditionally been excluded from orthobiologic formulations due to inflammation, oxidative stress, and hemolysis concerns. However, emerging evidence suggests that RBCs may play an active role in regenerative medicine, contributing to immune modulation, vascular support, and oxidative balance. Their interactions with macrophages, involvement in nitric oxide signaling, and release of extracellular vesicles suggest they may influence tissue repair more than previously assumed. Despite these potential benefits, RBC retention in orthobiologic preparations like platelet-rich plasma (PRP) and bone marrow aspirate concentrate (BMAC) remains controversial, with most protocols favoring their removal in the absence of robust translational clinical data. This review explores the biological functions of RBCs in regenerative medicine, their potential contributions to PRP and BMAC, and the challenges associated with their inclusion. While concerns about hemolysis and inflammation persist, controlled studies are needed to determine whether selective RBC retention could enhance musculoskeletal healing in some scenarios. Future research should focus on optimizing RBC processing techniques and evaluating their impact on clinical applications. Addressing these gaps will clarify whether RBCs represent an overlooked but valuable component in regenerative therapies or their exclusion remains justified.

Keywords: red blood cells; regenerative medicine; extracellular vesicles; immunomodulation; tissue engineering

1. Introduction

Regenerative medicine has transformed the treatment of musculoskeletal (MSK) disorders by introducing biologically active therapies that enhance tissue repair and modulate inflammation [1]. Orthobiologic formulations, including platelet-rich plasma (PRP) and

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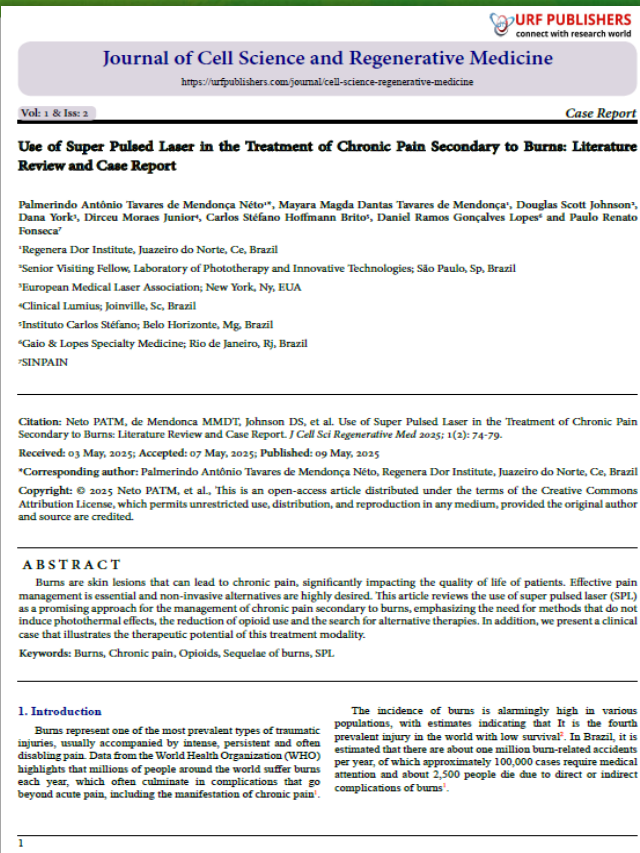
Use of Super Pulsed Laser in the Treatment of Chronic Pain Secondary to Burns: Literature Review and Case Report

- Palmerindo Antônio Tavares de Mendonça Néto
- Mayara Magda Dantas Tavares de Mendonça
- Douglas Scott Johnson
- Dana York
- Dirceu Moraes Junior
- Carlos Stéfano Hoffmann Brito
- Daniel Ramos Gonçalves Lopes
- Paulo Renato Fonseca

Publicação: 09 de Maio de 2025

Veículo: URF Publishers – Journal of Cell Science and Regenerative Medicine

Pesquisa completa aqui!



Orthobiologics Revisited: A Concise Perspective On Regenerative Orthopedics

- Fabio Ramos Costa
- Luyddy Pires
- Rubens Andrade Martins
- Marcia Santos
- Gabriel Silva Santos
- João Vitor Lana
- Bruno Ramos Costa
- Napoliane Santos
- Alex Pontes de Macedo
- Andre Kruel
- Jose Fabio Lana

Publicação: 2 de Abril de 2025

Veículo: MDPI – Current Issues in Molecular Biology

Pesquisa completa aqui!



current issues in
molecular biology



Review

Orthobiologics Revisited: A Concise Perspective on Regenerative Orthopedics

Fábio Ramos Costa ^{1,*}, Luyddy Pires ^{2,3}, Rubens Andrade Martins ⁴, Márcia Santos ⁵, Gabriel Silva Santos ^{2,3}, João Vitor Lana ⁶, Bruno Ramos Costa ⁷, Napoliane Santos ^{2,3}, Alex Pontes de Macedo ^{2,3}, André Kruel ³ and José Fábio Lana ^{2,3,6,8,9}

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Abstract: At the forefront of regenerative medicine, orthobiologics represent a spectrum of biological substances that offer promising alternatives for tissue repair and regeneration. Traditional surgical treatments often involve significant risks, extended recovery periods, and may not fully restore tissue functionality, creating a strong demand for less invasive options. This paper presents a concise overview of orthobiologics, reexamining their role within the broader landscape of regenerative medicine. Beginning with a brief introduction to orthobiologics, the paper navigates through various types of biological materials and their associated mechanisms of action and clinical applications. By highlighting platelet derivatives, bone marrow-derived products, and processed adipose tissue, among others, it underscores the pivotal role of orthobiologics in prompting biological responses like cellular proliferation, differentiation, and angiogenesis, thereby fostering tissue healing. Furthermore, this paper explores the diverse applications of orthobiologics in orthopedic conditions, outlining their utility in the treatment of bone and soft-tissue injuries. Addressing clinical considerations, it discusses safety profiles, efficacy, patient selection criteria, and emerging challenges. With the limitations of traditional medicine becoming more apparent, orthobiologics offer an innovative and less invasive approach to patient care. Looking forward, this paper approaches future directions in orthobiologics research, emphasizing the need for continued innovation and exploration. Through a concise perspective, this paper aims to provide clinicians, researchers, and stakeholders with a comprehensive understanding of orthobiologics and their evolving role in regenerative medicine.

Keywords: orthobiologics; stem cells; growth factors; regenerative medicine; tissue regeneration



The Role of Injectable Platelet-Rich Fibrin in Orthopedics: Where Do We Stand?

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Review

The Role of Injectable Platelet-Rich Fibrin in Orthopedics: Where Do We Stand?

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Abstract: Injectable Platelet-Rich Fibrin (i-PRF) has emerged as a promising tool in regenerative medicine, particularly in orthopedics, due to its unique biological properties and ease of preparation. i-PRF is an autologous platelet concentrate derived through a simple, anticoagulant-free centrifugation process, resulting in a liquid matrix enriched with fibrin, leukocytes, and growth factors. These components promote tissue regeneration, angiogenesis, and anti-inflammatory responses, making i-PRF suitable for bone and cartilage repair as well as drug delivery systems. This review discusses the history, biological mechanisms, and clinical applications of i-PRF in orthopedics, highlighting its potential advantages over traditional platelet-rich plasma (PRP). Furthermore, we address the challenges and limitations of i-PRF, including drug stability, release control, and bioactive interactions, underscoring the need for further research to optimize its therapeutic efficacy.

Keywords: platelet-rich fibrin; orthopedics; tissue regeneration; anti-inflammatory therapy; regenerative medicine

1. Introduction

Platelet-rich fibrin (PRF) is a second-generation platelet concentrate that was first introduced in the field of oral and maxillofacial surgery by Choukroun and colleagues [1]. PRF was initially used in oral and maxillofacial surgical procedures in 2001 by Choukroun et al., due to its simplicity, cost-effectiveness, and ease of handling [1]. This biological product was conceived as a promising alternative to existing bone grafts and platelet-rich plasma at the time [1].

This autologous biomaterial contains a dense fibrin matrix, along with leukocytes and a wide range of healing proteins [4]. Unlike other platelet preparations, such as PRP, i-PRF



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Cross-talks between osteoporosis and gut microbiome

- SS Jha
- Naveen Jeyaraman
- Madhan Jeyaraman
- Swaminathan Ramasubramanian
- Sathish Muthu
- Gabriel Silva Santos
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Cross-talks between osteoporosis and gut microbiome

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Abstract

The gut microbiome comprises a vast community of microbes inhabiting the human alimentary canal, playing a crucial role in various physiological functions. These microbes generally live in harmony with the host; however, when dysbiosis occurs, it can contribute to the pathogenesis of diseases, including osteoporosis. Osteoporosis, a systemic skeletal disease characterized by reduced bone mass and increased fracture risk, has attracted significant research attention concerning the role of gut microbes in its development. Advances in molecular biology have highlighted the influence of gut microbiota on osteoporosis through mechanisms involving immunoregulation, modulation of the gut-brain axis, and regulation of the intestinal barrier and nutrient absorption. These microbes can enhance bone

Transtrapezoidal Accessory Nerve Block with a Novel Injectable Solution: An Innovative Approach to the Treatment of Chronic Shoulder Pain

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Research Article

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Transtrapezoidal Accessory Nerve Block with a Novel Injectable Solution: An Innovative Approach to the Treatment of Chronic Shoulder Pain

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Abstract

This article presents an innovative technique for the management of chronic shoulder pain, a prevalent condition that can result from traumatic injuries, repetitive activities, and chronic conditions such as tendinitis and bursitis. The accessory nerve, which plays a crucial role in the motor innervation of the neck and shoulders, is often involved in compression syndromes that result in chronic pain.

The article describes a minimally invasive, ultrasound-guided technique for accessory nerve block. This technique allows real-time visualization of anatomical structures, increasing the accuracy and safety of the procedure. The combination of 5% glucose, 1% procaine, and 1% bupivacaine is used to provide pain relief, neuronal stabilization, and anesthetic support. Studies indicate that this multimodal approach can reduce the need for systemic pharmacological analgesia and promote functional recovery.

In addition to the description of the technique, the article reports three cases of treated patients, demonstrating the therapeutic efficacy of the proposed intervention. However, the article emphasizes the need for further studies to assess the durability of therapeutic effects and to establish optimized protocols for different patient profiles.

Keywords: Accessory nerve block; Chronic pain; Ultrasound guided intervention; Pain management; Anatomy; Compression syndromes; Diagnosis; Treatment.

INTRODUCTION

Shoulder pain is a condition that affects a substantial portion of the population, with prevalence ranging from 6.9% to 26% [1]. Causes include traumatic injuries, repetitive activities, and chronic conditions such as tendinitis and bursitis, often leading to a decrease in quality of life [2,3]. The diagnosis of shoulder pain can be complex due to the wide range of etiologies, including rotator cuff injuries, subacromial impingement, and glenohumeral arthritis [4,5]. Chronic shoulder pain often arises from injuries that are not properly treated or from repeated injuries over 4.5]. Chronic shoulder pain often arises from injuries that are not properly treated or from repeated injuries over time, resulting in conditions such

as Painful Shoulder Syndrome and adhesive capsulitis [6]. The treatment of this condition involves a multimodal approach, including physical therapy, pharmacological therapies, and surgical interventions [4,5]. Multidisciplinary approaches have been shown to be more effective, integrating supervised exercise, relaxation techniques, and regular physical therapy [3, 7].

Ultrasound-guided interventional procedures have become increasingly common in the treatment of chronic pain, including shoulder pain [4,8]. This approach allows real-time visualization of joint, tendons, muscle, and nerve structures, providing greater precision and safety in the administration of therapies [2,9-11]. Studies demonstrate that ultrasound-guided nerve blocks offer significant relief and improve functionality for patients with chronic pain [3,4]. In the context of this approach, the accessory nerve plays a key role in the mechanism of chronic pain in the shoulder and shoulder girdle [12,13]. Its motor and sensory innervation of key structures makes it a relevant target for innovative therapeutic interventions such as nerve blocks [4,15]. Exploring new techniques for refractory pain management can significantly contribute to improving patients' quality of life and reducing the overall impact of chronic pain [5,6].

This article aims to describe a minimally invasive, sonoguided, anesthetic technique for the management of chronic shoulder pain with accessory nerve block and to demonstrate its effectiveness with a series of clinical cases.

LITERATURE REVIEW

The accessory nerve is a mixed nerve whose main function is motor, innervating muscles crucial for neck and shoulder movement [12]. This

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The Regenerative Marriage Between High-Density Platelet-Rich Plasma and Adipose Tissue

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- Luga Podesta
- José Fábio Lana
- George Shapiro
- Rafael Barnabé Domingues
- Andre van Zundert
- Robert W. Alexander

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Review

The Regenerative Marriage Between High-Density Platelet-Rich Plasma and Adipose Tissue

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Abstract: The use of autologous biological preparations (ABPs) and their combinations fills the void in healthcare treatment options that exists between surgical procedures, like plastic reconstructive, cosmetic, and orthopedic surgeries; non-surgical musculoskeletal biological procedures; and current pharmaceutical treatments. ABPs, including high-density platelet-rich plasma (HD-PRP), bone marrow aspirate concentrates (BMACs), and adipose tissue preparations, with their unique stromal vascular fractions (SVFs), can play important roles in tissue regeneration and repair processes. They can be easily and safely prepared at the point of care. Healthcare professionals can employ ABPs to mimic the classical wound healing cascade, initiate the angiogenesis cascade, and induce tissue regenerative pathways, aiming to restore the integrity and function of damaged tissues. In this review, we will address combining autologous HD-PRP with adipose tissue, in particular the tissue stromal vascular fraction (t-SVF), as we believe that this bio cellular combination demonstrates a synergistic effect, where the HD-PRP constituents enhance the regenerative potential of t-SVF and its adipose-derived mesenchymal stem cells (AD-MSCs) and pericytes, leading to improved functional tissue repair, tissue regeneration, and wound healing in variety of clinical applications. We will address some relevant platelet bio-physiological aspects, since these properties contribute to the synergistic effects of combining HD-PRP with t-SVF, promoting overall better outcomes in chronic inflammatory conditions, soft tissue repair, and tissue rejuvenation.

Keywords: high-density platelet-rich plasma; tissue stromal vascular fraction; adipose-derived mesenchymal stem cells; autologous platelet exosomes; tissue repair

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PL-US GUIDED: Postero-Lateral Ultrasound Guided Technique for Bone Marrow Aspiration

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Review article



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PL-US GUIDED: Postero-Lateral Ultrasound Guided Technique for Bone Marrow Aspiration

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SUMMARY

The article addresses the ultrasound-guided bone marrow aspirate (BMA) collection technique, highlighting its importance in regenerative medicine. The traditional BMA collection technique involves blind approaches or fluoroscopy, which present challenges such as difficulty of access in obese patients and risks of radiation exposure. The ultrasound-guided technique allows real-time visualization of anatomical structures, facilitating the optimal location for puncture and minimizing complications. The study describes the collection of BMA by posteromedial approach, with the patient in the prone position, using local anesthesia and the Jamshidi needle. The posteromedial approach offers greater safety and comfort to the patient, reducing local trauma and recovery time. BMA collection is essential to obtain progenitor cells used in regenerative therapies, such as the treatment of osteoarthritis and tendon injuries. The technique described in the article represents a safe and effective alternative to traditional approaches, in line with trends towards minimally invasive and image-guided procedures. The use of ultrasound improves the accuracy of the puncture, resulting in less pain and greater efficiency in collection.

Keywords: Bone Marrow Aspirate (BMA); Ultrasonography; Posteromedial Approach; Minimally Invasive Technique; Guided Collection

Abbreviations: BMA: Bone Marrow Aspirate; CAGR: Compound Annual Growth Rate; PRP: Platelet-Rich Plasma; PRF: Platelet-Rich Fibrin; iPRF: Injectable PRF; SVF: Stromal Vascular Fraction; BMAC: Bone Marrow Aspirate Concentrate; P30S: Posterosuperior Iliac Spine; MSCs: Mesenchymal Stem Cells; PPM: Plasma Power Mix



Synergism between platelet-rich fibrin with superpulsed laser and pulsed magnetic field in the treatment of disc herniations: A therapeutic protocol

- Palmerindo Antônio Tavares de Mendonça Néto
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(RESEARCH ARTICLE)

Synergism between platelet-rich fibrin with superpulsed laser and pulsed magnetic field in the treatment of disc herniations: A therapeutic protocol

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Abstract

Herniated discs affect about 1% to 5% of the general population and are more common in adults between the ages of 30 and 50 years, the peak of productive age. Among the risk factors are obesity, sedentary lifestyle and activities that involve weightlifting. This condition often results in chronic pain, depression, work disability, and reduced daily functional capacity. Clinically, patients present with localized pain with or without irradiation, muscle weakness, tingling, and, in more severe cases, loss of sensation. The definitive diagnosis is obtained through imaging tests, such as CT scans or MRIs, which allow confirmation of the extent and location of the hernia. Therapeutic options range from conservative approaches, including physical therapy and analgesic and anti-inflammatory medications, to surgical interventions for cases where there is significant neurological impairment. Recently, innovative therapies such as superpulsed laser, pulsed magnetic field, and Orthobiological, such as injectable platelet-rich fibrin, have shown promising results. The combination of orthobiologicals with superpulsed laser and pulsed magnetic field offers an integrated approach to modulate the inflammatory response and promote tissue regeneration. This therapeutic synergy can provide effective symptomatic relief, injured tissue repair, and accelerated recovery. The regenerative approach to herniated discs, which combines orthobiological, superpulsed laser, and pulsed magnetic field, has the potential to revolutionize treatment by offering a minimally invasive, safe, and effective option for patients. Additional studies are needed to evaluate the statistical effectiveness and side effects of this innovative approach.

Keywords: Disc hernia; Non-surgical treatment; Minimally invasive treatment; Regenerative medicine; Orthobiological; Superpulsed laser treatment; Pulsed magnetic field

1. Introduction

Disc herniation is a statistically relevant condition, affecting about 1% to 5% of the general population, with a higher incidence in adults between 30 and 50 years of age, the peak of the productive period ^[1-3] and is the leading cause of spine surgery in adults ^[4]. Risk factors include obesity, sedentary lifestyle, and activities that require weightlifting. ^[5-7]

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Case report: Association of laser and magnetotherapy with iPRF for treatment of herniated disc

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- Douglas Scott Johnson
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(CASE REPORT)

Case report: Association of laser and magnetotherapy with iPRF for treatment of herniated disc

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Abstract

Lumbar disc herniation is one of the main causes of pain and disability, affecting 1% to 5% of the adult population, especially between 30 and 50 years of age. Conservative treatments include corticosteroids, anti-inflammatories, and physical therapy, with surgery being reserved for refractory cases. Surgical complications are possible, including pain and neurological sequelae. This study presents the clinical case of an extrusive disc herniation in a 49-year-old patient, treated with orthobiologics (iPRF), superpulsed laser and pulsed magnetic field, resulting in symptom improvement and total remission of the hernial process confirmed by Magnetic Resonance Imaging. The association between a minimally invasive approach proved to be effective, suggesting the feasibility of using combined therapies to treat disc herniations with remarkable clinical improvement in two months, without surgical risks and hospital costs. The synergy between iPRF, superpulsed laser, and pulsed magnetotherapy promotes cell recovery and inflammatory modulation.

Keywords: Disc hernia; Minimally invasive treatment; Regenerative medicine; Orthobiological; iPRF; Superpulsed laser; Pulsed magnetic field

1. Introduction

Herniated discs are an important cause of low back pain, a pain condition that causes several deficits in the lives of patients; in addition to the direct impact on work capacity, being a significant cause of absenteeism [1, 2, 3]. Lumbar disc herniation is a frequent condition that affects the spine, resulting in inflammation or compression of adjacent nerves and causing severe pain. The prevalence of this condition varies between 1% and 5% of the population, being the main cause of spine surgery in the adult population [3, 4, 5].

Lumbar disc herniation predominantly occurs between the fourth and fifth decades of life, affecting an average age group of 37 years, but it can occur in other age groups, from children to the elderly [5, 6]. In addition to affecting the most varied age groups, it is the most common degenerative alteration in the spine, in addition to being one of the main causes of temporary absence from work, resulting in significant lost workdays for workers who are possibly at the peak

* Corresponding author: Palmerindo Antônio Tavares de Mendonça Néto
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Personalized Multimodal Treatment for Adhesive Capsulitis: A Case Series on Regenerative Medicine and Noninvasive Therapies

- Napoliane Costa Santos
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- Palmerindo Antônio Tavares de Mendonça Néto
- Renata Takeyama de Oliveira
- Daiane Agostini
- José Fábio Lana

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Original Article

Journal of Regenerative Science 2024 July-December 4(2): 00-0

Personalized Multimodal Treatment for Adhesive Capsulitis: A Case Series on Regenerative Medicine and Noninvasive Therapies

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Abstract

Introduction: Adhesive capsulitis causes chronic shoulder pain and restricted range of motion (ROM). Conventional treatments often offer limited relief, prompting the need for innovative approaches, such as high-intensity pulsed electromagnetic field (PEMF) therapy, shockwave therapy, and orthobiologic injections. **Objective:** To evaluate the efficacy of a multimodal approach combining shockwave therapy, high-intensity PEMF therapy, orthobiologic injections, and complementary therapies in improving pain and shoulder function in patients with adhesive capsulitis. **Methods:** This retrospective case series included five patients treated in Indaiatuba, São Paulo, Brazil, between May 2023 and October 2024. Individualized multimodal protocols were performed. Pain and ROM were assessed pre- and post-treatment. **Discussion:** All patients showed significant improvements in pain and ROM after treatment. High-intensity PEMF therapy, shockwave therapy, and orthobiologics enhanced tissue regeneration, supported by complementary therapies. Personalized protocols optimized outcomes, with synergistic effects observed between treatments. **Conclusion:** A multimodal, personalized approach effectively reduced pain and improved function in adhesive capsulitis patients. This strategy shows promise, especially for those unresponsive to conventional treatments, warranting further research.

Keywords: Adhesive capsulitis, High intensity pulsed electromagnetic field therapy, Orthobiologics, Regenerative medicine, Shockwave therapy

Introduction

Adhesive capsulitis (AC) or frozen shoulder is a pathology characterized by progressive pain of spontaneous onset in the shoulder associated with stiffness, pain in the shoulder joint and severely limiting mobility. Such restriction is secondary to inflammation of the joint capsule with consequent thickening and adherence of this structure to itself or to the anatomical neck of the humerus [1, 2]. Such comorbidity occurs mainly in females aged 40–60 years, with an incidence of approximately 2%–5% in the general population. This condition not only affects physical activity but can also have profound psychological implications for individuals, leading to frustration and a diminished quality of life due to chronic discomfort [1, 3].

AC is a debilitating condition and understanding the multifaceted nature of AC is crucial. Recent studies indicate that early intervention with physical therapy can improve outcomes and reduce recovery time for some patients. Furthermore, other treatments, such as acupuncture or corticosteroid injections, may provide additional relief for patients who do not respond well to conventional therapies, highlighting the need for a personalized approach in the treatment of this complex condition [4, 5].

While conservative traditional treatment is the first-line approach, many patients experience prolonged recovery and residual functional limitations. The heterogeneity of responses to conservative treatment for adhesive capsulitis, with prolonged recovery in many cases,



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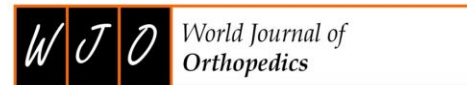
Gut microbiome and orthopaedic health: Bridging the divide between digestion and bone integrity

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- Madhan Jeyaraman
- Priya Dhanpal
- Swaminathan Ramasubramanian
- Lavanya Ragavanandam
- Sathish Muthu
- Gabriel Silva Santos
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Gut microbiome and orthopaedic health: Bridging the divide between digestion and bone integrity

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Abstract

The gut microbiome, a complex ecosystem of microorganisms in the digestive tract, has emerged as a critical factor in human health, influencing metabolic, immune, and neurological functions. This review explores the connection between the gut microbiome and orthopaedic health, examining how gut microbes impact bone density, joint integrity, and skeletal health. It highlights mechanisms linking gut dysbiosis to inflammation in conditions such as rheumatoid arthritis and osteoarthritis, suggesting microbiome modulation as a potential therapeutic strategy. Key findings include the microbiome's role in bone metabolism through

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Innovative Approaches in Knee Osteoarthritis Treatment: A Comprehensive Review of Bone Marrow-Derived Products

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- **Joseph Purita**
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biomedicines



Review

Innovative Approaches in Knee Osteoarthritis Treatment: A Comprehensive Review of Bone Marrow-Derived Products

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Abstract: Knee osteoarthritis (OA) is a chronic articular disease characterized by the progressive degeneration of cartilage and bone tissue, leading to the appearance of subchondral cysts, osteophyte formation, and synovial inflammation. Conventional treatments consist of non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, and glucocorticoids. However, the prolonged use of these drugs causes adverse effects. NSAIDs, for instance, are known to be nephrotoxic, increasing the damage to articular cartilage. New therapies capable of accelerating the process of tissue regeneration and repair are being discussed, such as the use of orthobiologics that are naturally found in the body and obtained through minimally invasive collection and/or laboratory manipulations. Bone marrow aspirate (BMA) and bone marrow aspirate concentrate (BMAC) are both rich in hematopoietic stem cells, mesenchymal stem cells (MSCs), and growth factors (GFs) that can be used in the healing process due to their anabolic and anti-inflammatory effects. The aim of this literature review is to assess the efficacy of BMA and BMAC in the treatment of knee OA based on the favorable results that researchers have obtained with the use of both orthobiologics envisaging an accelerated healing process and the prevention of OA progression.

Keywords: knee osteoarthritis; bone marrow aspirate; bone marrow aspirate concentrate; stem cells; regenerative medicine

1. Introduction

Knee osteoarthritis (KOA) is a disease characterized by the wear of articular cartilage and bone changes and may have several causes and risk factors. Bone sclerosis, capsular fibrosis, and osteophyte formation are the results of tissue growth [1]. KOA involves abnormal remodeling driven by inflammatory mediators within the joint (Figure 1). Pathological changes in KOA include articular cartilage degradation, subchondral bone thickening,

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Upper Crossed Syndrome and Scapulae Upper-Trapping: A Mesotherapy Protocol in Cervicoscapulobrachial Pain –The 8:1 Block

- Luyddy Pires
- Napoliane Santos
- João Vitor Lana
- Alex Pontes de Macedo
- Fábio Ramos Costa
- Gabriel Ohana Marques Azzini
- Tomas Mosaner
- Daniel de Moraes Ferreira Jorge
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Technical Note

Upper Crossed Syndrome and Scapulae Upper-Trapping: A Mesotherapy Protocol in Cervicoscapulobrachial Pain—The 8:1 Block

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Abstract: Upper Crossed Syndrome (UCS), described by Vladimir Janda, is characterized by postural changes involving the cervical spine and trunk, leading to biomechanical limitations and cervicoscapulobrachial pain. This study proposes a mesotherapy protocol, termed the 8:1 block, to address cervicoscapulobrachialgia by targeting the scapulae and associated musculature. The scapula, central to shoulder girdle kinematics, often exhibits dyskinesia and muscular imbalances, notably the pattern referred to as scapular upper trapping (SUT). SUT involves scapular elevation, medial rotation, and shoulder protraction, contributing to cervicobrachial pain. The protocol includes a comprehensive assessment of muscle tone changes and biomechanical considerations, highlighting the importance of the scapula in upper limb movement and posture. Key anatomical changes involve tightened upper trapezius, levator scapulae, and pectoralis minor muscles, with weakened middle trapezius and serratus anterior. The mesotherapy approach targets these imbalances through specific injection points to alleviate muscle tension and correct postural deviations. Case studies from our clinic demonstrate the protocol's effectiveness in reducing pain and restoring scapular biomechanics. Patients reported significant improvements in pain relief and functional outcomes, underscoring the clinical utility of the 8:1 block in treating cervicoscapulobrachialgia. This protocol offers a feasible, cost-effective intervention that enhances the efficacy of traditional therapeutic exercises by addressing underlying muscular and biomechanical dysfunctions. In conclusion, the 8:1 block mesotherapy protocol provides a novel approach to managing cervicoscapulobrachial pain by focusing on scapular biomechanics and muscle tension. Further studies are needed to validate these findings and refine the protocol for broader clinical application.

Keywords: upper crossed syndrome; scapular dyskinesia; cervicoscapulobrachialgia; mesotherapy protocol; scapular upper trapping

1. Introduction

Described by Vladimir Janda, the Upper Crossed Syndrome (UCS) is characterized by a syndromic postural change that involves the cervical spine and trunk [1] (Figure 1). Being

Regenerative Inflammation: The Mechanism Explained from the Perspective of Buffy-Coat Protagonism and Macrophage Polarization

- Rubens Andrade Martins
- Fábio Ramos Costa
- Luyddy Pires
- Márcia Santos
- Gabriel Silva Santos
- João Vitor Lana
- Bruno Ramos Costa
- Napoliane Santos
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- André Krue
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Review

Regenerative Inflammation: The Mechanism Explained from the Perspective of Buffy-Coat Protagonism and Macrophage Polarization

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Abstract: The buffy-coat, a layer of leukocytes and platelets obtained from peripheral blood centrifugation, plays a crucial role in tissue regeneration and the modulation of inflammatory responses. This article explores the mechanisms of regenerative inflammation, highlighting the critical role of the buffy-coat in influencing macrophage polarization and its therapeutic potential. Macrophage polarization into M1 and M2 subtypes is pivotal in balancing inflammation and tissue repair, with M1 macrophages driving pro-inflammatory responses and M2 macrophages promoting tissue healing and regeneration. The buffy-coat's rich composition of progenitor cells, cytokines, and growth factors—such as interleukin-10, transforming growth factor-β, and monocyte colony-stimulating factor—supports the transition from M1 to M2 macrophages, enhancing tissue repair and the resolution of inflammation. This dynamic interaction between buffy-coat components and macrophages opens new avenues for therapeutic strategies aimed at improving tissue regeneration and managing inflammatory conditions, particularly in musculoskeletal diseases such as osteoarthritis. Furthermore, the use of buffy-coat-derived therapies in conjunction with other regenerative modalities, such as platelet-rich plasma, holds promise for more effective clinical outcomes.

Keywords: buffy-coat; macrophage polarization; regenerative inflammation; platelet-rich plasma; mesenchymal stem cells



SDIMMER: A Proposed Clinical Approach to Optimize Cellular Physiology in Regenerative Medicine

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Communication

SDIMMER: A Proposed Clinical Approach to Optimize Cellular Physiology in Regenerative Medicine

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Abstract: SDIMMER is an acronym intended for use in both clinical practice and medical research. It facilitates a comprehensive evaluation of a patient's metabolic profile and serves as a mnemonic for the following key assessment areas: Sleep, Diet, Microbiome, Metabolism, Medications, Exams, and Rehabilitation. In the clinical setting, SDIMMER's primary objective is to monitor and manage the patient's metabolic status, particularly targeting low-grade chronic systemic inflammation, a hallmark of metabolic syndrome (MS). This inflammatory condition is characterized by elevated levels of circulating inflammatory cytokines and increased macrophage infiltration in peripheral tissues. SDIMMER aims to enhance the effectiveness of ortho-biological treatments by elevating growth factor levels, thereby enhancing patient outcomes. Additionally, SDIMMER emphasizes guiding patients toward positive lifestyle changes to improve overall quality of life and foster a healthier metabolism. SDIMMER introduces a patient metabolic profile quantification tool comprising 7 domains, totaling 35 items. Additionally, an instructional guide is provided to facilitate the application process. Its versatility spans various clinical and research domains, showcasing its potential to positively influence multiple fields.

Keywords: metabolism; systemic inflammation; clinical diagnosis; regenerative medicine

1. Introduction

The success of regenerative therapies hinges on many factors influencing the patient's overall health and response to treatment. Sleep patterns, dietary habits, microbiome composition, metabolic status, medication usage, and the patient's general health condition play pivotal roles among these factors. Numerous studies have highlighted the direct impact of these factors on the efficacy and outcome of regenerative interventions [1–3]. Therefore, a systematic and quantitative assessment of these parameters is imperative to mitigate biases in clinical research and optimize the outcomes of regenerative therapies.



Evolution and Innovations in Bone Marrow Cellular Therapy for Musculoskeletal Disorders: Tracing the Historical Trajectory and Contemporary Advances

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Pesquisa completa aqui!



Review

Evolution and Innovations in Bone Marrow Cellular Therapy for Musculoskeletal Disorders: Tracing the Historical Trajectory and Contemporary Advances

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Abstract: Bone marrow cellular therapy has undergone a remarkable evolution, significantly impacting the treatment of musculoskeletal disorders. This review traces the historical trajectory from early physiological references to contemporary scientific advancements. The groundbreaking work of Friedenstein in 1968, identifying fibroblast colony-forming cells in bone marrow, laid the foundation for future studies. Caplan's subsequent identification of mesenchymal stem cells (MSCs) in 1991 highlighted their differentiation potential and immunomodulatory properties, establishing them as key players in regenerative medicine. Contemporary research has focused on refining techniques for isolating and applying bone marrow-derived MSCs. These cells have shown promise in treating conditions like osteoarthritis, osteoarthritis, and tendon injuries thanks to their ability to promote tissue repair, modulate immune responses, and enhance angiogenesis. Clinical studies have demonstrated significant improvements in pain relief, functional recovery, and tissue regeneration. Innovations such as the ACH classification system and advancements in bone marrow aspiration methods have standardized practices, improving the consistency and efficacy of these therapies. Recent clinical trials have validated the therapeutic potential of bone marrow-derived products, highlighting their advantages in both surgical and non-surgical applications. Studies have shown that MSCs can reduce inflammation, support bone healing, and enhance cartilage repair. However, challenges remain, including the need for rigorous characterization of

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Preparing the soil: Adjusting the metabolic health of patients with chronic wounds and musculoskeletal diseases

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REVIEW ARTICLE

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Preparing the soil: Adjusting the metabolic health of patients with chronic wounds and musculoskeletal diseases

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Abstract

In recent years, systemic inflammation has emerged as a pivotal player in the development and progression of various degenerative diseases. This complex, chronic inflammatory state, often undetected, can have far-reaching consequences for the body's physiology. At the molecular level, markers such as C-reactive protein, cytokines and other inflammatory mediators serve as indicators of systemic inflammation and often act as predictors of numerous musculoskeletal diseases and even certain forms of cancer. The concept of 'meta-inflammation', specifically referring to metabolically triggered inflammation, allows healthcare professionals to understand inflammatory responses in patients with metabolic syndrome. Driven by nutrient excess and the

List of Abbreviations: AGEs, advanced glycation end products; AMPs, antimicrobial peptides; AP, alkaline phosphatase; ATP, adenosine triphosphate; BMD, bone mineral density; BMP, bone morphogenetic protein (BMP-2, BMP-4); CRP, C-reactive protein; CXCR2, C-X-C motif chemokine receptor 2; DHEA, dehydroepiandrosterone; ERK, extracellular signal-regulated kinase; GAGs, glycosaminoglycans; GIL, growth hormone; GLUT-1, glucose transporter 1; Hb, haemoglobin; IHA, glycidyl haemoglobin; IGF-1, insulin-like growth factor 1; IL, interleukin (IL-4, IL-10); LPS, lipopolysaccharide; MCP-1, monocyte chemoattractant protein-1; MMP, matrix metalloproteinase (MMP-3, MMP-9, MMP-13); MS, metabolic syndrome; OA, osteoarthritis; p38, p38 mitogen-activated protein kinase; PGE-2, prostaglandin E2; PPAR γ , peroxisome proliferator-activated receptor γ ; RANKL, receptor activator of nuclear factor kappa-B ligand; rhGF-1, recombinant human insulin-like growth factor 1; ROS, reactive oxygen species; Runx2, runt-related transcription factor 2; SASP, senescence-associated secretory phenotype; SCF, stem cell factor; SCFA, short-chain fatty acids; T2DM, type 2 diabetes mellitus; T3 and T4, triiodothyronine and thyroxine (thyroid hormones); Th, T helper cell; TIMP-3, tissue inhibitor of metalloproteinase-3; TNF-R2, tumour necrosis factor receptor 2; TNF- α , tumour necrosis factor- α ; Treg, regulatory T cell; TR- α and TR- β , thyroid hormone receptors alpha and beta.

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ViSCNOVAS: A Novel Classification System for Hyaluronic Acid-Based Gels in Orthobiologic Products and Regenerative Medicine

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- Luyddy Pires
- Rubens Andrade Martins
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- Gabriel Silva Santos
- José Fábío Lana

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Communication

ViSCNOVAS: A Novel Classification System for Hyaluronic Acid-Based Gels in Orthobiologic Products and Regenerative Medicine

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Abstract: Hyaluronic acid (HA), a naturally occurring polysaccharide, holds immense potential in regenerative medicine due to its diverse biological functions and clinical applications, particularly in gel formulations. This paper presents a comprehensive exploration of HA, encompassing its origins, molecular characteristics, and therapeutic roles in gel-based interventions. Initially identified in bovine vitreous humor, HA has since been found in various tissues and fluids across vertebrate organisms and bacterial sources, exhibiting consistent physicochemical properties. The synthesis of HA by diverse cell types underscores its integral role in the extracellular matrix and its relevance to tissue homeostasis and repair. Clinical applications of HA, particularly in addressing musculoskeletal ailments such as osteoarthritis, are examined, highlighting its efficacy and safety in promoting tissue regeneration and pain relief. Building upon this foundation, a novel classification system for HA-based interventions is proposed, aiming to standardize treatment protocols and optimize patient outcomes. The ViSCNOVAS classification system refers to viscosity, storage, chain, number, origin, volume, amount, and size. This classification is specifically designed for HA-based orthobiologic products used in regenerative medicine, including orthopedics, sports medicine, aesthetics, cosmetic dermatology, and wound healing. It aims to provide clinicians with a structured framework for personalized treatment strategies. Future directions in HA research are also discussed, emphasizing the need for further validation and refinement of the proposed classification system to advance the field of regenerative medicine. Overall, this manuscript elucidates the biological functions of hyaluronic acid and its potential in clinical practice while advocating for standardization to enhance patient care in various regenerative applications.

Keywords: hyaluronic acid; orthobiologics; classification; regenerative medicine; clinical applications



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1. Introduction

Hyaluronic acid (HA), often referred to as hyaluronan, is a naturally occurring biological compound found in numerous tissues and fluids within the body [1]. Notably, HA possesses unique gel-forming properties, making it a crucial component in various medical and cosmetic applications. These properties enable HA to form hydrogels that exhibit excellent biocompatibility, viscoelasticity, and water retention capabilities, which are essential for its role in regenerative medicine. It can be obtained from various sources,

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Nebulized Glutathione as a Key Antioxidant for the Treatment of Oxidative Stress in Neurodegenerative Conditions

- João Vitor Lana
- Alexandre Rios
- Renata Takeyama
- Napoliane Santos
- Luyddy Pires
- Gabriel Silva Santos
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- Joseph Purita
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Review

Nebulized Glutathione as a Key Antioxidant for the Treatment of Oxidative Stress in Neurodegenerative Conditions

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Abstract: Glutathione (GSH), a tripeptide synthesized intracellularly, serves as a pivotal antioxidant, neutralizing reactive oxygen species (ROS) and reactive nitrogen species (RNS) while maintaining redox homeostasis and detoxifying xenobiotics. Its potent antioxidant properties, particularly attributed to the sulfhydryl group (-SH) in cysteine, are crucial for cellular health across various organelles. The glutathione-glutathione disulfide (GSH-GSSG) cycle is facilitated by enzymes like glutathione peroxidase (GPx) and glutathione reductase (GR), thus aiding in detoxification processes and mitigating oxidative damage and inflammation. Mitochondria, being primary sources of reactive oxygen species, benefit significantly from GSH, which regulates metal homeostasis and supports autophagy, apoptosis, and ferroptosis, playing a fundamental role in neuroprotection. The vulnerability of the brain to oxidative stress underscores the importance of GSH in neurological disorders and regenerative medicine. Nebulization of glutathione presents a novel and promising approach to delivering this antioxidant directly to the central nervous system (CNS), potentially enhancing its bioavailability and therapeutic efficacy. This method may offer significant advantages in mitigating neurodegeneration by enhancing nuclear factor erythroid 2-related factor 2 (NRF2) pathway signaling and mitochondrial function, thereby providing direct neuroprotection. By addressing oxidative stress and its detrimental effects on neuronal health, nebulized GSH could play a crucial role in managing and potentially ameliorating conditions such as Parkinson's Disease (PD) and Alzheimer's Disease (AD). Further clinical research is warranted to elucidate the therapeutic potential of nebulized GSH in preserving mitochondrial health, enhancing CNS function, and combating neurodegenerative conditions, aiming to improve outcomes for individuals affected by brain diseases characterized by oxidative stress and neuroinflammation.

Keywords: glutathione; nebulization; oxidative stress; neurological disorders; aging; regenerative medicine



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Profound Properties of Protein-Rich, Platelet-Rich Plasma Matrices as Novel, Multi-Purpose Biological Platforms in Tissue Repair, Regeneration, and Wound Healing

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- José Fábio Lana
- Robert W. Alexander
- Ignacio Dallo
- Elizaveta Kon
- Mary A. Ambach
- André van Zundert
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Review

Profound Properties of Protein-Rich, Platelet-Rich Plasma Matrices as Novel, Multi-Purpose Biological Platforms in Tissue Repair, Regeneration, and Wound Healing

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Abstract: Autologous platelet-rich plasma (PRP) preparations are prepared at the point of care. Contribution cellular density separation acquires a fresh unit of blood into three main fractions: a platelet-poor plasma (PPP) fraction, a stratum rich in platelets (platelet concentrate), and variable leukocyte bioformulation and erythrocyte fractions. The employment of autologous platelet concentrates facilitates the biological potential to accelerate and support numerous cellular activities that can lead to tissue repair, tissue regeneration, wound healing, and, ultimately, functional and structural repair. Normally, after PRP preparation, the PPP fraction is discarded. One of the less well-known but equally important features of PPP is that particular growth factors (GFs) are not abundantly present in PRP, as they reside outside of the platelet alpha granules. Precisely, insulin-like growth factor-1 (IGF-1) and hepatocyte growth factor (HGF) are mainly present in the PPP fraction. In addition to their roles as angiogenesis activators, these plasma-based GFs are also known to inhibit inflammation and fibrosis, and they promote keratinocyte migration and support tissue repair and wound healing. Additionally, PPP is known for the presence of exosomes and other macromolecules, exerting cell-cell communication and cell signaling. Newly developed ultrafiltration technologies incorporate PPP processing methods by eliminating, in a fast and efficient manner, plasma water, cytokines, molecules, and plasma proteins with a molecular mass (weight) less than the pore size of the filters. Consequently, a viable and viscous protein concentrate of functional total proteins, like fibrinogen, albumin, and alpha-2-macroglobulin is created. Consolidating a small volume of high platelet concentrate with a small volume of highly concentrated protein-rich PPP creates a protein-rich, platelet-rich plasma (PR-PRP) biological preparation. After the activation of proteins, mainly fibrinogen, the PR-PRP matrix retains and facilitates interactions between invading resident cells, like macrophages, fibroblast, and mesenchymal stem cells (MSCs), as well as the embedded concentrated PRP cells and molecules. The administered PR-PRP biologic will ultimately undergo fibrinolysis, leading to a sustained release of concentrated cells and molecules that have been retained in the PR-PRP matrix until the matrix is dissolved. We will discuss the unique biological and tissue reparative and regenerative properties of the PR-PRP matrix.

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Orthobiologic Management Options for Degenerative Disc Disease

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Pesquisa completa aqui!



Review

Orthobiologic Management Options for Degenerative Disc Disease

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Abstract: Degenerative disc disease (DDD) is a pervasive condition that limits quality of life and burdens economies worldwide. Conventional pharmacological treatments primarily aimed at slowing the progression of degeneration have demonstrated limited long-term efficacy and often do not address the underlying causes of the disease. On the other hand, orthobiologics are regenerative agents derived from the patient's own tissue and represent a promising emerging therapy for degenerative disc disease. This review comprehensively outlines the pathophysiology of DDD, highlighting the inadequacies of existing pharmacological therapies and detailing the potential of orthobiologic approaches. It explores advanced tools such as platelet-rich plasma and mesenchymal stem cells, providing a historical overview of their development within regenerative medicine, from foundational *in vitro* studies to preclinical animal models. Moreover, the manuscript delves into clinical trials that assess the effectiveness of these therapies in managing DDD. While the current clinical evidence is promising, it remains insufficient for routine clinical adoption due to limitations in study designs. The review emphasizes the need for further research to optimize these therapies for consistent and effective clinical outcomes, potentially revolutionizing the management of DDD and offering renewed hope for patients.

Keywords: disc disease; orthobiologics; inflammation; orthopedics; regenerative medicine

1. Introduction

Degenerative disc diseases (DDD) encompass a wide and heterogeneous set of health conditions which can affect all musculoskeletal and nervous tissues along the spine [1]. DDDs are frequently associated with pain syndromes, radiculopathy, spondylitis, spondylolisthesis, stenosis, fractures, tumors, and osteoporosis [1]. DDD is linked to significant pain and disability, generating a major socioeconomic burden given its high global prevalence [2]. Patients often present pseudoradicular pain, mostly due to degenerative

The Biological Role of Platelet Derivatives in Regenerative Aesthetics

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Pesquisa completa aqui!



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Review

The Biological Role of Platelet Derivatives in Regenerative Aesthetics

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Abstract: Bioproducts derived from platelets have been extensively used across various medical fields, with a recent notable surge in their application in dermatology and aesthetic procedures. These products, such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), play crucial roles in inducing blood vessel proliferation through growth factors derived from peripheral blood. PRP and PRF, in particular, facilitate fibrin polymerization, creating a robust structure that serves as a reservoir for numerous growth factors. These factors contribute to tissue regeneration by promoting cell proliferation, differentiation, and migration and collagen/elastin production. Aesthetic medicine harnesses these effects for diverse purposes, including hair restoration, scar treatment, striae management, and wound healing. Furthermore, these biological products can act as adjuvants with other treatment modalities, such as laser therapy, radiofrequency, and microneedling. This review synthesizes the existing evidence, offering insights into the applications and benefits of biological products in aesthetic medicine.

Keywords: platelet-rich plasma; platelet-rich fibrin; growth factors; tissue regeneration; aesthetic medicine

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1. Introduction

Biological products are diverse substances, including vaccines, growth factors, immunomodulators, monoclonal antibodies, and hematological components. Various studies have demonstrated the use of numerous biologics in almost every field of medicine. The use of autologous hematological components, especially platelet-rich plasma (PRP), has become a highly attractive therapeutic tool for various applications since the biological functions of these products go beyond hemostasis [1].

According to the International Olympic Committee, PRP is an autologous preparation derived from whole blood in which platelets are concentrated in a small fraction of the plasma [2] (Figure 1).



Sacral Bioneuromodulation: The Role of Bone Marrow Aspirate in Spinal Cord Injuries

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Pesquisa completa aqui!



Review

Sacral Bioneuromodulation: The Role of Bone Marrow Aspirate in Spinal Cord Injuries

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Abstract: Spinal cord injury (SCI) represents a severe trauma to the nervous system, leading to significant neurological damage, chronic inflammation, and persistent neuropathic pain. Current treatments, including pharmacotherapy, immobilization, physical therapy, and surgical interventions, often fall short in fully addressing the underlying pathophysiology and resultant disabilities. Emerging research in the field of regenerative medicine has introduced innovative approaches such as autologous orthobiologic therapies, with bone marrow aspirate (BMA) being particularly notable for its regenerative and anti-inflammatory properties. This review focuses on the potential of BMA to modulate inflammatory pathways, enhance tissue regeneration, and restore neurological function disrupted by SCI. We hypothesize that BMA's bioactive components may stimulate reparative processes at the cellular level, particularly when applied at strategic sites like the sacral hiatus to influence lumbar centers and higher neurological structures. By exploring the mechanisms through which BMA influences spinal repair, this review aims to establish a foundation for its application in clinical settings, potentially offering a transformative approach to SCI management that extends beyond symptomatic relief to promoting functional recovery.

Keywords: spinal cord injury; neuromodulation; orthobiologics; bone marrow aspirate; regenerative medicine



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1. Introduction

Spinal cord trauma is a complex injury that causes a series of disabling problems and functional deficits in patients [1]. Neurological injury is the most serious and debilitating alteration experienced by these patients. SCI interrupts nerve impulse conduction, affecting the ascending, descending and propriospinal pathways. This impairment can cause sensory, motor, proprioceptive or mixed deficits [2]. Such deficits can have devastating effects on the patient's life, causing severe dependence on performing daily activities and personal hygiene [2]. According to the American Spinal Injury Association (ASIA), the loss of motor, sensory, or autonomic functions characterizes SCI, which can be complete or incomplete.



The role of orthobiologics in chronic wound healing

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REVIEW ARTICLE

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The role of orthobiologics in chronic wound healing

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Abstract

Chronic wounds, characterized by prolonged healing processes, pose a significant medical challenge with multifaceted aetiologies, including local and systemic factors. Here, it explores the complex pathogenesis of chronic wounds, emphasizing the disruption in the normal phases of wound healing, particularly the inflammatory phase, leading to an imbalance in extracellular matrix (ECM) dynamics and persistent inflammation. Senescent cell populations further contribute to impaired wound healing in chronic lesions. Traditional medical management focuses on addressing underlying causes, but many chronic wounds resist to conventional treatments, necessitating innovative approaches. Recent attention has turned to autologous orthobiologics, such as platelet-rich plasma (PRP), platelet-rich fibrin (PRF) and mesenchymal stem cells (MSCs), as potential regenerative interventions. These biologically derived materials, including bone marrow aspirate/concentrate (BMA/BMAC) and adipose tissue-derived stem cells (ADSCs), exhibit promising cytokine content and regenerative potential. MSCs, in particular, have emerged as key players in wound healing, influencing inflammation and promoting tissue regeneration. This paper reviews relevant scientific literature regarding basic science and brings real-world evidence regarding the use of orthobiologics in the treatment of chronic wounds, irrespective of aetiology. The discussion highlights the

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Conservative Treatment Approach of Achilles Tendon Ruptures with Orthobiologics: Case Series

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Case Series

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Conservative Treatment Approach of Achilles Tendon Ruptures with Orthobiologics: Case Series

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¹¹Abstract

The Achilles Tendon (AT) is one of the strongest tendons in the body. It is also the most frequently ruptured tendon with increasing incidence. Unlike other tendons, AT ruptures are highly correlated with physical activity. In fact, more than 75% of AT ruptures occur during sports maneuvers. AT rupture is a prevalent and debilitating condition linked to overuse injuries in the ankle and foot. Managing this condition is often complex due to the inadequate vascularity of tendons, relying on synovial fluid diffusion for nutrient supply. The weakened strength resulting from AT rupture can heighten the risk of further complications. While surgical interventions are commonly employed as the primary treatment, challenges may persist in the postoperative period. In contrast, therapeutic interventions with orthobiologics and shockwave therapy have demonstrated notable success in regenerative procedures. In this case series, 3 patients received multiple sessions of bone

marrow aspiration, injectable platelet-rich fibrin and extracorporeal shockwave therapy. In the initial sessions, they already exhibited satisfactory healing results as assessed through functional measures, MRI findings, and pain scores. The patients successfully resumed sports activities without complaints, and follow-up MRI scans indicated evident signs of AT restoration. This case series highlights the safe and effective use of autologous orthobiologic products and shockwave therapy as viable alternatives for enhancing the healing process in musculoskeletal tissue injuries.

Method: Patients received the following treatments: a single Bone Marrow Aspiration (BMA) and then injectable Platelet-Rich Fibrin (i-PRF) injections fortnightly for 12 weeks, in addition to a weekly session of Extracorporeal Shock Wave Therapy (ESWT). The patients were reassessed at all follow-ups with physical evaluation and ultrasound examination. In addition, we also recommended lifestyle adjustments emphasizing the importance of sleep, diet and medications for better tissue recovery. At the end of 12 weeks, we requested a new magnetic resonance imaging of the left ankle for a comparative study, which revealed a significant improvement in the radiological findings. The results of this case report suggest that the application of orthobiologics plus ESWT expedites healing and rehabilitation time and reduces costs and risks inherent to the surgical procedure, which is particularly important in elderly patients and/or with co-morbidities. This approach may therefore represent a viable alternative for the accelerated recovery of musculoskeletal tissue injuries with safety and efficacy.

Keywords: Case Series, Achilles Tendon, Bone Marrow Aspiration, Platelet-Rich Fibrin, Shockwave Therapy, Regenerative Medicine.

Introduction

The Achilles tendon is an important lower limb structure that inserts in plantar flexion of the ankle, thus being one of the strongest tendons yet highly susceptible to injuries. It is formed by the convergence of the tendons of the medial and lateral gastrocnemius and soleus muscles, inserting into the posterior surface of the calcaneus [1].

Between the origin and insertion of the tendons that make up the calcaneus, the fibers rotate 90°, so the fibers of the gastrocnemius insert laterally, and those of the soleus medially [2]. In the topography of this rotation of tendon fibers, the most vulnerable area of the tendon is found, around 2 to 6 cm from its insertion in the calcaneus, where blood supply is deficient [3].

The AT may undergo biochemical (degenerative) or biochemical (inflammatory) changes [4]. AT disorders are more common in individuals who participate in endurance sports that involve repetitive loading of the foot. The rising incidence of ruptures is related to an increase in the participation of the population in recreational and competitive sports and is therefore one of the most common orthopedic disorders in sports medicine [5].

Acute rupture is primarily related to sudden forced plantar flexion during weight bearing with the knee fully extended. Therefore, athletes play sports that require explosive acceleration, sudden changes in direction or jumping and running are at greater risk [5,6]. Patients with an AT rupture usually describe a history of severe,



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The Synergistic Effects of Hyaluronic Acid and Platelet-Rich Plasma for Patellar Chondropathy

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Review

The Synergistic Effects of Hyaluronic Acid and Platelet-Rich Plasma for Patellar Chondropathy

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Abstract: Musculoskeletal disorders are increasingly prevalent worldwide, causing significant socio-economic burdens and diminished quality of life. Notably, patellar chondropathy (PC) is among the most widespread conditions affecting joint structures, resulting in profound pain and disability. Hyaluronic acid (HA) and platelet-rich plasma (PRP) have emerged as reliable, effective, and minimally invasive alternatives. Continuous research spanning from laboratory settings to clinical applications demonstrates the numerous advantages of both products. These encompass lubrication, anti-inflammation, and stimulation of cellular behaviors linked to proliferation, differentiation, migration, and the release of essential growth factors. Cumulatively, these benefits support the rejuvenation of bone and cartilaginous tissues, which are otherwise compromised due to the prevailing degenerative and inflammatory responses characteristic of tissue damage. While existing literature delves into the physical, mechanical, and biological facets of these products, as well as their commercial variants and distinct clinical uses, there is limited discussion on their interconnected roles. We explore basic science concepts, product variations, and clinical strategies. This comprehensive examination provides physicians with an alternative insight into the pathophysiology of PC as well as biological mechanisms stimulated by both HA and PRP that contribute to tissue restoration.

Keywords: hyaluronic acid; platelet-rich plasma; patellar chondropathy; regenerative medicine; orthopedics

1. Introduction

Patellar chondropathy (PC), also referred to informally as “runner’s knee”, is an orthopedic condition characterized by visible radiological alterations in patellar cartilage and pain in the anterior aspect of the knee [1]. This condition commonly affects younger individuals, and the initial changes include swelling, edema, and cartilage softening (Figure 1). Notorious factors that contribute to PC are trauma, patellofemoral instability, bony anatomic variations, cartilage vulnerability, abnormal patellar kinematics, or occupational hazards [1].

Although sometimes reversible [1,2], depending on the disease stage (Table 1), PC may progress into patellofemoral osteoarthritis (OA) if left untreated [1]. Significant

Bone Marrow Aspirate and Injectable Platelet Rich Fibrin for Achilles Tendon Rupture

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Journal of
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A SCITECHNOL JOURNAL

Mini Review

Bone Marrow Aspirate and Injectable Platelet Rich Fibrin for Achilles Tendon Rupture

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Abstract

Achilles tendon rupture is a frequent ailment tied to overuse injuries of the ankle and foot. Given the tendon's limited vascularization, which depends on diffusion from synovial fluid for nutrient intake, managing this condition poses challenges. The weakened state post-rupture can predispose one to further injuries. Although surgical interventions often lead to the best results, challenges can arise during recovery. Meanwhile, the use of orthobiologics for non-invasive treatment has shown promising outcomes in various regenerative medicine applications. Notably, autologous treatments like bone marrow aspirate (BMA) and injectable platelet-rich fibrin (i-PRF) have gained traction in clinical scenarios.

BMA is a reservoir of diverse cell populations and molecules pivotal for tissue regeneration. PRF, on the other hand, is a dense concoction of platelets, growth factors, cytokines, leukocytes, and a sturdy fibrin matrix conducive to cellular functions.

Utilizing a combination of these two orthobiologic entities could amplify their individual effects, optimizing the healing process by fostering tissue growth, hastening new blood vessel formation, and modulating immune responses.

With this understanding, we advocate for the joint use of BMA and i-PRF as a potent orthobiologic solution, aiming to improve the healing trajectory of Achilles tendon ruptures within the sphere of regenerative orthopedics.

Keywords

Achilles tendon rupture; Bone marrow aspirate; Platelet-rich fibrin; Orthobiologics; Regenerative medicine

Introduction

Achilles tendon rupture is a relatively common injury that occurs when the tendon, located at the back of the ankle, tears or ruptures. This injury can have a significant impact on mobility and athletic performance. Epidemiologically, Achilles tendon ruptures are most commonly seen in middle-aged individuals, particularly males, who participate in physical activities that involve repetitive jumping or sudden changes in direction. The prevalence of Achilles tendon ruptures is estimated to be around 18 to 37 cases per 100,000 people per year, with an increasing incidence noted in recent years [1-3].

The Achilles tendon is the thickest and strongest tendon in the human body. It originates in the calf region, specifically from the fusion of the gastrocnemius muscle and the soleus muscle. The gastrocnemius muscle has two heads, medial and lateral, which cross the knee joint. Deep to the gastrocnemius lies the soleus muscle. Together, these muscles form the triceps surae, and their conjoint tendon is known as the Achilles tendon [1-3]. The Achilles tendon has three main vascular areas: the posterior artery supplies the midsection

of the tendon, while the posterior tibial artery supplies the proximal and distal sections. The mid-substance of the tendon has relatively poor vascularization, which may contribute to a higher incidence of pathology in that region [1-3].

The length of the Achilles tendon averages about 15 cm, with variations ranging from 11 to 26 cm. Its width changes along its course: it measures around 6.8 cm (4.5-8.6 cm) at its origin and narrows to approximately 1.8 cm (range 1.2-2.6 cm) in the midsection. As it approaches the calcaneus (heel bone), the Achilles tendon becomes more rounded and has a width of about 3.4 cm (2.0-4.4 cm) at its insertion site on the posterior surface of the calcaneus [1-3]. The Achilles tendon is connected to both the soleus and gastrocnemius muscles. The exact proportion of these insertions varies among individuals. Studies on cadavers have shown that in approximately 52% of cases, 12% of the tendon fibers originate from the soleus muscle, while 40% come from the gastrocnemius muscle. In 10% of cases, an equal contribution is observed, and in 13% of cadavers, more than 60% of the contribution arises from the gastrocnemius muscle [1-3].

The main motivation for the development of this study is based on the favorable results that researchers have obtained with the use of autologous products derived from bone marrow aspirate (BMA) and platelet concentrates such as platelet-rich fibrin (PRF) in accelerating the healing process and improving degenerative conditions. We believe that the association of the rich cellular and molecular components from BMA and PRF might establish an effective therapeutic methodology for the treatment of patients with Achilles tendon rupture.

Etiopathogenesis

Symptoms of an Achilles tendon rupture can vary, but one common and distinctive symptom reported by many individuals is a sudden and audible "popping" or "snapping" sound at the time of injury. This sound is often accompanied by a sharp pain in the back of the leg or ankle. The popping sensation occurs when the Achilles tendon tears or ruptures, and it is caused by the sudden release of tension within the tendon fibers [4].



Recovery of Achilles Tendon Rupture with Bone Marrow Aspirate Matrix: A Case Report

- Rodrigo Vicente
- Gabriel Silva Santos
- Madhan Jeyaraman
- Lucas Furtado da Fonseca
- Daniel Shuiti Igarashi Ueno
- Mauricio D'arc Palmieri
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Recovery of Achilles Tendon Rupture with Bone Marrow Aspirate Matrix: A Case Report

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Abstract

Achilles Tendon (AT) rupture is a common debilitating condition associated with ankle and foot overuse injuries. This disorder can often prove to be challenging since tendons are poorly vascularized structures that rely on synovial fluid diffusion in order to obtain nutrients. The deficit in strength due to AT rupture may increase the risk of additional injuries and complications. Surgical interventions are usually the first choice of treatment, but problems may still persist during follow-up. Conversely, the administration of orthobiologics has revealed high success rates in several procedures associated with regenerative medicine. Popular autologous alternatives, such as Bone Marrow Aspirate (BMA), are often utilized in clinical settings. Our patient received only one session of "BMA matrix" injections, displaying satisfactory healing based on functional assessments, Magnetic Resonance Imaging (MRI) results, and pain scores. The patient was able to return to sports with no complaints and MRI scans obtained during follow-up revealed clear signs of AT restoration. Here, we discuss a safe and effective administration of an autologous BMA product as a feasible alternative for the enhanced healing of a musculoskeletal tissue injury.

Keywords: Case report; Achilles tendon; Orthobiologics; Bone marrow aspirate; Regenerative medicine.

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Platelet-Rich Plasma Power-Mix Gel (ppm)—An Orthobiologic Optimization Protocol Rich in Growth Factors and Fibrin

- José Fábio Lana
- Joseph Purita
- Peter Albert Everts
- Palmerindo Antonio Tavares De Mendonça Neto
- Daniel de Moraes Ferreira Jorge
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- Madhan Jeyaraman
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Review

Platelet-Rich Plasma Power-Mix Gel (ppm)—An Orthobiologic Optimization Protocol Rich in Growth Factors and Fibrin

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Abstract: Platelet- and fibrin-rich orthobiologic products, such as autologous platelet concentrates, have been extensively studied and appreciated for their beneficial effects on multiple conditions. Platelet-rich plasma (PRP) and its derivatives, including platelet-rich fibrin (PRF), have demonstrated encouraging outcomes in clinical and laboratory settings, particularly in the treatment of musculoskeletal disorders such as osteoarthritis (OA). Although PRP and PRF have distinct characteristics, they share similar properties. The relative abundance of platelets, peripheral blood cells, and molecular components in these orthobiologic products stimulates numerous biological pathways. These include inflammatory modulation, augmented neovascularization, and the delivery of pro-anabolic stimuli that regulate cell recruitment, proliferation, and differentiation. Furthermore, the fibrinolytic system, which is sometimes overlooked, plays a crucial role in musculoskeletal regenerative medicine by regulating proteolytic activity and promoting the recruitment of inflammatory cells and mesenchymal stem cells (MSCs) in areas of tissue regeneration, such as bone, cartilage, and muscle. PRP acts as a potent signaling agent; however, it diffuses easily, while the fibrin from PRF offers a durable scaffolding effect that promotes cell activity. The combination of fibrin with hyaluronic acid (HA), another well-studied orthobiologic product, has been shown to improve its scaffolding properties, leading to more robust fibrin polymerization. This supports cell survival, attachment, migration, and proliferation. Therefore, the administration of the “power mix” containing HA and autologous PRP + PRF may prove to be a safe and cost-effective approach in regenerative medicine.

Keywords: platelet-rich plasma; platelet-rich fibrin; hyaluronic acid; orthobiologics; osteoarthritis; regenerative medicine



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1. Introduction

Osteoarthritis (OA) is acknowledged as a major degenerative and progressive joint disease responsible for significant pain and disability in the adult population [1]. The incidence of OA across the globe has risen significantly in the last few decades due to metabolic syndrome and aging [2–4]. This disease can often be challenging to treat as it presents a multifactorial nature, being mainly characterized by the physiological and architectural changes in the joint compartment as a whole [5]. It is highly influenced

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Angiogenesis and Tissue Repair Depend on Platelet Dosing and Bioformulation Strategies Following Orthobiological Platelet-Rich Plasma Procedures: A Narrative Review

- Peter A. Everts
- **José Fábio Lana**
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Review

Angiogenesis and Tissue Repair Depend on Platelet Dosing and Bioformulation Strategies Following Orthobiological Platelet-Rich Plasma Procedures: A Narrative Review

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Abstract: Angiogenesis is the formation of new blood vessel from existing vessels and is a critical first step in tissue repair following chronic disturbances in healing and degenerative tissues. Chronic pathoanatomic tissues are characterized by a high number of inflammatory cells; an overexpression of inflammatory mediators; such as tumor necrosis factor- α (TNF- α) and interleukin-1 (IL-1); the presence of mast cells, T cells, reactive oxygen species, and matrix metalloproteinases; and a decreased angiogenic capacity. Multiple studies have demonstrated that autologous orthobiological cellular preparations (e.g., platelet-rich plasma (PRP)) improve tissue repair and regenerate tissues. There are many PRP devices on the market. Unfortunately, they differ greatly in platelet numbers, cellular composition, and bioformulation. PRP is a platelet concentrate consisting of a high concentration of platelets, with or without certain leukocytes, platelet-derived growth factors (PGFs), cytokines, molecules, and signaling cells. Several PRP products have immunomodulatory capacities that can influence resident cells in a diseased microenvironment, inducing tissue repair or regeneration. Generally, PRP is a blood-derived product, regardless of its platelet number and bioformulation, and the literature indicates both positive and negative patient treatment outcomes. Strangely, the literature does not designate specific PRP preparation qualifications that can potentially contribute to tissue repair. Moreover, the literature scarcely addresses the impact of platelets and leukocytes in PRP on (neo)angiogenesis, other than a general one-size-fits-all statement that "PRP has angiogenic capabilities". Here, we review the cellular composition of all PRP constituents, including leukocytes, and describe the importance of platelet dosing and bioformulation strategies in orthobiological applications to initiate angiogenic pathways that re-establish microvasculature networks, facilitating the supply of oxygen and nutrients to impaired tissues.

Keywords: angiogenesis; tissue repair; platelet-rich plasma; platelet dose; bioformulation; leukocytes; platelet-rich fibrin; orthobiology; biosurgery

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An update on stem cell and stem cell-derived extracellular vesicle-based therapy in the management of Alzheimer's disease

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- Sathish Muthu
- Naveen Jeyaraman
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Review article

An update on stem cell and stem cell-derived extracellular vesicle-based therapy in the management of Alzheimer's disease

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 Clinical trial

ABSTRACT

Globally, neurological diseases pose a major burden to healthcare professionals in terms of the management and prevention of the disorder. Among neurological diseases, Alzheimer's disease (AD) accounts for 50%–70% of dementia and is the fifth leading cause of mortality worldwide. AD is a progressive, degenerative neurological disease, with the loss of neurons and synapses in the cerebral cortex and subcortical regions. The management of AD remains a debate among physicians as no standard and specific "disease-modifying" modality is available. The concept of "Regenerative Medicine" is aimed at regenerating the degenerated neural tissues to reverse the pathology in AD. Genetically modified engineered stem cells modify the course of AD after transplantation into the brain. Extracellular vesicles (EVs) are an emerging new approach in cell communication that involves the transfer of cellular materials from parental cells to recipient cells, resulting in changes at the molecular and signaling levels in the recipient cells. EVs are a

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Cannabidiol for musculoskeletal regenerative medicine

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Pesquisa completa aqui!

Minireview

Cannabidiol for musculoskeletal regenerative medicine

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Impact Statement

Cannabidiol (CBD) has gained a lot of significance from orthopedic and sports medicine physicians due to its potential part in the treatment of chronic pain in musculoskeletal (MSK) conditions. CBD plays vital physiological roles in human health that go well beyond immunomodulation, anti-inflammation, and antinociception. Recent investigations show that CBD also enhances cell proliferation and migration, especially in human MSCs. CBD is still relatively new in MSK medicine, and even though new studies are emerging, the clinical application of CBD requires more robust data from clinical trials to further elucidate the mechanisms that contribute to the improvement of MSK structures.

Abstract

Chronic musculoskeletal (MSK) pain is one of the most prevalent causes, which lead patients to a physician's office. The most common disorders affecting MSK structures are osteoarthritis, rheumatoid arthritis, back pain, and physical disability. Although there are many known management strategies currently in practice, phytotherapeutic compounds have recently begun to rise in the medical community, especially cannabidiol (CBD). This natural, non-intoxicating molecule derived from the cannabis plant has shown interesting results in many preclinical studies and some clinical settings. CBD plays vital roles in human health that go well beyond the classic immunomodulatory, anti-inflammatory, and antinociceptive properties. Recent studies demonstrated that CBD also improves cell proliferation and migration, especially in mesenchymal stem cells (MSCs). The foremost objective of this review article is to discuss the therapeutic potential of CBD in the context of MSK regenerative medicine. Numerous studies listed in the literature indicate that CBD possesses a significant capacity to modulate mammalian tissue to attenuate and reverse the notorious hallmarks of chronic musculoskeletal disorders (MSDs). The most of the research included in this review report common findings like immunomodulation and stimulation of cell activity associated with tissue regeneration, especially in human MSCs. CBD is considered safe and well tolerated as no serious adverse effects were reported. CBD promotes many positive effects which can manage detrimental alterations brought on by chronic MSDs. Since the application of CBD for MSK health is still undergoing expansion, additional randomized clinical trials are warranted to further clarify its efficacy and to understand its cellular mechanisms.

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Keywords: Cannabidiol, orthopedics, regenerative medicine, inflammation, exosome

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Intra-Articular Hyaluronic Acid in Osteoarthritis and Tendinopathies: Molecular and Clinical Approaches

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Pesquisa completa aqui!



biomedicines



Review

Intra-Articular Hyaluronic Acid in Osteoarthritis and Tendinopathies: Molecular and Clinical Approaches

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Abstract: Musculoskeletal diseases continue to rise on a global scale, causing significant socio-economic impact and decreased quality of life. The most common disorders affecting musculoskeletal structures are osteoarthritis and tendinopathies, complicated orthopedic conditions responsible for major pain and debilitation. Intra-articular hyaluronic acid (HA) has been a safe, effective, and minimally invasive therapeutic tool for treating these diseases. Several studies from bedside to clinical practice reveal the multiple benefits of HA such as lubrication, anti-inflammation, and stimulation of cellular activity associated with proliferation, differentiation, migration, and secretion of additional molecules. Collectively, these effects have demonstrated positive outcomes that assist in the regeneration of chondral and tendinous tissues which are otherwise destroyed by the predominant catabolic and inflammatory conditions seen in tissue injury. The literature describes the physicochemical, mechanical, and biological properties of HA, their commercial product types, and clinical applications individually, while their interrelations are seldom reported. Our review addresses the frontiers of basic sciences, products, and clinical approaches. It provides physicians with a better understanding of the boundaries between the processes that lead to diseases, the molecular mechanisms that contribute to tissue repair, and the benefits of the HA types for a conscientious choice. In addition, it points out the current needs for the treatments.

Keywords: hyaluronic acid; orthopedics; orthobiologics; inflammation; viscosupplementation; regenerative medicine

1. Introduction

Hyaluronic acid (HA), commonly referred to as hyaluronan, is a natural biological copolymer present in many tissues and fluids [1]. HA was first isolated as glycosaminoglycan (GAG) in 1934 by Meyer and Palmer from bovine vitreous humor. The term “hyaluronic acid” is broken down into hyaloid, which means vitreous, and uronic acid [1]. Posteriorly, HA was identified in other organs and tissue types, such as skin, joints, and the human umbilical cord, to name a few. Researchers discovered that this product could also be synthesized by many bacterial species such as *Escherichia coli*, *Bacillus subtilis*, and *Streptococcus zooepidemicus* via fermentation [2]. Conveniently, the chemical structure and

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Bone Marrow Aspirate Concentrate Improves Outcomes in Adults With Osteochondral Dissecans of the Talus and Achilles Rupture

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- Isabella Martins Zaia
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- Rodrigo Fernando Guercia
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Pesquisa completa aqui!

Systematic Review

Bone Marrow Aspirate Concentrate Improves Outcomes in Adults With Osteochondral Dissecans of the Talus and Achilles Rupture



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Purpose: The objective of this systematic literature review was to investigate the effects of the clinical application of bone marrow aspirate (BMA) and/or bone marrow aspirate concentrate (BMAC) in tendon and cartilage injuries in the foot and ankle. **Methods:** A search of the Embase, MEDLINE/PubMed, CINAHL, and Cochrane databases was performed in January 2021. The risk of bias of the studies was assessed using the tool "A Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies." The outcomes analyzed included pain reduction and functional improvement with the use of BMA/BMAC in patients with tendon and cartilage injuries in the foot and ankle. **Results:** Eleven studies met the inclusion criteria for analysis, involving a total of 527 subjects with osteochondral lesions (OCLs) of the talus, cartilage lesions of the talus, and acute Achilles tendon rupture. BMAC was applied alone in 4 studies, and in 7 studies, it was compared with other techniques such as matrix-induced autologous chondrocyte implantation, particulate juvenile articular cartilage, or microfracture. Interventions demonstrated improved function and reduced foot and ankle pain and showed no serious adverse effects. **Conclusions:** Evidence indicates that BMAC provides good clinical results, with improved function and reduced pain in adults with OCL and cartilage lesions of the talus and acute Achilles tendon rupture. **Level of Evidence:** Level IV, systematic review of level II to IV studies.

The feet and ankles can be affected by acute and chronic traumatic injuries to bones, ligaments, and tendons, as well as degenerative changes and inflammatory conditions that result in pain and functional disability.¹⁻³ In this sense, foot and ankle surgeons diagnose and treat different diseases conservatively or surgically.⁴ Treatment options include surgical procedures with reparative or restorative techniques and

pharmacologic and nonpharmacologic treatments that can be used to reduce pain, maintain function, accommodate existing deformity, and prevent new deformities.^{3,5,6} In addition, recent research has demonstrated that biological agents can provide excellent clinical results by optimizing and accelerating the healing of musculoskeletal tissue.⁷ Available biological treatments include bone marrow aspirate/bone marrow aspirate concentrate (BMA/BMAC), mesenchymal stem/stromal cells (MSCs), autologous blood products such as platelet-rich plasma, autologous chondrocyte implantation, and autologous matrix-induced chondrogenesis.^{8,9} Most of these treatments have shown promising results in relation to bone and cartilage regeneration.⁹

BMA and BMAC emerged as feasible alternatives to orthoplastic reconstruction. MSCs, growth factors, and other bone marrow-derived biological components can be found in bone marrow products. Notable effects include enhanced proliferation and angiogenesis as well as impeded secretion of proinflammatory cytokines.^{10,11} Thus, considering both the anti-inflammatory and regenerative effect, BMA and BMAC can be an important treatment for cartilage regeneration.

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Platelet-Rich Plasma Gel Matrix (PRP-GM): Description of a New Technique

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- Bruno Lima Rodrigues
- Stephany Cares Huber
- Maria Helena Andrade Santana
- Lucas Furtado da Fonseca
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Pesquisa completa aqui!



Technical Note Platelet-Rich Plasma Gel Matrix (PRP-GM): Description of a New Technique

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Abstract: Several musculoskeletal conditions are triggered by inflammatory processes that occur along with imbalances between anabolic and catabolic events. Platelet-rich plasma (PRP) is an autologous product derived from peripheral blood with inherent immunomodulatory and anabolic properties. The clinical efficacy of PRP has been evaluated in several musculoskeletal conditions, including osteoarthritis, tendinopathy, and osteonecrosis. When used in combination with hyaluronic acid (HA), a common treatment alternative, the regenerative properties of PRP are significantly enhanced and may provide additional benefits in terms of clinical outcomes. Recently, a new PRP-derived product has been reported in the literature and is being referred to as “plasma gel”. Plasma gels are obtained by polymerizing plasminic proteins, which form solid thermal aggregates cross-linked with fibrin networks. Plasma gels are considered to be a rich source of growth factors and provide chemotactic, migratory, and proliferative properties. Additionally, clot formation and the associated fibrinolytic reactions play an additional role in tissue repair. There are only a few scientific articles focusing on plasma gels. Historically, they have been utilized in the fields of aesthetics and dentistry. Given that the combination of these products (PRP, HA, and plasma gel) could enhance tissue repair and wound healing, in this technical note, we propose a novel regenerative approach, named “PRP-HA cellular gel matrix” (PRP-GM), in which leukocyte-rich PRP (LR-PRP) is mixed with a plasma gel (obtained by heating the plasma up) and HA in one syringe using a three-way stopcock. The final product contains a fibrin- α -albumin network entangled with HA's polymers, in which the cells and biomolecules derived from PRP are attached and released gradually as fibrinolytic reactions and hyaluronic acid degradation occur. The presence of leukocytes, especially monocytes and macrophages, promotes tissue regeneration, as type 2 macrophages (M2) possess an anti-inflammatory feature. In addition, HA promotes the viscosupplementation of the joint and induces an anti-inflammatory response, resulting in pain relief. This unique combination of biological molecules may contribute to the optimization of regenerative protocols suitable for the treatment of degenerative musculoskeletal diseases.

Keywords: platelet-rich plasma; hyaluronic acid; autologous biomaterials; regenerative medicine; orthopedics



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Extracorporeal Shockwave Treatment for Low Back Pain: A Descriptive Review of The Literature

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Biologic Orthopedic Journal

Review Article
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EXTRACORPOREAL SHOCKWAVE TREATMENT FOR LOW BACK PAIN: A DESCRIPTIVE REVIEW OF THE LITERATURE

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Abstract

Low back pain is a common symptom in patients with chronic musculoskeletal conditions, affecting several individuals. In most cases, low back pain can often prove to be nonspecific or even multifactorial. Current treatment approach is based on surgical and noninvasive interventions, including pharmacological, psychological, physiotherapeutic, or complementary strategies. Extracorporeal shock wave therapy (ESWT) is a type of noninvasive mechanical therapy that has become popular in recent years due to its applicability in the treatment of various musculoskeletal disorders, especially in the lumbar spine of individuals with osteoporosis, sacroiliitis, and even spinal cord disorders. The objective of this manuscript is to review the scientific evidence supporting the application of this therapy in the management of low back pain, and give a brief description of the treatment techniques used in clinical settings. The articles included in this descriptive review were selected from databases using the Google Scholar tool, from which a total of 13 applicable studies matching the topic were included. Despite the need for more clinical trials, shock waves have been applied in medical health for many years with satisfactory results. Its application in the treatment of lumbar spine disorders has been shown to be advantageous in the management of pathological progression, such as the natural wear and tear process of musculoskeletal structures. In this sense, shockwave therapy may represent a viable alternative for the treatment of lumbar spine disorders; however, its therapeutic effects and mechanisms require further elucidation.

Keywords: low back pain; shockwave therapy; regenerative medicine; orthopedics; musculoskeletal medicine

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Full Recovery from O'Donoghue's Triad with Autologous Bone Marrow Aspirate Matrix: A Case Report

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- André Atsushi Sugano
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- Tomas Mosaner
- Gabriel Silva Santos
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Pesquisa completa aqui!



Case Report

Full Recovery from O'Donoghue's Triad with Autologous Bone Marrow Aspirate Matrix: A Case Report

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Abstract: O'Donoghue's triad is an extremely debilitating condition. Although there are many conventional treatments available, there is still no consensus regarding the most effective rehabilitation protocol for a full recovery. Surgical interventions have become an ordinary consideration, but problems may still persist even after the surgical procedure. Orthobiologics, however, have gained considerable popularity in regenerative medicine. Notable autologous alternatives, such as bone marrow aspirate (BMA), are often utilized in clinical settings. To our knowledge, the administration of BMA products for the management of O'Donoghue's triad has not been thoroughly investigated in the literature. In this case report we describe a full recovery from O'Donoghue's triad with BMA matrix in a patient who was recalcitrant to surgical intervention due to fear of complications. Our patient received three BMA matrix injections with four-week intervals, exhibiting significant recovery according to pain scores, functional assessment outcomes, and magnetic resonance imaging (MRI) results. The patient returned to normal activities with no complaints and MRI evidence at follow-up showed significant signs of structural restoration of the musculoskeletal tissues. Here, we demonstrate that autologous BMA products are a feasible alternative for the accelerated recovery of musculoskeletal tissue injury with safety and efficacy.

Keywords: case report; knee injury; anterior cruciate ligament; orthobiologics; bone marrow aspirate



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1. Introduction

ACL ruptures can occur in contact sports and also in noncontact situations during sudden direction changes, cutting maneuvers, or during landing after a jump. Few prospective studies have investigated the biomechanical risk factors of ACL injuries, but it seems that the injury is linked to poor neuromuscular control of the knee-stabilizing muscles and to the dynamic valgus condition to which the knee can be subjected even in the context of contact sports [1]. This severe injury usually affects proximal structures, including the meniscus, surrounding musculature, critical neurovascular structures, and other ligaments [2]. Moreover, it is also related to a higher risk of a knee re-injury and long-term medical disability due to early osteoarthritis occurring in half of the individuals 10–15 years later [3]. The ACL is a pivotal structure in knee joints and its main function is to avoid anterior translation of the tibia. It also stabilizes internal tibial rotation and valgus angulation at the knee [2]. Upon complete extension, the ACL can absorb up to 75% of loading and approximately 85% between 30 and 90 degrees of flexion [2]. ACL injuries promote biomechanical instability and reduced magnitude of coupled rotation during flexion. For reference, the tensile strength of this ligament is of about 2200 Newtons; however, this threshold may change due to advanced age and repetitive loading. ACL force increases in equal proportion to the increasing magnitude of the anterior drawer force [4].

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The Mechanism of Action between Pulsed Radiofrequency and Orthobiologics: Is There a Synergistic Effect?

- Daniel de Moraes Ferreira Jorge
- Stephany Cares Huber
- Bruno Lima Rodrigues
- Lucas Furtado Da Fonseca
- Gabriel Ohana Marques Azzini
- Carlos Amílcar Parada
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Review

The Mechanism of Action between Pulsed Radiofrequency and Orthobiologics: Is There a Synergistic Effect?

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Abstract: Radiofrequency energy is a common treatment modality for chronic pain. While there are different forms of radiofrequency-based therapeutics, the common concept is the generation of an electromagnetic field in the applied area, that can result in neuromodulation (pulsed radiofrequency—PRF) or ablation. Our specific focus relates to PRF due to the possibility of modulation that is in accordance with the mechanisms of action of orthobiologics. The proposed mechanism of action of PRF pertaining to pain relief relies on a decrease in pro-inflammatory cytokines, an increase in cytosolic calcium concentration, a general effect on the immune system, and a reduction in the formation of free radical molecules. The primary known properties of orthobiologics constitute the release of growth factors, a stimulus for endogenous repair, analgesia, and improvement of the function of the injured area. In this review, we described the mechanism of action of both treatments and pertinent scientific references to the use of the combination of PRF and orthobiologics. Our hypothesis is a synergistic effect with the combination of both techniques which could benefit patients and improve the life quality.

Keywords: pulsed radiofrequency; orthobiologics; neuromodulation; growth factors

1. Introduction

Radiofrequency (RF) energy-based procedures, whether conventional, ablative or pulsed, represent a technique commonly performed for chronic pain in a variety of musculoskeletal conditions [1–3].

Pulsed radiofrequency (PRF) is derived from conventional RF with the aim of a less destructive RF-based treatment to be applied to the afferent nerve pathways of injured tissues [4]. PRF creates an electromagnetic field with the aim of functionally disrupting the neuronal membrane, which modulates gene expression, affecting the release of cytokines [5]. The application of PRF is based on the delivery of a train of sinusoidal electrical bursts (5–20 ms length) in the radiofrequency range (500 kHz) at a repetitive rate of a few hertz (2–5 Hz) [6] (Figure 1).

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Photobiomodulation therapy for osteoarthritis: Mechanisms of action

- Fábio Pericinato Giolo
- Gabriel Silva Santos
- Victor Fontes Pacheco
- Stephany Cares Huber
- Kaue Franco Malange
- Bruno Lima Rodrigues
- Fernanda Bassora
- Tomas Mosaner
- Gabriel Azzini
- Lucas Leite Ribeiro
- Carlos Amílcar Parada
- José Fábio Santos Duarte Lana

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Photobiomodulation therapy for osteoarthritis: Mechanisms of action

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Specialty type: Medicine, research and experimental

Fábio Pericinato Giolo, Department of Physical Therapy, Brazilian Institute of Regenerative Medicine, Indaiatuba 13334-170, Brazil

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Gabriel Silva Santos, Stephany Cares Huber, Bruno Lima Rodrigues, Biomedical Science, Brazilian Institute of Regenerative Medicine, Indaiatuba 13334-170, Brazil

Peer-review model: Single blind

Victor Fontes Pacheco, Tomas Mosaner, Gabriel Azzini, Lucas Leite Ribeiro, José Fábio Santos Duarte Lana, Department of Orthopedics, Brazilian Institute of Regenerative Medicine, Indaiatuba 13334-170, Brazil

Peer-review report's scientific quality classification

Kaue Franco Malange, Carlos Amílcar Parada, Neurobiology of Pain and Regenerative Medicine, The University of Campinas, Campinas 13083-862, Brazil

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

P-Reviewer: Al-Omari B, United Arab Emirates; Xu G, China

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Abstract

Photobiomodulation (PBM) is a non-invasive therapeutic modality with demonstrated effects in many fields related to regenerative medicine. In the field of orthopedics, in particular, PBM at various wavelengths has demonstrated the capacity to trigger multiple biological effects associated with protective mechanisms in musculoskeletal tissues. The articles cited in this review show that devices operating close to or within the near infrared range at low intensities can provoke responses which favor the shift in the predominant catabolic microenvironment typically seen in degenerative joint diseases, especially osteoarthritis (OA). These responses include proliferation, differentiation and expression of proteins associated with stable cell cycles. Additionally, PBM can also modulate oxidative stress, inflammation and pain by exerting regulatory effects on immune cells and blocking the transmission of pain through sensory neuron fibers, without adverse events. Collectively, these effects are essential in order to control the progression of OA, which is in part attributed to exacerbated inflammation



Platelet-rich plasma application in diabetic ulcers: A review

- Victoria Pereira Simão
- Carolina Souza Cury
- Gabriel Mota Zamariolli Tavares
- Gabriel Calixto Ortega
- Arthur Cichetto Ribeiro
- Gabriel Silva Santos
- José Fábio Santos Duarte Lana

Publicação: 02 de Junho de 2022
Veículo: WJD - World Journal of
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MINIREVIEWS

Platelet-rich plasma application in diabetic ulcers: A review

Victoria Pereira Simão, Carolina Souza Cury, Gabriel Mota Zamariolli Tavares, Gabriel Calixto Ortega, Arthur Cichetto Ribeiro, Gabriel Silva Santos, José Fábio Santos Duarte Lana

Specialty type: Orthopedics

Provenance and peer review: Unsolicited article; Externally peer reviewed.

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Peer-review report's scientific quality classification

Grade A (Excellent) 0
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Abstract

There are 422 million diabetic people in the world. 25% of these individuals are diagnosed with diabetic foot ulcer (DFU). 20% of patients with DFU will suffer amputation of the lower limbs. Following amputation procedures, the mortality rate of patients is over 70% in 5 years. Diabetes has no cure and, therefore, treatment aims to prevent and treat its complications. Autologous platelet-rich plasma (PRP) has been shown to be a therapeutic tool for many types of disorders, including the treatment of DFU. This manuscript aims to carry out a review to provide more knowledge about the efficacy and safety of autologous PRP for wound closure in patients with DFU. The majority of studies included in this review state that PRP promotes improvement of DFU lesions by accelerating tissue healing processes. However, many studies have a small sample size and thus require larger sample range in order to improve robustness of data in the literature.

Key Words: Diabetic foot ulcer; Platelet-rich plasma; Wound healing; Tissue regeneration; Inflammation

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Application of Sygen® in Diabetic Peripheral Neuropathies—A Review of Biological Interactions

- Marcelo Amaral Coelho
- Madhan Jeyaraman
- Naveen Jeyaraman
- Ramya Lakshmi Rajendran
- André Atsushi Sugano
- Tomas Mosaner
- Gabriel Silva Santos
- João Vitor Bizinotto Lana
- Anna Vitória Santos Duarte Lana
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- Prakash Gangadaran
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Publicação: 18 de Maio de 2022
Veículo: MDPI - Bioengineering

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Review

Application of Sygen® in Diabetic Peripheral Neuropathies—A Review of Biological Interactions

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Abstract: This study investigates the role of Sygen® in diabetic peripheral neuropathy, a severe disease that affects the peripheral nervous system in diabetic individuals. This disorder often impacts the lower limbs, causing significant discomfort and, if left untreated, progresses into more serious conditions involving chronic ulcers and even amputation in many cases. Although there are management strategies available, peripheral neuropathies are difficult to treat as they often present multiple causes, especially due to metabolic dysfunction in diabetic individuals. Gangliosides, however, have long been studied and appreciated for their role in neurological diseases. The monosialotetrahexosylganglioside (GM1) ganglioside, popularly known as Sygen, provides beneficial effects such as enhanced neurite sprouting, neurotrophin, neuroprotection, anti-apoptosis, and anti-excitotoxic activity, being particularly useful in the treatment of neurological complications that arise from diabetes. This product mimics the roles displayed by neurotrophins, improving neuronal function and immunomodulation by attenuating exacerbated inflammation in neurons. Furthermore, Sygen assists in axonal stabilization and keeps nodal and paranodal regions of myelin fibers organized. This maintains an adequate propagation of action potentials and restores standard peripheral nerve function. Given the multifactorial nature of this complicated disorder, medical practitioners must carefully screen the patient to avoid confusion and misdiagnosis. There are several studies analyzing the role of Sygen in neurological disorders. However, the medical literature still needs more robust investigations such as randomized clinical trials regarding the administration of this compound for diabetic peripheral neuropathies, specifically.

Keywords: diabetic peripheral neuropathy; gangliosides; sygen; neuroprotection; regenerative medicine

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Stromal Vascular Fraction for Knee Osteoarthritis – An Update

- José Fábio Santos Duarte Lana
- Anna Vitória Santos Duarte Lana
- Lucas Furtado da Fonseca
- Marcelo Amaral Coelho
- Guilherme Gabriel Marques
- Tomas Mosaner
- Lucas Leite Ribeiro
- Gabriel Ohana Marques Azzini
- Gabriel Silva Santos
- Eduardo Fonseca
- Marco Antonio Percepe de Andrade

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REVIEW ARTICLE

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Stromal Vascular Fraction for Knee Osteoarthritis – An Update

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Abstract

Orthobiologics never cease to cause popularity within the medical science field, distinctly in regenerative medicine. Recently, adipose tissue has been an object of interest for many researchers and medical experts due to the fact that it represents a novel and potential cell source for tissue engineering and regenerative medicine purposes. Stromal vascular fraction (SVF), for instance, which is an adipose tissue derivative, has generated optimistic results in many scenarios. Its biological potential can be harnessed and administered into injured tissues, particularly areas in which standard healing is disrupted. This is a typical feature of osteoarthritis (OA), a common degenerative joint disease which is outlined by persistent inflammation and destruction of surrounding tissues. SVF is known to carry a large amount of stem and progenitor cells, which are able to perform self-renewal, differentiation, and proliferation. Furthermore, they also secrete several cytokines and several growth factors, effectively sustaining immune modulatory effects and halting the escalated pro-inflammatory status of OA. Although SVF has shown interesting results throughout the medical community, additional research is still highly desirable in order to further elucidate its potential regarding musculoskeletal disorders, especially OA.

Keywords: Stromal vascular fraction; Orthobiologics; Osteoarthritis; Regenerative medicine; Adipose tissue.

Introduction

Osteoarthritis (OA) has long affected many individuals. This orthopedic condition remains the most common degenerative and progressive joint disease and is a major cause of pain and disability in adult populations, taking hold of approximately 7% of the global population [1]. According to the Global Burden of Disease (GBD) 2019 paper results, the number of people affected by OA rose 48% globally in between 1990 and 2019, which put OA at the 13th place for highest cause (long-term) with disability in the same year [2]. The increase in OA cases is likely attributed to factors such as aging and manifestation of poor metabolic health, especially incidences such as obesity [3-5].

OA is highly influenced by the exchanges between local, systemic and external factors, which consequently dictate the disease's progression and the way patients respond to its treatment processes [6]. Typical observations which characterize OA encompasses a continuous loss of articular cartilage, formation of osteophytes, thickening of the subchondral bone, exaggerated synovial inflammation, degeneration of ligaments and menisci as well as joint hypertrophy [6]. Several handling strategies have been proposed. Conservative methods such as administration of pharmacological agents only lead to temporary pain alleviation, rather than targeting the problem root cause [7].

Usually, health care providers may prescribe a course of multiple combined drugs for different OA stages, with the objective of controlling inflammatory nociceptive pain. Non-steroidal anti-inflammatory drugs (NSAIDs), other analgesics and corticosteroids, for example, may be commonly prescribed to aid in pain management. However, chronic NSAID use is of great concern as reported. Although NSAIDs effectively mitigate pain, they are also responsible for the increased risk of several adverse events, such as peptic ulcer disease, acute renal failure, and myocardial infarction [8]. Non-pharmacological strategies are usually limited to physical therapy, low impact exercise, weight loss, physical aids, and nerve ablation. In severe cases, however, such as grade IV OA, surgical interventions with joint replacement procedures may be unavoidable and therefore extremely detrimental to the patient [9,10].

These obstacles have led researchers to explore non-surgical alternatives, such as prescribing orthobiologics in particular. Orthobiologics are biologic products derived from substances that are naturally found in the human body which can mitigate the healing process of orthopedic injuries. Popular examples include platelet-rich plasma (PRP), hyaluronic acid (HA) and bone marrow aspirate/concentrate (BMA/BMAC), as well as adipose tissue-derived stem cells (ADSCs) [11,12]. According to the literature, these biological materials contain cytokines, monokines, and

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Application of Orthobiologics in Achilles Tendinopathy: A Review

- Luciano C. Ramires
- Madhan Jeyaraman
- Sathish Muthu
- Navaladi Shankar
- Gabriel Silva Santos
- Lucas Furtado da Fonseca
- José Fábio Lana
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Review

Application of Orthobiologics in Achilles Tendinopathy: A Review

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Abstract: Orthobiologics are biological materials that are intended for the regeneration of bone, cartilage, and soft tissues. In this review, we discuss the application of orthobiologics in Achilles tendinopathy, more specifically. We explain the concepts and definitions of each orthobiologic and the literature regarding its use in tendon disorders. The biological potential of these materials can be harnessed and administered into injured tissues, particularly in areas where standard healing is disrupted, a typical feature of Achilles tendinopathy. These products contain a wide variety of cell populations, cytokines, and growth factors, which have been shown to modulate many other cells at local and distal sites in the body. Collectively, they can shift the state of escalated inflammation and degeneration to reestablish tissue homeostasis. The typical features of Achilles tendinopathy are failed healing responses, persistent inflammation, and predominant catabolic reactions. Therefore, the application of orthobiologic tools represents a viable solution, considering their demonstrated efficacy, safety, and relatively easy manipulation. Perhaps a synergistic approach regarding the combination of these orthobiologics may promote more significant clinical outcomes rather than individual application. Although numerous optimistic results have been registered in the literature, additional studies and clinical trials are still highly desired to further illuminate the clinical utility and efficacy of these therapeutic strategies in the management of tendinopathies.

Keywords: Achilles tendinopathy; orthobiologics; regenerative medicine

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The Association between Gut Microbiota and Osteoarthritis: Does the Disease Begin in the Gut?

- Luciano C. Ramires
- Gabriel Silva Santos
- Rafaela Pereira Ramires
- Lucas Furtado da Fonseca
- Madhan Jeyaraman
- Sathish Muthu
- Anna Vitória Lana
- Gabriel Azzini
- Curtis Scott Smith
- José Fábio Lana

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Veículo: MDPI - International Journal of Molecular Sciences

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International Journal of
Molecular Sciences



Review

The Association between Gut Microbiota and Osteoarthritis: Does the Disease Begin in the Gut?

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Abstract: Some say that all diseases begin in the gut. Interestingly, this concept is actually quite old, since it is attributed to the Ancient Greek physician Hippocrates, who proposed the hypothesis nearly 2500 years ago. The continuous breakthroughs in modern medicine have transformed our classic understanding of the gastrointestinal tract (GIT) and human health. Although the gut microbiota (GMB) has proven to be a core component of human health under standard metabolic conditions, there is now also a strong link connecting the composition and function of the GMB to the development of numerous diseases, especially the ones of musculoskeletal nature. The symbiotic microbes that reside in the gastrointestinal tract are very sensitive to biochemical stimuli and may respond in many different ways depending on the nature of these biological signals. Certain variables such as nutrition and physical modulation can either enhance or disrupt the equilibrium between the various species of gut microbes. In fact, fat-rich diets can cause dysbiosis, which decreases the number of protective bacteria and compromises the integrity of the epithelial barrier in the GIT. Overgrowth of pathogenic microbes then release higher quantities of toxic metabolites into the circulatory system, especially the pro-inflammatory cytokines detected in osteoarthritis (OA), thereby promoting inflammation and the initiation of many disease processes throughout the body. Although many studies link OA with GMB perturbations, further research is still needed.

Keywords: osteoarthritis; gut microbiota; metabolic syndrome; systemic inflammation

1. Introduction

Osteoarthritis (OA) has long been considered a degenerative disease that affects the hyaline cartilage alone. This orthopedic disorder still remains one of the most common degenerative and progressive joint diseases and a major cause of pain and disability in adults, affecting approximately 7% of the global population [1]. The Global Burden of Disease (GBD) 2019 study results revealed that the number of individuals affected by this

Bone Marrow Aspirate for Delayed Union due to Severe Thoracic Rib Trauma

- Marcelo Braga
- Vitor Carreira Braga
- Thiago Setti
- Gabriel Silva Santos
- José Fábio Lana

Publicação: 03 de Setembro de 2021
Veículo: HSOA - Journal of Stem Cells Research, Development & Therapy

Pesquisa completa aqui!



Stem Cells Research, Development & Therapy

Case Report

Bone Marrow Aspirate for Delayed Union due to Severe Thoracic Rib Trauma

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Abstract

Study Design: Case report

Objectives: The objective is report a case of delayed union due to severe thoracic rib trauma involving multiple fractures by evaluation, interventional strategy and follow-up.

Background: Delayed union due to severe trauma is an impactful condition responsible for progressive deformity and pain where surgical intervention may still prove to be challenging in terms of success rates. Rib fracture is the most common form of blunt thoracic injury affecting multiple costal structures in all types of thoracic trauma. Typical conservative treatments are usually limited to brace application and only for the control of pain in acute circumstances. Rib fracture is still an important communicator of trauma severity, as morbidity and mortality can increase according to the number of fractured ribs.

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Braga M, et al., J Stem Cells Res Dev Ther 2021, 7: 077
DOI: 10.24966/SRDT-2080100077

HSOA Journal of

Stem Cells Research, Development & Therapy

Materials and Methods: Computed tomography (CT) of the costal arches was performed in both diagnosis and follow-up. The patient received Bone Marrow Aspirate (BMA) infiltration treatment to treat the delayed union of fractured bones.

Results: All of the fractured ribs (from the 2nd to the 12th) with multiple affected regions were apparently consolidated. The bone over-ride on the 5th, 6th, 7th, 9th and 10th ribs, were also consolidated. There was no evidence of chest wall collapse or instability, and there was no evidence of anomalous joints or even pseudarthrosis. The titanium showed no evidence of abnormalities. Patient exhibited significant pain improvement with BMA treatment.

Conclusion: In this peculiar setting, the infiltrations with BMA proved to be an efficient alternative tool for the treatment of severe thoracic rib trauma and delayed union. The patient returned with no complaints and CT evidence indicated that all of the fractured ribs had complete consolidation. Pain and functional outcome of the chest wall in terms of stability improved with the help of this orthopedic alternative.

Keywords: Bone marrow aspirate; Delayed union; Fracture; Orthopedics; Thoracic trauma

Key Points

- A 48-year-old man with a history of epilepsy fell off the roof of his house and suffered severe thoracic trauma, multiple rib fractures on the right rib cage, from the 2nd to the 12th ribs, affecting multiple points in the same costal arch.
- The condition was also associated with hemothorax, and unstable chest, as of September 2019. Signs of pain were detected in the right hemithorax. After 3 months, with no signs of consolidation of these fractures (Figure 1) a conclusion was found, characterizing it as possible pseudoarthrosis.
- The patient was submitted to two sessions of BMA injections for the management of delayed union. The first session occurred in February 2020, and the second one in June 2020.
- Delayed union was significantly improved with just two sessions with BMA administration. Three months after the first infiltration procedure the patient returned to the office and showed expressive improvements in pain and significant consolidation of fractured areas.

Introduction

The ribs are vital structures of the thoracic cage. Rib trauma can affect the lungs, mediastinum and other thoracoabdominal structures that rely on the integrity of the ribs for adequate protection [1]. Thoracic trauma usually arise from blunt or penetrating forces and can be broadly classified as chest wall, pulmonary or cardiovascular injury. Rib fractures are the most common form of blunt thoracic injuries affecting multiple points of these structures in all types of thoracic trauma [2]. Depending on the severity of traumatic rib injuries, key complications can encompass acute pain, hemothorax, pneumothorax, extensor, extensor humeralis, acute vascular injury and pulmonary



Characterization of autologous platelet rich plasma (PRP) and its biological effects in patients with Behçet's Disease

- Stephany Cares Huber
- Silmara Aparecida de Lima Montalvão
- Zoraida Sachetto
- Jose Fabio Santos Duarte Lana
- Joyce Maria Annichino-Bizzacchi

Publicação: 27 de Agosto de 2021

Veículo: JSRM – Regenerative Therapy

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Nebulization of glutathione and N-Acetylcysteine as an adjuvant therapy for COVID-19 onset

- José Fábio Santos Duarte Lana
- Anna Vitória Santos Duarte Lana
- Quézia Souza Rodrigues
- Gabriel Silva Santos
- Riya Navani
- Annu Navani
- Lucas Furtado da Fonseca
- Gabriel Ohana Marques Azzini
- Thiago Setti
- Tomas Mosaner
- Claudio Lopes Simplicio
- Taís Mazzini Setti

Publicação: 08 de Agosto de 2021

Veículo: Elsevier - Advances in Redox Research

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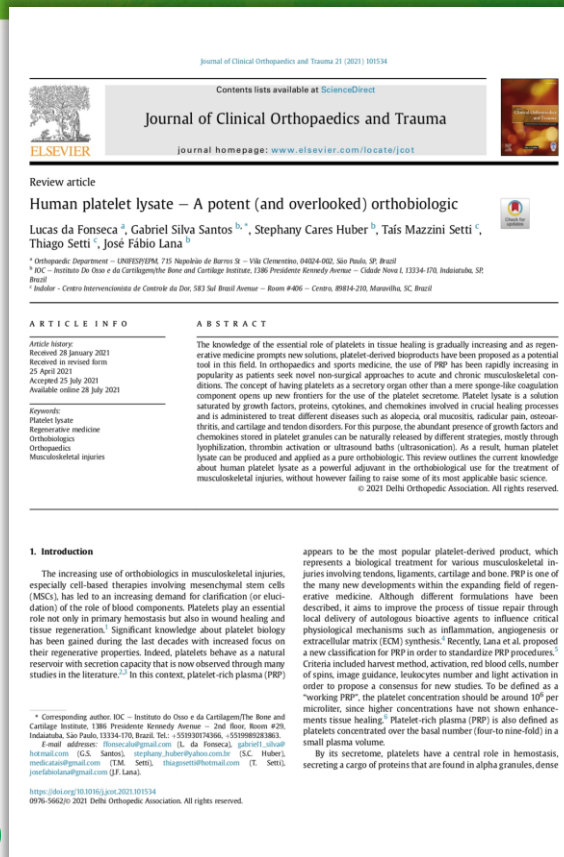


Human platelet lysate - A potent (and overlooked) orthobiologic

- Lucas da Fonseca
- Gabriel Silva Santos
- Stephany Cares Huber
- Taís Mazzini Setti
- Thiago Setti
- José Fábio Lana

Publicação: 28 de Julho de 2021
Veículo: Elsevier - Journal of Clinical Orthopaedics and Trauma

Pesquisa completa aqui!



The regenerative mechanisms of platelet-rich plasma: A review

- Rafael Gonzalez dos Santos
- Gabriel Silva Santos
- Natasha Alkass
- Tania Liana Chiesa
- Gabriel Ohana Azzini
- Lucas Furtado da Fonseca
- Antonio Fernando dos Santos
- Bruno Lima Rodrigues
- Tomas Mosaner
- José Fábio Lana

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Veículo: Elsevier - Cytokine

Pesquisa completa aqui!



Orthobiologics in the treatment of hip disorders

- André Vinícius Saueressig Kruel
- Lucas Leite Ribeiro
- Paulo David Gusmão
- Stephany Cares Huber
- José Fábio Santos Duarte Lana

Publicação: 26 de Abril de 2021

Veículo: WJSC - World Journal of Stem Cells

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MINIREVIEWS

Orthobiologics in the treatment of hip disorders

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Author contributions: All authors contributed to the study conception and design. The body of the manuscript was written by Kruel A; Literature research was conducted by Ribeiro LL; Gusmão PD revised the draft and made suggestions for improvement; Huber SC formatted the manuscript and made all the necessary adjustments in order to prepare the manuscript for the submission process; Lana JPD acted as the group leader, designing the main concepts and subtopics of discussion presented in the manuscript, critically revising both the initial and final versions of the manuscript before submission.

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Abstract

Orthobiologics are biological materials that are intended for the regeneration or healing of bone, cartilage and soft tissues. In this review we discuss the use of orthobiologics for hip disorders providing an update. The orthobiologics included in this article are hyaluronic acid, platelet rich plasma, bone marrow, adipose tissue and expanded mesenchymal stem cells. We explain the concepts and definitions of each orthobiological product, and the literature regarding its use in the hip joint. The paucity of guidelines for the production and characterization of the biological products leads to uneven results across the literature. Each biologic therapy has indications and benefits; however, noteworthy are the characterization of the orthobiologics, the application method and outcome analysis for further improvement of each technique.

Key Words: Orthobiologics; Hip disorders; Platelet-rich plasma; Mesenchymal stem cells; Bone marrow; Adipose tissue

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WJSC | <https://www.wjstc.com>

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April 26, 2021 | Volume 13 | Issue 4 |



Bone Marrow Aspirate Matrix: A Convenient Ally in Regenerative Medicine

- José Fábio Lana
- Lucas Furtado da Fonseca
- Gabriel Azzini
- Gabriel Santos
- Marcelo Braga
- Alvaro Motta Cardoso Junior
- William D. Murrell
- Alberto Gobbi
- Joseph Purita
- Marco Antonio Percope de Andrade

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Veículo: MDPI - International Journal of Molecular Sciences

Pesquisa completa aqui!



International Journal of
Molecular Sciences



Review

Bone Marrow Aspirate Matrix: A Convenient Ally in Regenerative Medicine

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Abstract: The rise in musculoskeletal disorders has prompted medical experts to devise novel effective alternatives to treat complicated orthopedic conditions. The ever-expanding field of regenerative medicine has allowed researchers to appreciate the therapeutic value of bone marrow-derived biological products, such as the bone marrow aspirate (BMA) clot, a potent orthobiologic which has often been dismissed and regarded as a technical complication. Numerous in vitro and in vivo studies have contributed to the expansion of medical knowledge, revealing optimistic results concerning the application of autologous bone marrow towards various impactful disorders. The bone marrow accommodates a diverse family of cell populations and a rich secretome; therefore, autologous BMA-derived products such as the “BMA Matrix”, may represent a safe and viable approach, able to reduce the costs and some drawbacks linked to the expansion of bone marrow. BMA provides—it eliminates many hurdles associated with its preparation, especially in regards to regulatory compliance. The BMA Matrix represents a suitable alternative, indicated for the enhancement of tissue repair mechanisms by modulating inflammation and acting as a natural biological scaffold as well as a reservoir of cytokines and growth factors that support cell activity. Although promising, more clinical studies are warranted in order to further clarify the efficacy of this strategy.

Keywords: tissue healing; bone marrow aspirate clot; fibrin matrix; hyaluronic acid; regenerative medicine; orthobiologics

1. Introduction

The rise in musculoskeletal disorders has been a great cause of concern in recent decades. Major health organizations such as the World Health Organization (WHO) confirm that musculoskeletal diseases are the highest contributor to global disability [1]. These health conditions can affect both young and elderly populations by putting bones, joint and muscle tissues at risk and generating a detrimental socioeconomic and psychosocial impact. Current interventional strategies are divided into pharmacological and nonpharmacological alternatives. Popular nonpharmacological strategies usually employ exercise,

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Biofat grafts as an orthobiologic tool in osteoarthritis: An update and classification proposal

- Rafael da Rocha Macedo
- Lucas Furtado da Fonseca
- José Fábio Santos Duarte Lana
- Tomas Mosaner
- Joseph Purita
- MAP de Andrade
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- Patricio Centurion

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 Meta-Analysis

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Biofat grafts as an orthobiologic tool in osteoarthritis: An update and classification proposal

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Author contributions: Purita J wrote the manuscript; Lana [BS] proposed the research subtopics; Fonseca LFD was responsible for navigating the literature and sharing the relevant studies that were included in this review; de Andrade JM and Rodrigues LM showed significant knowledge regarding the use of orthobiologics in regenerative medicine; Mosaner T formatted the citations and compiled the references; Centurion P and Purita J revised and formatted the body of the manuscript, verifying spelling, punctuation and grammatical errors; Macedo RBR created Table 1 and was also responsible for reviewing and approving all the modifications made to the manuscript, from draft to final version.

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Abstract

Among degenerative musculoskeletal disorders, osteoarthritis remains one of the main causes of pain and disability in the adult population. Current available alternatives to alleviate symptoms include conservative treatments such as physical therapy, anti-inflammatory drugs and an educational approach to lifestyle modification. The use of certain analgesics, such as opiates and corticosteroids offer short-term results but does not address the etiological source of pain and disability. In addition, prolonged use of such medications can cause additional complications. Therefore, the demand for regeneration of joint cartilage has led to an alternative approach called 'orthobiologics'. This alternative is based on cellular and molecular components capable of inducing and promoting tissue repair. Products derived from adipose tissue have been studied as an excellent source of orthobiologics in an attempt to promote joint cartilage repair. However,



Platelet-rich plasma vs bone marrow aspirate concentrate: An overview of mechanisms of action and orthobiologic synergistic effects

- José Fábio Santos Duarte Lana
- Lucas Furtado da Fonseca
- Rafael da Rocha Macedo
- Tomas Mosaner
- William Murrell
- Ashok Kumar
- Joseph Purita
- Marco Antonio Percepe de Andrade

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Platelet-rich plasma vs bone marrow aspirate concentrate: An overview of mechanisms of action and orthobiologic synergistic effects

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Author contributions: Purita J wrote the manuscript; de Andrade MAP proposed the research subtopics; Kumar A was responsible for navigating the literature and sharing the relevant studies that were included in this review; Murrell W and da Fonseca LF shared significant knowledge regarding the use of orthobiologics in regenerative medicine; Mosaner T formatted the citations and compiled the references; Macedo RR revised and formatted the body of the manuscript and verified spelling, punctuation and grammatical errors; Lana JFSD was responsible for reviewing and approving all the modifications made to the manuscript from draft to final version.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

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Abstract

The use of orthobiologics as a novel therapy for the treatment of numerous musculoskeletal disorders has increased considerably over the past decade. Currently, there are multiple alternatives available as suitable treatments; however, the use of autologous blood-derived products such as platelet-rich plasma (PRP), bone marrow aspirate (BMA) and BMA concentrate (BMAC), specifically, is expanding. Although many investigations attempted to demonstrate the effectiveness of these therapies, even with positive results, the literature lacks standardized protocols and overall accuracy in study designs, which leads to variance and difficulty in reproducibility of protocols. The efficacy of PRP for the treatment of cartilage, bone and muscle tissues is well known.



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The role of Glutathione as an adjunct therapy in the treatment of patients with COVID-19-Related Acute Respiratory Syndrome

- Taís Mazzini Setti
- Thiago Setti
- Lucas Furtado da Fonseca
- Stephany Cares Huber
- Gabriel Silva Santos
- José Fábio Santos Duarte Lana

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Research Article,

The role of Glutathione as an adjunct therapy in the treatment of patients with COVID-19-Related Acute Respiratory Syndrome

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Abstract:

Covid-19 is a novel coronavirus disease that has been (SARS-CoV-2) responsible for a worldwide pandemic of infectious pneumonia associated with severe acute respiratory syndrome. Although in most cases the disease can be resolved on its own, in severe or critical cases, patients can ultimately pass away, mainly due to the diffuse and massive alveolar damage associated with disease progression. One in four patients will be admitted to the Intensive Care Unit (ICU). A constant characteristic in severely affected patients is the exacerbated systemic inflammatory response. This is attributed to the excessive immune response mediated by cytokine secretion, which therefore causes acute lung injury, acute respiratory distress syndrome, multiple organ failure and even death. Currently, there are no effective antiviral agents and there are no fully elucidated or validated therapeutic options that can halt disease progression in some patients. Therefore, there is an urgent need for new treatments to delay the excessive inflammatory response and accelerate the repair of functional lung tissue in these patients. Glutathione may fit these criteria because it has some properties which can be associated with antiviral effects and it also participates in immune responses with the ability to balance oxidative stress.

Key words: acute respiratory syndrome, COVID-19, glutathione.

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Preparing the Soil: Targeting Meta-Inflammation in Musculoskeletal Regenerative Medicine

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- Lucas Furtado da Fonseca
- José Fábio Santos Duarte Lana
- Gabriel Azzini

Publicação: 2021
Veículo: ISAKOS - Global Link

Pesquisa completa aqui!

CURRENT CONCEPTS

Preparing the Soil: Targeting Meta-Inflammation in Musculoskeletal Regenerative Medicine



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Introduction

It is well known that the rise in metabolic syndrome (MS) has become a major health burden across the globe. Excessive caloric intake and poor dietary habits pave the way for the progression of "meta-inflammation," which disrupts metabolic equilibrium and eventually aggravates low-grade chronic inflammation throughout the body¹.

By definition, meta-inflammation is a state of chronic inflammation mediated by macrophages that are present in certain locations such as the liver, muscle, adipose tissue, pancreas, colon, and brain². These cells are known to coordinate immune activity and homeostasis, taking on different roles and displaying many cellular properties, depending on time and various biochemical stimuli³. Meta-inflammation can disrupt proper cell signaling and macrophage polarization, a process that also appears to be linked to MS. While meta-inflammation and disrupted cell signaling have been associated with MS and other autoimmune disorders, other unknowns still remain to be explored with regard to the origins and initiatory mechanisms of this disorder. In any case, this disorder still poses a great challenge for orthopaedic surgeons and other medical practitioners as chronic inflammation has been shown to harm musculoskeletal structures⁴. Musculoskeletal complications may be treated with conservative alternatives as well as novel therapeutic interventions such as the application of orthobiologics, which are regenerative therapies that are used to facilitate the healing of variety of tissues. Popular examples include hyaluronic acid, platelet-rich plasma, bone marrow, adipose tissue, and expanded mesenchymal stem cells⁵. In order to promote a more effective response, however, medical professionals must "prepare the soil" before managing a patient with an orthobiologic intervention. In other words, the target tissue must be biologically receptive to therapeutic agents. This goal can be achieved by designing health protocols that modulate an individual's metabolic profile with the inclusion of dietary modifications, intermittent fasting, health supplements (minerals and vitamins), hormonal regulation, and other alternatives.

The objective of this review is to discuss some but not all of the known biologic soil-preparation alternatives in the fight against meta-inflammation, demonstrating the importance of primarily addressing low-grade chronic inflammation preceding interventional therapies.

Macrophage Polarization

The polarization of macrophages has been broadly divided into two distinct phenotypes (M1 and M2), which are attributed to the corresponding Th1 and Th2 (T helper) cell responses⁶. The M1 macrophages have been classically associated with inflammatory responses. These responses are usually mediated by certain inflammatory agents such as interferon- γ (IFN- γ) and lipopolysaccharide (LPS), which allows these cells to develop microbicidal and proinflammatory properties, a main feature of this specific phenotype. M1 receptors for cytokines and LPS, in turn, allow signal transduction, which results in the expression of well-known inflammatory mediators such as inducible nitric oxide synthase (iNOS), tumor necrosis factor- α (TNF- α), and chemokine (C-C motif) ligand 2 (CCL2/MCP-1)⁷.

Platelet-Rich Plasma: New Performance Understandings and Therapeutic Considerations in 2020

- Peter Everts
- Kentaro Onishi
- Prathap Jayaram
- José Fábio Lana
- Kenneth Mautner

Publicação: 21 de Outubro de 2020
Veículo: MDPI - International Journal of Molecular Sciences

Pesquisa completa aqui!



Review

Platelet-Rich Plasma: New Performance Understandings and Therapeutic Considerations in 2020

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Received: 2 October 2020; Accepted: 19 October 2020; Published: 21 October 2020



Abstract: Emerging autologous cellular therapies that utilize platelet-rich plasma (PRP) applications have the potential to play adjunctive roles in a variety of regenerative medicine treatment plans. There is a global unmet need for tissue repair strategies to treat musculoskeletal (MSK) and spinal disorders, osteoarthritis (OA), and patients with chronic complex and recalcitrant wounds. PRP therapy is based on the fact that platelet growth factors (PGFs) support the three phases of wound healing and repair cascade (inflammation, proliferation, remodeling). Many different PRP formulations have been evaluated, originating from human, in vitro, and animal studies. However, recommendations from in vitro and animal research often lead to different clinical outcomes because it is difficult to translate non-clinical study outcomes and methodology recommendations to human clinical treatment protocols. In recent years, progress has been made in understanding PRP technology and the concepts for bioformulation, and new research directives and new indications have been suggested. In this review, we will discuss recent developments regarding PRP preparation and composition regarding platelet dosing, leukocyte activities concerning innate and adaptive immunomodulation, serotonin (5-HT) effects, and pain killing. Furthermore, we discuss PRP mechanisms related to inflammation and angiogenesis in tissue repair and regenerative processes. Lastly, we will review the effect of certain drugs on PRP activity, and the combination of PRP and rehabilitation protocols.

Keywords: platelet-rich plasma; regenerative medicine; platelet dosing; neutrophils; monocytes; lymphocytes; inflammation; angiogenesis; serotonin; analgesic effects; immunomodulation; rehabilitation

1. Introduction

Autologous platelet-rich plasma (PRP) is the processed liquid fraction of autologous peripheral blood with a platelet concentration above the baseline [1]. PRP therapies have been used for various indications for more than 30 years, resulting in considerable interest in the potential of autologous PRP in regenerative medicine. The term orthobiologics has recently been introduced for the treatment of musculoskeletal (MSK) disorders, with promising results for the regenerative capacity of the heterogeneous biological active PRP cellular cocktail. Currently, PRP therapies are suitable treatment options with clinical benefits, with encouraging patient outcomes reported [2–4]. However,

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www.mdpi.com/journal/ijms



The protective role of glutathione in osteoarthritis

- Thiago Setti
- Miguel Gustavo Luz Arab
- Gabriel Silva Santos
- Natasha Alkass
- Marco Antonio Percope Andrade
- José Fábio Santos Duarte Lana

Publicação: 06 de Setembro de 2020
Veículo: Elsevier - Journal of Clinical Orthopaedics and Trauma

Pesquisa completa aqui!



Bone marrow aspirate clot: A feasible orthobiologic

- Jose Fábio Santos Duarte Lana
- Lucas Furtado da Fonseca
- Tomas Mosaner
- Clauber Eduardo Tieppo
- Gabriel Ohana Marques Azzini
- Lucas Leite Ribeiro
- Thiago Setti
- Joseph Purita

Publicação: 05 de Julho de 2020
Veículo: Elsevier - Journal of Clinical Orthopaedics and Trauma

Pesquisa completa aqui!



Metabolic syndrome and subchondral bone alterations: The rise of osteoarthritis - A review

- Gabriel Ohana Marques Azzini
- Gabriel Silva Santos
- Silvia Beatriz Coutinho Visoni
- Vitor Ohana Marques Azzini
- Rafael Gonzales dos Santos
- Stephany Cares Huber
- José Fábio Lana

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Veículo: Elsevier - Journal of
 Clinical Orthopaedics and Trauma

Pesquisa completa aqui!



Bone marrow-derived products: A classification proposal – bone marrow aspirate, bone marrow aspirate concentrate or hybrid?

- Joseph Purita
- José Fábio Santos Duarte Lana
- Morey Kolber
- Bruno Lima Rodrigues
- Tomas Mosaner
- Gabriel Silva Santos
- Carolina Calari-Oliveira
- Stephany Cares Huber

Publicação: 26 de Abril de 2020
Veículo: WJSC - World Journal of Stem Cells

Pesquisa completa aqui!



Submit a Manuscript: <https://www.wj-sc.com>

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WJSC 2020

Bone marrow-derived products: A classification proposal – bone marrow aspirate, bone marrow aspirate concentrate or hybrid?

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Author contributions: Purita J and Kolber M wrote the manuscript. Lana JPSD and Rodrigues BL designed the ACH classification concepts. Huber SC and Calari-Oliveira C created Tables 1 and 2 and completed the reference list. Santos GS proposed the schematic representation of the ACH classification illustrated in Figure 1 and Mosaner T reviewed the literature to validate information.

Conflict of interest statement: The authors declare no conflict of interests for this article.

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Abstract

Degenerative musculoskeletal disorders are one of the top causes of pain and disability in the adult population. Current available alternatives to mitigate symptoms include conservative treatments such as the administration of pharmacological agents and an educative approach towards lifestyle modification. The use of certain analgesics, such as opiates and corticosteroids, delivers short term results but do not address the etiological source of pain and disability. Also, prolonged use of such medications may cause additional complications. Therefore, the demand for musculoskeletal tissue regeneration has led to an alternative approach referred to as "orthobiologics". This alternative is based on cellular and molecular components capable of inducing and promoting tissue repair. Bone marrow (BM) aspirate (BMA) and concentrate are well-known orthobiologics used to treat musculoskeletal conditions. Orthobiologics derived from the BM have been discussed in the literature; however, the lack of standardization regarding collection and processing protocols presents a challenge for generalization of study outcomes and determination of efficacy. Since BM-derived orthobiologics have not yet been classified, to our knowledge, this manuscript proposes the ACH-classification system, which speaks to BMA (A), BMA and concentrate (C) and hybrid (H), which combines A and C. This classification proposes and describes 8 parameters that are relevant for the quality of biological products. The more parameters used would imply greater characterization and complexity of the evaluation of the biological product used.

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Extracorporeal shock wave therapy mechanisms in musculoskeletal regenerative medicine

- Claudio Lopes Simplicio
- Joseph Purita
- William Murrell
- Gabriel Silva Santos
- Rafael Gonzales dos Santos
- Jose Fábio Santos Duarte Lana

Publicação: 12 de Fevereiro de 2020
Veículo: Elsevier - Journal of Clinical Orthopaedics and Trauma

Pesquisa completa aqui!



The Regenerative Medicine Potential of PRP in Elite Athlete Injuries

- Alex Pontes De Macedo
- José Fábio Santos Duarte Lana
- Carolina Masini Pedrozo
- Ivan Corrêa Bottene
- Jose Renan Moyses De Medeiros
- Letícia Queiroz Da Silva

Publicação: 03 de Fevereiro de 2020
Veículo: Fortune Journals of Rheumatology

Pesquisa completa aqui!

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DOI: 10.26502/fjr.26880014



Review Article

The Regenerative Medicine Potential of PRP in Elite Athlete Injuries

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Abstract

Despite the health benefits of sports and physical activities, sports injuries rank among the major public health problems due to the important social and economic impact on society. A significant proportion of these injuries remain difficult to treat, and many athletes suffer from decreased performance and longstanding pain and discomfort, especially the high-performance athletes. Non-surgical alternatives have been studied, and the use of the Platelet-Rich Plasma (PRP) is one of the most popular solutions due to its chemotactic,

proliferative and anabolic responses through the delivery of growth factors. However, there are many unanswered questions concerning the composition of PRP, the individual blood product characteristics, the distinct protocols of production, and the different methods of application, all of which compromise the real evaluation of PRP efficacy. In addition, not much is known about its response in professional athletes and how these differ across sports. This review discusses the current literature regarding the use of PRP in the

Fortune Journal of Rheumatology

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Hyaluronic acid and fibrin from L-PRP form semi-IPNs with tunable properties suitable for use in regenerative medicine

- Bruna Alice Gomes de Melo
- Carla Giometti França
- José Luis Dávila
- NilzaAlzira Batista
- Carolina Caliar-Oliveira
- Marcos Akira d'Ávila
- Ângela Cristina Malheiros Luzo
- José Fábio Santos Duarte Lana
- Maria Helena Andrade Santana

Publicação: 13 de Dezembro de 2019
Veículo: Elsevier - Materials Science & Engineering C

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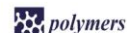


Association of Platelet-Rich Plasma and Auto-Crosslinked Hyaluronic Acid Microparticles: Approach for Orthopedic Application

- Andréa Arruda Martins Shimojo
- Adriana da Silva Santos Duarte
- **José Fábio Santos Duarte Lana**
- Ângela Cristina Malheiros Luzo
- Ana Rita Fernandes
- Elena Sanchez-Lopez
- Eliana Barbosa Souto
- Maria Helena Andrade Santana

Publicação: 26 Setembro de 2019
Veículo: MDPI - Polymers

Pesquisa completa aqui!



Article

Association of Platelet-Rich Plasma and Auto-Crosslinked Hyaluronic Acid Microparticles: Approach for Orthopedic Application

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Abstract: Platelet-rich plasma (PRP) associated with high molecular weight hyaluronic acid (HA) has been clinically used for tissue regeneration in orthopedics. Despite the recognized beneficial clinical outcomes (e.g., early pain control, improvement of patients' functional limitation and longer-term effectiveness compared to PRP and HA alone in mild and moderate osteoarthritis treatments), its use is still challenging and controversial due to lack of standardization of association practical protocols. Moreover, most studies neglect the matrix structure, that generates the ultimate properties of the association among platelets, fibrin network and the microparticles. In the present work, we aimed to analyze the influence of the PRP/HA association with a controlled matrix structure on the stability, rheological behavior, release of growth factors and in vitro proliferation of human adipose-derived mesenchymal cells (h-AdMSCs). The attenuation of the negative charge of HA was also evaluated. Pure PRP (P-PRP) (i.e., plasma enriched with platelets and poor in leukocytes) was prepared by centrifugation and activated with serum and calcium chloride (aP-PRP). Autocrosslinked hyaluronic acid (aHA) was prepared by organocatalyzed auto-esterification and structured in microparticles (aHA) by shearing. The attenuation of the negative charge of aHA was performed with chitosan (CHT) by polyelectrolyte complexation yielding aHA-CHT. The results showed that microparticles (MPs) have viscoelastic properties, extrusion force and swelling ratio appropriate for injectable applications. The association of aP-PRP with the controlled structure of aHA and aHA-CHT formed a matrix composed of platelets and of a fibrin network with fibers around 160 nm located preferably on the surface of the MPs with an average diameter of 250 µm. Moreover, aP-PRP/aHA and aP-PRP/aHA-CHT associations were non-toxic and supported controlled growth factor (PDGF-AB and TGF-β1) release and in vitro proliferation of h-AdMSC with a similar pattern to that of aP-PRP alone. The best h-AdMSC proliferation was obtained with the aP-PRP/aHA-CHT⁷⁵ indicating that the charge attenuation improved the cell

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www.mdpi.com/journal/polymers



Centrifugation Conditions in the L-PRP Preparation Affect Soluble Factors Release and Mesenchymal Stem Cell Proliferation in Fibrin Nanofibers

- Bruna Alice Gomes de Melo
- Ângela Cristina Malheiros Luzo
- José Fábio Santos Duarte Lana
- Maria Helena Andrade Santana

Publicação: 27 de Julho de 2019
Veículo: MDPI - Molecules

Pesquisa completa aqui!



Article

Centrifugation Conditions in the L-PRP Preparation Affect Soluble Factors Release and Mesenchymal Stem Cell Proliferation in Fibrin Nanofibers

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Abstract: Leukocyte and platelet-rich plasma (L-PRP) is an autologous product that when activated forms fibrin nanofibers, which are useful in regenerative medicine. As an important part of the preparation of L-PRP, the centrifugation parameters may affect the release of soluble factors that modulate the behavior of the cells in the nanofibers. In this study, we evaluated the influences of four different centrifugation conditions on the concentration of platelets and leukocytes in L-PRP and on the anabolic/catabolic balance of the nanofiber microenvironment. Human adipose-derived mesenchymal stem cells (h-AdMSCs) were seeded in the nanofibers, and their viability and growth were evaluated. L-PRPs prepared at 100× g and 100 + 400× g released higher levels of transforming growth factor (TGF)-β1 and platelet-derived growth factor (PDGF)-BB due to the increased platelet concentration, while inflammatory cytokines interleukin (IL)-8 and tumor necrosis factor (TNF)-α were more significantly released from L-PRPs prepared via two centrifugation steps (100 + 400× g and 800 + 400× g) due to the increased concentration of leukocytes. Our results showed that with the exception of nanofibers formed from L-PRP prepared at 800 + 400× g, all other microenvironments were favorable for h-AdMSC proliferation. Here, we present a reproducible protocol for the standardization of L-PRP and fibrin nanofibers useful in clinical practices with known platelet/leukocyte ratios and in vitro evaluations that may predict in vivo results.

Keywords: platelet; leukocyte; L-PRP; centrifugation; fibrin; nanofiber; growth factor; cytokine; mesenchymal stem cells

1. Introduction

In the past few years, the benefits of autologous leukocyte- and platelet-rich plasma (L-PRP) have been evidenced in the treatment of many types of diseases [1–6]. Aside from growth factors (GFs) released from the platelets' alpha granules, L-PRP contains inflammatory cytokines secreted from leukocytes that act in synergy to modulate the migration, proliferation, and differentiation of autologous cells through different pathways that lead to tissue regeneration [7–11]. Depending on the site, the degree of the injury (acute or chronic), and treatment phase (early or late stage of healing), the leukocyte fraction must be adjusted from poor-leukocyte PRP (P-PRP) to L-PRP [12–14]. Modern classifications systems consider the platelet and leukocyte levels, aside from other conditions, such as the number of centrifugation spins, activation, the presence of erythrocytes, and guided applications [15–18].

Molecules 2019, 24, 2729; doi:10.3390/molecules24132729

www.mdpi.com/journal/molecules



Procedures Guided by Ultrasonography in Injectable Treatments in Knee, Hip and Shoulder Pathologies

- Renato Luiz Bevilacqua de Castro
- Sergio Ricardo Neto Breno Pazinato Antoni
- José Fábio Lana
- Fernanda Santiago Bassora

Publicação: 25 de Junho de 2019

Veículo: Fortune Journal of Rheumatology

Pesquisa completa aqui!

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Review Article

Procedures Guided by Ultrasonography in Injectable Treatments in Knee, Hip and Shoulder Pathologies

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Abstract

The pathologies of the musculoskeletal system continue to be one of the main causes of the reduction of quality of life and are the main causes of disability with increasing incidence. The use of ultrasound equipment has gained importance, mainly with the improvement of image quality and technology. Currently, ultrasound has become the main diagnostic tool in traumatic, inflammatory and degenerative lesions in soft tissue conditions, and in the monitoring of joints, ligaments, cartilage and muscles. This work aims to present a review of the indicators of the use of intervention techniques with ultrasound equipment in musculoskeletal system disorders in knee, shoulder and hip joints.

Keywords: Shoulder; Knee; Hip; Ultrasonography

1. Introduction

The pathologies of the musculoskeletal system continue to be one of the main causes of the reduction of quality of life. Recently, the Arthritis Research, an English reputed institution demonstrated that between the years 2000 and 2015, the pathologies of the musculoskeletal system in the United Kingdom were the principal causes of disabilities, with an increase of 5% in this period and an increasing incidence curve [1]. In this scenario, the use of ultrasound equipment has gained importance, mainly with the improvement of image quality and technology. Currently,

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Leukocyte-rich PRP versus leukocyte-poor PRP - The role of monocyte/macrophage function in the healing cascade

- **José Fábio Lana**
- **Stephany Cares Huber**
- **Joseph Purita**
- **Claudia H. Tambeli**
- **Gabriel Silva Santos**
- **Christian Paulus**
- **Joyce M. Annichino-Bizzacchi**

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Pesquisa completa aqui!

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Leukocyte-rich PRP versus leukocyte-poor PRP - The role of monocyte/macrophage function in the healing cascade

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Regeneration

ABSTRACT

The mechanism of action of Platelet Rich Plasma (PRP) is thought to be related to the biomolecules present in α-granules. However, for the healing process to occur, an inflammatory phase is also deemed necessary. Leukocytes present in the inflammatory phase release both pro- and anti-inflammatory molecules. The latter may play an important role in the process of "inflammatory regeneration". Thus, we propose that in the context of healing, both platelets and leukocytes play an important role, specifically due to the macrophage's plasticity to switch from the M1 to M2 function. Therefore, we propose that PRP products derived from the buffy coat may be more beneficial than detrimental from a standpoint of the regenerative potential of PRP.

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1. Introduction

Platelet Rich Plasma (PRP) has been the focus of many published studies in the medical as well as veterinary¹ and dental² literature both as a stand-alone therapy as well as in conjunction with Stem Cells and scaffold materials. Specific to medical clinical trials, there is an increasing interest in PRP as evidenced by the large number of registered clinical trials. Currently there are 302 registered clinical trials for a variety of medical conditions (www.clinicaltrials.com).

PRP contains an autologous mixture of a variety of cells with a primary focus on platelets concentrated above baseline³. Platelets contain granules with a wide range of active biomolecules. When the platelets are activated, they release these biomolecules, which stimulate the natural healing cascade⁴⁻⁶. The primary focus of published studies as well as the hypothesis behind the therapeutic

efficacy of PRP relies on this biomolecule release from the α-granules.

The cell type and concentration of cells within a PRP preparation other than platelets may also include White Blood Cells, Red Blood Cells and a small fraction of stem cells⁷. The impact of the various PRP cell components other than platelets remains a subject of some controversy in the literature. This specifically applies to the recovery of leukocytes such as neutrophils due to their established release of inflammatory cytokines and metalloproteinases which can exacerbate the early inflammatory response to tissue injury⁸. This way, leukocyte-rich platelet-rich plasma (LR-PRP) and leukocyte-poor platelet-rich plasma (LP-PRP) have been the focus of debate over the past few years without a consensus. However, these and other variables should be considered in the questions for the ideal biologic activity of a PRP product. These variables include platelet number, the presence of white blood cells, the level of growth factors and the use of image guidance for its administration, among others. Recently, Lana et al. (2017) have published an article incorporating a broad variety of variables in a classification system termed MAASPRP. In summary, this new classification focuses on the method of PRP preparation (M), the use or lack of exogenous

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Impact on the quality of life of patients suffering from osteoarthritis of the knee after intra-articular administration of bone marrow mononuclear cells

- Marcus Valadares Guimarães
- Dalton Lopes Terra
- José Fábio Santos Duarte Lana
- Paula Alexandra da Graça Morais

Publicação: 12 de Abril de 2019

Veículo: Clinical and Medical Investigations

Pesquisa completa aqui!

Clinical and Medical Investigations



Research Article

ISSN: 2398-5763

Impact on the quality of life of patients suffering from osteoarthritis of the knee after intra-articular administration of bone marrow mononuclear cells

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Abstract

Objective: The aim of this study was to evaluate the combined treatment of BMMCs alone or in combination of arthroscopic debridement and lavage in treatment of knee OA, through response image and quality of life questionnaire. In comparison to the mesenchymal stem cells (MSC), the effectiveness is lower, however the costs for manipulation and laboratory handling make it difficult to use in clinical practice.

Design: This was a pilot, longitudinal and prospective trial with two years of follow-up. Twenty-one patients with patellofemoral osteoarthritis who met the study criteria were included. The patients were divided into three groups: BMMCs+arthroscopy, BMMCs+lavage, BMMCs. Clinical outcomes were evaluated using SF-36 questionnaire at baseline and two years after the procedure.

Results: In this study, it was verified a high recovery of BMMCs and platelets, especially with manual separation. It was not observed differences in SF-36 when comparing the three groups, however the evaluation of SF-36 baseline and two years of follow-up in each one of the three groups, it was showed an improvement in 3-4 parameters. The MRI showed an improvement in the stroke, subchondral bone and cartilage size in the patella and femur.

Conclusion: This study demonstrated that OA showed a significant improvement, measured by quality life questionnaire, only with the use of BMMCs, showing no improvement with the combination of arthroscopy or joint lavage. In this way, the use of BMMCs is well accepted, a presented impact on parameters of SF-36. None of the patients underwent total knee arthroplasty. A study with a higher number of patients is of great value to assess the safety and efficacy of BMMCs application.

Introduction

Articular cartilage has a limited intrinsic capacity to regenerate spontaneously after injury, often leading to pain and disability. It is generally believed that cartilage lesions progress to osteoarthritis (OA). OA of the knee is one of the most chronic degenerative joint diseases, affecting the quality of life of patient. Prompt intervention for symptomatic lesions make possible prevention of evolution to OA as well as to provide symptom relief. Conventional treatment modalities may be useful for relief of symptoms in the short term; however, they do not restore the natural articular cartilage integrity or prevent the deterioration [1]. In addition, the surgery for knee replacement provides a solution for severe OA [2]. The conservative non-surgical treatments include analgesics, nonsteroidal and steroid anti-inflammatory drugs and corticosteroids [3,4]. When the conservative treatment fails to control the symptoms and functional limitations occur, surgery should be considered to treat the cartilage lesion and the anatomical abnormalities. Conventional methods used to regenerate anomalies of the articular cartilage include microfractures, multiple perforation, abrasion and microfracture with limited results [5].

Orthobiologics is a thriving area of research and development, aimed specifically at preventing further degeneration and disease by restoring native biology, structure, and function. Cell-based therapy is a form of regenerative medicine that introduces new cells to repair damaged tissue [1]. Nowadays, there are a variety of orthobiologics such as: whole blood therapy, traditional platelet-rich plasma (PRP), autologous conditioned serum (ACS) or autologous conditioned serum, bone marrow aspirate, adipose derived stem cells, allograft of mesenchymal stem cells are the most well-studied and prevalent grafts of current use [6]. In this study we focus on autologous mononuclear cells obtained from bone marrow (BMMCs). In cell therapy, the majority of studies have used mesenchymal stem cells derived from bone marrow (BMSC). It is important to note that, the BMMCs, enriched with BMSCs have shown to be beneficial [7]. Previous clinical trials have demonstrated beneficial effects in osteoarthritis of femoral head, relieving pain and prevents the progression of osteoarthritis. The number of cells used increased 3 folds basal number, reaching 35×10^6 cells/mL [8]. We published a study evaluating the use of BMMCs and arthroscopy to treat patellofemoral osteoarthritis and verified promising results, reducing signs of patellofemoral AO and ensure the patient satisfaction with a safe return to social life and sports and improvement in functional scores, restoring the articular cartilage of subchondral bone [9]. However, the use of BMMCs for OA is not

plasma (PRP), autologous conditioned serum (ACS) or autologous conditioned serum, bone marrow aspirate, adipose derived stem cells, allograft of mesenchymal stem cells are the most well-studied and prevalent grafts of current use [6]. In this study we focus on autologous mononuclear cells obtained from bone marrow (BMMCs). In cell therapy, the majority of studies have used mesenchymal stem cells derived from bone marrow (BMSC). It is important to note that, the BMMCs, enriched with BMSCs have shown to be beneficial [7]. Previous clinical trials have demonstrated beneficial effects in osteoarthritis of femoral head, relieving pain and prevents the progression of osteoarthritis. The number of cells used increased 3 folds basal number, reaching 35×10^6 cells/mL [8]. We published a study evaluating the use of BMMCs and arthroscopy to treat patellofemoral osteoarthritis and verified promising results, reducing signs of patellofemoral AO and ensure the patient satisfaction with a safe return to social life and sports and improvement in functional scores, restoring the articular cartilage of subchondral bone [9]. However, the use of BMMCs for OA is not

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Key words: patellofemoral joint, osteoarthritis, bone marrow mononuclear cells

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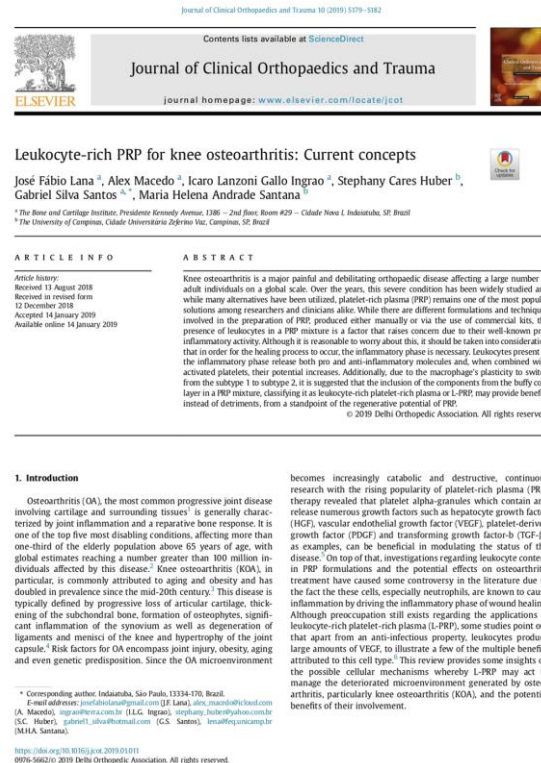


Leukocyte-rich PRP for knee osteoarthritis: Current concepts

- José Fábio Lana
- Alex Macedo
- Icaro Lanzoni Gallo Ingraio
- Stephany Cares Huber
- Gabriel Silva Santos
- Maria Helena Andrade Santana

Publicação: 14 de Janeiro de 2019
Veículo: Elsevier - Journal of Clinical Orthopaedics and Trauma

Pesquisa completa aqui!



Orthobiologic Treatment for Knee Osteoarthritis: A Cost Effectiveness Choice

- José Fábio Santos Duarte Lana
- Renato Bevilacqua de Castro
- Bruno Lima Rodrigues
- Carolina Calilari Oliveira
- Stephany Cares Huber
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- William D Murrel
- Mathew Nicholls

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Carolina Calilari Oliveira, Biomed J Sci & Tech Res



Review Article

Open Access

Orthobiologic Treatment for Knee Osteoarthritis: A Cost Effectiveness Choice



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Abstract

Osteoarthritis (OA) is the most prevalent joint disease and a common cause of joint pain, functional loss, and disability. Besides focusing only on pain relief, conventional treatments have shown some serious adverse effects, especially with the use of corticosteroids. In the severe cases of OA, the prothetic joint replacement is necessary. Thus, the OA treatment represents important economic consequences. In this way, orthobiologics are emerging as an alternative option for the treatment of knee osteoarthritis as they promote tissue regeneration. It comprises intra-articular injections of Platelet Rich Plasma, bone marrow aspirate concentrate, isolated and expanded stem cells. There has been an increasing interest in this approach over the years. Clinical trials using orthobiologics showed that when this therapy is used alone or in combination it is safe and effective in pain relief and function improvement. In addition, several *in vitro* studies have shown its regenerative properties. The goal of this article is to review the current options in this approach and its fundamental aspects, focusing on costs, mechanisms of action and reports of clinical trials.

Abbreviations: OA: Osteoarthritis; MMPs: Matrix Metalloproteinases; BMAC: Bone Marrow Aspirate Concentrate; AT: Adipose Tissue; SDF-1: Stromal Derived Factor; PDGF: Platelet Derived Growth Factor; HA: Hyaluronic Acid; RCT: Randomized Clinical Trial; LA: PRP: Leukocyte-Rich; LP-PRP: Leukocyte-Poor PRP; VAS: Visual Analogic Scale; IROC: International Knee Documentation Committee; MSCs: Mesenchymal Stem Cells; HSCs: Hemopoietic Stem Cells; GM-CSF: Granulocyte-Macrophage Colony Stimulating Factor; BMP-2: Bone Morphogenetic Protein; OAOS: Osteoarthritis Research Society International; SVF: Stromal Vascular Cell Fraction; AMPT: Amniotic Micro Fragmented Fat Tissue; FDA: Food and Drug Administration; KOOS: Knee Injury and Osteoarthritis Outcome Score; IgG: Immunoglobulin G; MHC-1: Major Histocompatibility Complex; G-CSF: Granulocyte Colony Stimulating Factor

Introduction

Knee Osteoarthritis (OA) is one of the most prevalent joint diseases in the world. Its pathology is characterized by progressive degeneration of cartilage and bone tissue, leading to the appearance of subchondral cysts and formation of osteophytes [1,2]. Aetiological factors are also joint specific, in this context, knee OA is a major cause of pain and locomotor disability worldwide. Thus, knee OA patients are subject to functional loss that leads to a reduced quality of life [3]. The epidemiology of the disorder is multifactorial,

however, the main risk factors for knee OA are overweight and obesity, previous knee injuries and female gender [3]. Besides that, the increasing of life expectancy and population aging are associated with the increased of OA incidence [4]. Beyond the personal and social consequences, the lower-limb OA, specifically hip and knee OA may have various economic consequences for patients and burdens for patients health systems in worldwide [4]. In knee OA patients incurred total of \$9,466 annual medical costs

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The Role of Thyroid Hormones on Management of Cartilaginous Joint Disorders

- Gabriel Ohana Marques Azzini
- Silvia Beatriz Coutinho Visoni
- Gabriel Silva Santos
- Stephany Cares Huber
- Alex Macedo
- Icaro Lanzoni Gallo Ingraio
- José Fábio Santos Duarte Lana

Publicação: 14 de Novembro 2018

Veículo: JP - Novel Techniques in Arthritis & Bone Research

Pesquisa completa aqui!



Novel Techniques in
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The Role of Thyroid Hormones on Management of Cartilaginous Joint Disorders



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Abstract

The purpose of the present research is to demonstrate the involvement of thyroid hormones and function on orthopedic health, particularly focusing on the management of cartilaginous joint disorders. There is more than sufficient evidence in the literature suggesting that fluctuations in levels of thyroid hormones, that is, deficiency as well as excess, can lead to a wide array of complications and even the manifestation of systemic diseases. Several studies demonstrate the indispensable biological value of thyroid hormones and their role in diverse mammalian target tissues, especially in skeletal cells and chondrocytes. The investigations discussed in this article also shed light on cellular and molecular mechanisms of hormonal regulation, interaction and even thread further into the genetic perspective behind the metabolic processes. It is also well known that thyroid hormone receptors TRα1 and TRβ1 are both expressed in the skeleton, growth plate chondrocytes, bone marrow, osteoblasts and even stromal cells. Developmental type II is expressed in all skeletal cells, further suggesting their relevance in human health, largely to thyroid hormone impact on cartilage, appreciable studies evaluate the potential of parathyroid hormones in stimulating chondrocytes, ultimately suggesting that timing and duration of hormone application are vital, as chondrocytes seem to require time to adapt and respond to hormonal stimuli. Alternative approaches indicate that the implementation of small doses of dietary iodine in individuals with deficits in concentration of this micronutrient show significant changes and can be helpful in regulating thyroid status.

Keywords: Thyroid Hormones; Osteoarthritis; Metabolism; Cartilage; Bone

Introduction

When it comes to musculoskeletal disorders, osteoarthritis (OA) is the most frequent and age-related degenerative joint disorder, typically characterized by degeneration of articular joint cartilage. Conventional methods for managing OA such as non-steroidal anti-inflammatory drugs (NSAIDs) may intervene in common symptoms such as joint pain, stiffness and limited function, but does not reverse the disease process itself [1]. Obesity is known to be a risk factor for knee osteoarthritis (KOA) while age remains the major risk factor for the occurrence of OA, even though all of the exact mechanisms by which age is involved in the etiology of OA have not been completely elucidated yet [2]. The pathological changes associated with the progression of OA usually encompasses biomechanical forces as well as multiple autocrine, paracrine and endocrine cellular events which all contribute to dysregulation of tissue homeostasis within the affected joint [3]. Thyroid hormones drive many complex actions

in almost all tissues during the developmental stages in life, from childhood to adulthood. The skeleton is an important target tissue of triiodothyronine, the active form of the thyroid hormone (T3) and can illustrate the cellular and molecular processes that occur as a response from thyroid hormones. However, the mechanism of action of these hormones in bone and cartilage, specifically, continue to be studied for further clarification [4]. There is evidence in the literature, particularly in vitro studies, indicating that progenitor cells and immature chondrocytes are the major T3 target cells [5], which brings attention to thyroid hormones and their diverse physiological effects on the human body, motivating investigation of the possible ways for them to assist in the management of cartilaginous joint disorders.

Regulation of Thyroid Hormones: The hormones secreted by the thyroid gland are important regulators of endochondral ossification [6]. The thyroid gland is responsible for the

New Tech Arthritis Bone Res 3(1): 117-140 MS ID: 555811 (2018)

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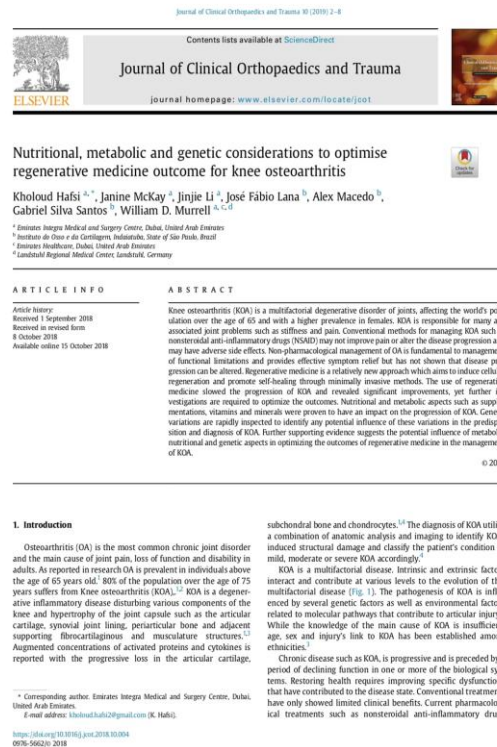


Nutritional, metabolic and genetic considerations to optimise regenerative medicine outcome for knee osteoarthritis

- Kholoud Hafsi
- Janine McKay
- Jinjie Li
- José Fábio Lana
- Alex Macedo
- Gabriel Silva Santos
- William D. Murrell

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Veículo: Elsevier - Journal of Clinical Orthopaedics and Trauma

Pesquisa completa aqui!



Treatment of male pattern alopecia with platelet-rich plasma: A double-blind controlled study with analysis of platelet number and growth factor levels

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- Silmara A. L. Montalvão
- Rebeca B. B. Cancela
- Francesca A. R. Silva
- Aline Urban Stephany C. Huber
- José Luiz R. C. Junior
- José Fábio S. D. Lana
- Joyce M. Annichinno-Bizzacchi

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Pesquisa completa aqui!

Treatment of male pattern alopecia with platelet-rich plasma: A double-blind controlled study with analysis of platelet number and growth factor levels



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Background: Promising results with platelet-rich plasma (PRP) in androgenetic alopecia that could be associated with platelet number and growth factor levels were described.

Objective: Analyze the platelet count and growth factor levels in PRP and their correlation with hair growth parameters evaluated by using the TrichoScan (Tricholog GmbH, Freiburg, Germany).

Methods: A total of 26 patients were randomized to receive 4 subcutaneous injections of PRP or saline. Hair growth, hair density, and percentage of anagen hairs were evaluated by using the TrichoScan method before injection, 15 days after the last injection, and again 3 months after the last injection. Growth factors (platelet-derived growth factor, epidermal growth factor, and vascular endothelial growth factor) were measured by the Luminex method (Millipore, Bedford, MA).

Results: We demonstrated a significant increase in hair count ($P = .0016$), hair density ($P = .012$) and percentage of anagen hairs ($P = .007$) in the PRP group versus in the control group, without correlation with platelet counts or quantification of the growth factors in PRP.

Limitations: Other growth factors that could be related to response to PRP were not evaluated.

Conclusion: Our data favor the use of PRP as a therapeutic alternative in the treatment of androgenetic alopecia. The lack of association between platelet count, platelet-derived growth factor, epidermal growth factor, and vascular endothelial growth factor levels and clinical improvement suggest that other mechanisms could be involved in this response. (J Am Acad Dermatol 2019;80:694-700.)

Key words: alopecia; hair loss; platelet-rich plasma; PRP.

Androgenetic alopecia (AGA) is characterized by pattern hair loss and is considered the most common type of alopecia in both men and women.¹ A progressive process of hair follicle miniaturization develops until follicles become ineffective at producing hair.² The development and progression of AGA are the result of action of

Abbreviations used

AGA: androgenetic alopecia
EGF: epidermal growth factor
PDGF: platelet-derived growth factor
PRP: platelet platelet-rich plasma
VEGF: vascular endothelial growth factor

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Correlation between Sex Hormone Deficiency and Osteoarthritis

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- Murrell WD
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Pesquisa completa aqui!

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Gratis

Review Article

Journal of Bone Biology and Osteoporosis Correlation between Sex Hormone Deficiency and Osteoarthritis

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Abstract

This literature review explores recent and past investigations carried out by researchers in various settings pertaining to the orthopaedic field of medicine, in attempts to show a possible connection between the deficit in sex hormone levels and the potential consequences it brings about on orthopaedic health, namely, osteoarthritis. There is some evidence in the literature suggesting that suboptimal concentrations of steroid hormones can negatively impact bone health, making it more susceptible to physical injury, especially when the hormone in question is estrogen. Several studies have shown that this biomolecule is quite essential to human health due to its effects on not only sexual development and function but also on bone metabolism, in both men and women. Investigations revolving around estrogenic compounds reveal their significance in physical capacitation of adult individuals, since it has already been found that estrogens play a pivotal role on bone maintenance by directly interacting with osteocytes, osteoblasts, osteoclasts and even T cells, to name a few examples. Large scale studies also bring up plausible evidence by evaluating the links between measured sex steroid concentrations and incidence of osteoarthritic joint replacement in adults. Taking that into consideration, there is sufficient motivation to look into hormonal fluctuation in adult individuals, calling for suitable medical intervention in order to keep a patient's health under control, avoiding and even treating the detrimental effects caused by the deficiency of certain steroid hormones.

Keywords: Osteoarthritis, Estrogen, Testosterone, Bone metabolism, Menopause

Introduction

Osteoarthritis (OA) is a major degenerative joint disease which can affect more than one quarter of the global population in individuals over the age of 18. This disease is typically defined by the following observations: progressive loss of articular cartilage, thickening of the subchondral bone, and formation of osteophyte, significant inflammation of the synovial as well as degeneration of ligaments and menisci of the knee and hypertrophy of the

joint capsule. Risk factors for OA encompass joint injury, obesity, aging and even genetic predisposition [1-3]. The pathological changes involved in the progression of OA are caused by biomechanical forces as well as multiple autocrine, paracrine and endocrine cellular events which all contribute to perturbations of tissue homeostasis within the affected joint [4],[5]. Gonadal steroid hormones, such as Estrogen (E) and Testosterone (T), for example, are molecules that are biosynthesized in the body and play a key role in sexual development and reproduction, which

J Bone Biol Osteoporosis, 4(1): 82-88 (2018)

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Patellofemoral Osteoarthritis: Treatment with Autologous Bone Marrow Mononuclear Cells and Arthroscopic Surgery, a Prospective Study

- Marcus Valladares Guimarães
- Paula Alexandra da Graça Morais Rios
- Milton Artur Ruiz
- José Carlos Pinto Noronha
- Dalton Lopes Terra
- José Fábio Santos Duarte Lana

Publicação: 14 de Janeiro de 2018
Veículo: Stem Cells & Regenerative Medicine

Pesquisa completa aqui!

Research Article

Stem Cell & Regenerative Medicine

Patellofemoral Osteoarthritis: Treatment with Autologous Bone Marrow Mononuclear Cells and Arthroscopic Surgery, a Prospective Study

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ABSTRACT

Objective: The aim of this study was to evaluate the treatment using BMNCs and arthroscopy in PF OA through functional questionnaires and MRI evaluations in a two year follow up. The use of mononuclear cells derived from bone marrow (BMNCs) is under investigation, and in vitro and pre-clinic studies showed promising results. In comparison to the mesenchymal stem cells (MSC), the effectiveness is lower, however the costs for manipulation and laboratory handling make it difficult to use in clinical practice.

Design: This was a pilot, longitudinal and prospective trial and 8 patients with patellofemoral osteoarthritis who met the study criteria were included. All of the patients underwent arthroscopic debridement and received an injection of autologous BMNCs. Clinical outcomes were evaluated using SF-36 and the TKSS questionnaire at baseline, one and two years after the procedure.

Results: In this study, an improvement in all of the evaluated parameters of the questionnaire was verified even after two years following the applications. The functional score of TKSS showed a significant improvement in one and two years in comparison to the baseline ($p < 0.001$). A significant improvement in SF-36 for all of the domains ($p < 0.001$) was also verified. In addition, an improvement in the MRI images of the patients was noticed, which indicates patellar cartilage recovery.

Conclusion: The procedure of the arthroscopy and the application of BMNCs has proved promising results to reduce the signs of PF OA and ensure the patient satisfaction with a safe return to social life and sports practice. The completed questionnaire confirmed a clear improvement and a strong impact on the quality of life of the patients with the regeneration of their articular cartilage and restored subchondral bone. These results offer a wide perspective for future studies with the use of BMNC to treat articular diseases.

Stem Cells Regen Med. 2018

Volume 2 | Issue 1 | 1 of 6



Distribution, Recovery and concentration of Platelets and Leukocytes in L-PRP prepared by Centrifugation

- Bruna Alice Gomes de Melo
- Andréa Arruda Martins Shimojo
- Amanda Gomes Marcelino Perez
- José Fábio Santos Duarte Lana
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Publicação: 01 de Janeiro de 2018

Veículo: Colloids and Surfaces B - Biointerfaces

Pesquisa completa aqui!

DISTRIBUTION, RECOVERY AND CONCENTRATION OF PLATELETS AND LEUKOCYTES IN L-PRP PREPARED BY CENTRIFUGATION

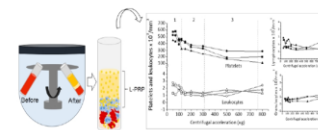
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Graphical abstract



Leukocyte and platelet-rich plasma (L-PRP) composition can be modulated by centrifugal acceleration.

Highlights

- Preparation of L-PRP by centrifuging the whole blood at different accelerations.
- Erythrocyte behavior influenced the distribution of platelets and leukocytes in the blood layers.
- Lower accelerations favored the location of platelets in the upper layer and leukocytes in the bottom layer.
- Leukocytes concentrated only after a second spin step.
- Three specific platelet/leukocyte and lymphocyte/granulocyte ratios were set from different acceleration ranges.

Contributions for classification of platelet rich plasma – proposal of a new classification: MARSPILL

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Publicação: 31 de Julho de 2017
Veículo: FSG - Future Medicine

Pesquisa completa aqui!

Special Report



Contributions for classification of platelet rich plasma – proposal of a new classification: MARSPILL

Platelet-rich plasma (PRP) has emerged as a significant therapy used in medical conditions with heterogeneous results. There are some important classifications to try to standardize the PRP procedure. The aim of this report is to describe PRP contents studying cellular and molecular components, and also propose a new classification for PRP. The main focus is on mononuclear cells, which comprise progenitor cells and monocytes. In addition, there are important variables related to PRP application incorporated in this study, which are the harvest method, activation, red blood cells, number of spins, image guidance, leukocytes number and light activation. The other focus is the discussion about progenitor cells presence on peripheral blood which are interesting due to neovascularogenesis and proliferation. The function of monocytes (in tissue-macrophages) are discussed here and also its plasticity, a potential property for regenerative medicine treatments.

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Keywords: growth factors • leukocytes • mononuclear cells • platelet-rich plasma
 • regenerative medicine

Platelet-rich plasma (PRP) can be considered as a form of autologous conditioned serum therapy, which contains a high concentration of growth factors (GFs) and cytokines. It plays important actions in various stages of regeneration and tissue repair [1].

According to the literature, PRP activation bursts the release of platelet α -granules, which are rich in proteins and GFs, such as PDGF, TGF- β , IGF, VEGF and EGF. All these molecules are important in different stages of tissue regeneration. They act as regulatory agents, stimulating chemotaxis and cellular differentiation and proliferation [2-5].

PRP has been widely investigated and used in medicine (orthopedics [6,7], dermatology [8] and plastic surgery), odontology [9] and veterinary medicine [10,11] due to its properties and simplicity to obtain the product. It is obtained with the use of commercial kits or not automated techniques (see Annex) that

results in different types of PRP. Despite the increasing number of studies and some classifications published, there is no consensus regarding the classification used for different types of PRP. These procedures are obtained via machine or in house. As a consequence, different terminologies may be observed for the same type of PRP and vice-versa [12]. Given the numerous classifications presented, the purpose of this report is to describe the main types of PRP in the literature. And also, from the critical analysis of these publications, to propose a terminology based on the main parameters used during the preparation of PRP. Thus, some variables, such as automated method (machine) or not, spin cycles number, activation form, presence or absence of cells, fibrin and concentration of different factors and cytokines that compose PRP, must not only be well defined, but also be easily identified.

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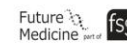
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The use of platelet rich plasma in the treatment of refractory Crohn's disease

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Pesquisa completa aqui!

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Original Article

The use of platelet rich plasma in the treatment of refractory Crohn's disease

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Abstract: Crohn's disease (CD) is a complex and multifactorial pathology. About 40% of patients cease to respond after available clinical therapy. Platelet rich plasma (PRP) is an alternative therapy widely used in the orthopedics and dentistry fields. Most recently, it has been studied in dermatological affections and autoimmune diseases. The aim was to evaluate the role of Platelet rich plasma (PRP) for refractory CD patients. Five patients diagnosed with ileocolic CD were selected. These patients were not taking any medication for at least two months and were resistant to biological therapy for at least one year. Growth factors, C-reactive protein, platelet and regulatory T cell frequency were measured at two different times: before treatment and after 12 injections of PRP (once a week). The activity of the disease was based on clinical and endoscopic indices. The endoscopic score after PRP decreased in comparison to the baseline in four patients. Four patients had clinical remission, including the absence of joint pain. Two patients with perianal CD showed a decrease of discharge. No adverse effects such as allergic reactions were observed. Our findings suggest a short-term benefit of PRP for most refractory CD patients in this case series.

Keywords: Platelet rich plasma, Crohn's disease, inflammatory bowel disease

Introduction

Crohn's disease (CD) is a chronic inflammatory bowel disease with unknown etiology, and it may affect any part of the gastrointestinal tract, especially the terminal ileum. CD is characterized by the formation of ulcers, fistulas and strictures, with periods of worsening and remission [1]. Immune factors are directly associated with CD: the patients present Th1/Th17 and Treg (regulatory T cell) disorders, which support the inflammatory symptoms [2]. The conventional clinical treatments comprise the use of immunosuppressive drugs and biological therapy. Besides the side effects, after a period of drug intake, 40% of the patients no longer respond to the treatment [3]. Therefore, the search for new effective treatments to induce a remission is needed.

Platelet-rich plasma (PRP) is a result of peripheral blood processing. It presents high concentration

of platelet [4]. This concentration is up to five times higher than the baseline platelet count (about 1 million platelet per microliter) [4, 5]. Recent studies are evaluating the functions of platelets more broadly, beyond hemostatic functions. Platelets participate in the inflammation process by releasing substances able to modulate inflammatory response by cell interactions to endothelial cells and leukocytes. PDGF, TGF- β , CD40L and CD154 are found among the immunomodulatory factors [6]. TGF- β is the main immunosuppressive molecule that influences Treg differentiation. This became evident in a study of immune thrombocytopenia, characterized by a decrease of Treg and TGF- β that showed a functional and quantitative Treg restoration after being treated with therapies that increase the platelet count [7]. Due to the immunomodulatory characteristics, especially Treg differentiation by TGF- β , PRP has the potential of being a therapeutic option for refractory CD. The objective of this study



Randomized controlled trial comparing hyaluronic acid, platelet-rich plasma and the combination of both in the treatment of mild and moderate osteoarthritis of the knee

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- Clarissa V. Souza
- Mary A. Ambach Hunter

- Vincent Aline Urban-Paffaro
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Veículo: Journal of Stem Cells & Regenerative Medicine

Pesquisa completa aqui!



RESEARCH ARTICLE

JSRM Code: 012020300011

Randomized controlled trial comparing hyaluronic acid, platelet-rich plasma and the combination of both in the treatment of mild and moderate osteoarthritis of the knee

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Objective: This study aimed at evaluating the clinical effects of Platelet Rich Plasma (PRP) and Hyaluronic Acid (HA) as individual treatments for mild to moderate Osteoarthritis (OA) and also examines the potential synergistic effects of PRP in combination with HA. Research continues to emerge examining the potential therapeutic efficacy of HA and PRP as autologous injectable treatments for joint arthritis. However, there is a paucity of research investigating the effects of combining HA and PRP on pain and functional status in patients with OA.

Design: In this multi-center, randomized, controlled, double blind, prospective trial, 105 patients with mild to moderate knee osteoarthritis, who met the study criteria, were randomly allocated to one of three interventions: HA (n=36), PRP (n=36), or HA+PRP (n=33). Each patient received 3 intra-articular knee injections of their assigned substance, with 2 week intervals between each injection. Clinical outcomes were evaluated using the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and Visual Analogue Scale (VAS) questionnaire at baseline and after 1, 6 and 12 months.

Results: The study showed that the PRP group had significant reduction in VAS scores at 1 (p=0.003), 3 (p=0.0001), 6 (p=0.0001) and 12 (p=0.0001) months when compared to HA. In addition, the PRP group illustrated greater improvement in WOMAC physical activity scale at 12 months (p=0.008) when compared to the HA group. Combining HA and PRP resulted in a significant decrease in pain (p<0.0001) and functional limitation (p<0.0001) when compared to HA alone at 1 year post treatment, and significantly increased physical function at 1 (p<0.0001) and 3 (p<0.01) months when compared to PRP alone.

Conclusion: The findings of the study support the use of autologous PRP as an effective treatment of mild to moderate knee osteoarthritis. It also shows that the combination of HA and PRP resulted to better outcomes than HA alone up to 1 year and PRP alone up to 3 months. Furthermore, the results suggest that combination of PRP and HA could potentially provide better functional outcomes in the first 30 days after treatment with both PRP and HA alone.

Key Words: Hyaluronic acid, Joint pathology, Knee, Osteoarthritis, Platelet-rich plasma

Introduction

Osteoarthritis of the knee joint has a great impact on physical performance and is considered one of the ten major causes of disability in the world. Standard conservative treatments for knee osteoarthritis include: weight loss, physical exercise, use of non-steroid anti-inflammatory agents, analgesics, injection of hyaluronic acid (HA) and injection of glucocorticoids¹⁻². Although standard conservative measures can provide symptomatic improvements, they are not without their limitations. Steroid injections are common practice among practitioners, including orthopedic surgeons, however, prolonged use of such pharmacologic treatments may have adverse effects on existing cartilage³. Also, chronic use of anti-inflammatory medications may cause nephrotoxicity and gastrointestinal side effects⁴. However, recently, orthobiologic injections have emerged as a potentially safe and efficacious option for joint Osteoarthritis.

Hyaluronic Acid (HA) is currently a widely used injectable treatment for degenerative joint pathology. It is a glycosaminoglycan that acts as a backbone for proteoglycans of

the extracellular matrix⁵, providing increased joint lubrication. Studies have demonstrated that HA has positive therapeutic efficacy for knee osteoarthritis with initial efficacy at 4 weeks, and peak effectiveness at 8 weeks which lasts for up to 6 months^{6,7}. When compared to continuous oral NSAIDs or other anti-inflammatory medications, HA has illustrated comparable, if not greater, therapeutic effects on knee OA with a better safety profile^{8,9}.

Autologous platelet rich plasma (PRP) has also emerged as an alternative in the context of injectable treatment for OA. PRP is comprised of a potent cellular milieu containing platelet concentrations above baseline, as well as an undifferentiated mixture of anti-inflammatory, pro-inflammatory, anabolic and catabolic mediators in an attempt to stimulate a supra-physiologic response and elicit the body's natural healing potential. Currently, most studies on PRP are anecdotal or case reports with small sample sizes. However, larger randomized controlled trials have demonstrated superior efficacy in terms such as tendinopathy¹⁰ and knee osteoarthritis¹¹.

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In vitro study of the role of thrombin in platelet rich plasma (PRP) preparation: utility for gel formation and impact in growth factors release

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- Letícia Queiroz da Silva
- Aline Urban Paffaro Francesca
- Aparecida Ramos da Silva
- Bruno Lima Rodrigues
- **José Fabio Santos Duarte Lana**
- Joyce Maria Annichinno-Bizzacchi

Publicação: 30 de Maio 2016
Veículo: Journal of Stem Cells & Regenerative Medicine

Pesquisa completa aqui!



RESEARCH ARTICLE

JSRM Code: 01201030002

In vitro study of the role of thrombin in platelet rich plasma (PRP) preparation: utility for gel formation and impact in growth factors release

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Introduction: The use of PRP has been studied for different fields, with promising results in regenerative medicine. Until now, there is no study in the literature evaluating thrombin levels in serum, used as autologous thrombin preparation. Therefore, in the present study we evaluated the role played by different thrombin concentrations in PRP and the impact in the release of growth factors. Also, different activators for PRP gel formation were evaluated. **Methods:** Thrombin levels were measured in different autologous preparations: serum, L-PRP (PRP rich in leukocytes) and T-PRP (thrombin produced through PRP added calcium gluconate). L-PRP was prepared according to the literature, with platelets and leukocytes being quantified. The effect of autologous thrombin associated or not with calcium in PRP gel was determined by measuring the time of gel formation. The relationship between thrombin concentration and release of growth factors was determined by growth factors (PDGF- $\alpha\alpha$, VEGF and IGF) multiplex analysis. **Results:** A similar concentration of thrombin was observed in serum, L-PRP and T-PRP (8.13 nM, 8.63 nM and 7.56 nM, respectively) with a high variation between individuals (C%: 35.07, 43 and 58.42, respectively). T-PRP and serum with calcium chloride showed similar results in time to promote gel formation. The increase of thrombin concentrations (2.66, 8 and 24 nM) did not promote an increase in growth factor release. **Conclusions:** The technique of using serum as a thrombin source proved to be the most efficient and reproducible for promoting PRP gel formation, with some advantages when compared to other activation methods, as this technique is easier and quicker with no need of consuming part of PRP. Noteworthy, PRP activation using different thrombin concentrations did not promote a higher release of growth factors, appearing not to be necessary when PRP is used as a suspension.

Key Words: Platelet Rich Plasma, Thrombin, gel, Leukocytes, Growth factor

Introduction

Platelet rich plasma (PRP) is defined as a concentrate preparation that increases between 4 to 9 folds the basal number of platelets, in reduced plasma volume^[1]. Platelets contain over 1100 proteins including growth factors, messengers of the immune system, enzymes, enzyme inhibitors and other bioactive compounds. These factors can improve tissue repair by diverse mechanisms including regulation of inflammation, angiogenesis, synthesis and remodeling of new tissue^[2-3]. For these reasons, PRP has been used in different fields: odontology^[4], plastic surgery^[5], orthopedics^[6], wound healing^[7] and dermatology^[8] with promising results. However, biomolecules are known to be quickly released from PRP, losing their activity in a short period of time which could represent a challenge in clinical practice^[9].

PRP preparations have been used since 1970s, however they became popular in 1990s. Since then, different protocols emerged to prepare PRP including commercial systems^[10]. Despite the promising results published by different research groups, the heterogeneity of protocols for PRP preparation available, render the evaluation of a consistent therapeutic effect quite difficult. *In vitro* studies evidenced that the different methodologies used in the preparation of PRP can affect biological aspects and clinical effects, which depend on several variables, particularly platelet and growth factor concentration, presence or absence of leukocytes and the type of activation^[11].

PRP is usually prepared by double centrifugation of anticoagulated blood. The first spin is to separate red blood cells and plasma; the second spin is to concentrate platelets. Despite the existing PRP standardization proposals, there is no consensus regarding centrifugation force or duration. This absence of a standard PRP preparation inhibits any comparisons of treatment efficacy obtained by different research groups. The inclusion or not of leukocytes is also widely discussed in the literature. PRP with leukocytes (L-PRP) presents different biologic activity, which could modify the therapeutic effect^[11].

Another important issue is the activation for growth factor release. This activation can be induced by bovine or autologous thrombin, calcium chloride, collagen, freeze & thaw cycles and mechanical trauma. Collagen and thrombin activate platelets by different mechanisms. For the activation of platelets by collagen, they must first adhere to collagen and then become active by it through a second receptor. This kind of platelet activation may require a longer mechanism than the cleavage process of thrombin-activated platelet activation^[12]. Park and collaborators demonstrated that thrombin is a strong agonist for induction of PRP cytokines and growth factors release when compared to ADP + calcium or collagen^[13]. Once PRP activation is achieved, a fibrin network begins to form with a rapid growth factor release during the first hour, continuing to release cytokines and growth factors from their mRNA for at least another 7 days^[14,15].

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Fibrin network architectures in pure platelet-rich plasma as characterized by fiber radius and correlated with clotting time

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Publicação: 17 de Maio de 2014
Veículo: Journal of Materials Science

Pesquisa completa aqui!

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Fibrin network architectures in pure platelet-rich plasma as characterized by fiber radius and correlated with clotting time

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Abstract Fibrin networks are obtained through activation of platelet-rich plasma (PRP) for use in tissue regeneration. The importance of fibrin networks relies on mediation of release of growth factors, proliferation of tissue cells and rheological properties of the fibrin gels. Activation of PRP usually involves the decomposition of fibrinogen by agonists, in a wide range of concentrations. Therefore fibrin networks with a large structural diversity are formed, making comparative evaluations difficult. In order to standardize the fibrin networks, we used the statistical techniques central composite rotatable design and response-surface analysis, to correlate the radius of the fibers with the ratios between the agonists (autologous serum/calcium chloride) and agonist/PRP. From an individual and interactive analysis of the variables, architectures characterized by thick, medium and thin fibers were delineated on the response-surface. Furthermore, the

architectures were correlated with coagulation time. This approach is valuable for standardizing the PRP preparation for clinical applications.

1 Introduction

Platelet-rich plasma (PRP) is an autologous preparation that concentrates platelets in a small volume of plasma [1]. Platelets are rich in growth factors (GFs), which play an important role in the healing process and tissue regeneration. PRP has the necessary biopolymers, such as fibrinogen and thrombin, and also calcium for the formation of fibrin networks whereby the GFs from platelets are released [2]. Among the various classifications of PRPs, the most current classifications consider networks from platelet concentrates in plasma that are low in leukocytes (pure PRP, or P-PRP); rich in leukocytes (L-PRP), including the leukocyte layer from the centrifugation of whole blood; rich in fibrin and platelets (P-PRF); and rich in leukocytes and fibrin (L-PRF) [3].

The preparation of P-PRP and L-PRP is a sequential process that involves two main steps: (1) the separation and concentration of platelets and (2) platelet activation and the formation of fibrin networks. The events in the second step are similar to those in the natural coagulation cascade: fibrinogen is cleaved by thrombin and is responsible for the processes of hemostasis, platelet adhesion and aggregation toward to form a fibrin network, the structural scaffold of blood clots [4]. The conversion of fibrinogen into networks of fibrin fibers occurs through a series of steps. After vessel injury, thrombin cleaves fibrinogen at four sites, catalyzing the hydrolytic removal of fibrinopeptides A and B, which exposes binding sites in fibrinogen's central domain. These sites interact with complementary sites in the end domains

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Relevant Aspects of Centrifugation Step in the Preparation of Platelet-Rich Plasma

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Research Article

Relevant Aspects of Centrifugation Step in the Preparation of Platelet-Rich Plasma

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Introduction. Platelet-Rich Plasma (PRP) is rich in growth factors, playing important role in tissue healing. The wide variation of reported protocols for preparation of PRP leads to variable compositions, which induce different biological responses and prevent results comparison. This study aims to highlight relevant aspects of the centrifugation step to obtain reproducible results and overall quality. **Material and Methods.** Samples of blood were collected from 20 healthy donors that have signed free informed consent. Two centrifugation steps (spins) were analyzed for the influence of centrifugal acceleration, time, processed volume, and platelet gradient. The Post-Platelet-Rich Plasma (P-PRP) was characterized in platelet concentration, integrity, and viability (α -selectin measurement). **Results.** Lower centrifugal accelerations favour platelet separation. The processing of 3.5 mL of blood at 100 ×g for 10 min (1st spin), 400 ×g for 10 min (2nd spin), withdrawing 2/3 of remnant plasma, promoted high platelet recovery (70–80%) and concentration (5x) maintaining platelet integrity and viability. The recovery of platelets was reduced for a larger WB volume (8.5 mL) processed. **Conclusion.** Centrifugal acceleration, time, WB processed volume, and minimization of the platelet gradient before sampling are relevant aspects to ensure reproducible compositions within the autologous nature of PRP.

1. Introduction

Platelet-Rich Plasma (PRP) is an autologous preparation that concentrates platelets in a small volume of plasma [1]. Platelets are rich in growth factors, which play an important role in tissue healing. Numerous studies have demonstrated the clinical application and notable results of PRP in dentistry [2], oral maxillofacial surgery [3], plastic surgery [4], orthopedics [5], rheumatology [6], and the treatment of different types of injuries that include chronic wounds [7, 8] and muscle injuries [9].

PRP is made for two purposes: one for harvesting platelets for therapeutic purposes and the other for testing for platelet function in PRP using aggregometry. In this work it was studied for therapeutic purposes only.

The wide variation in the reported protocols for obtaining PRP may lead to samples with different compositions that may induce different biological responses [1]. Despite these variations, all protocols follow a generic sequence that consists of blood collection, an initial centrifugation to separate red blood cells (RBC), subsequent centrifugations to concentrate platelets, and other components and an activation of the sample by adding a platelet agonist (Figure 1). Prior to the platelet activation step, variables in the process that may influence the platelet integrity along with the composition and effectiveness of the PRP include the number of spins, centrifugal acceleration, and time period of centrifugation [10]. In addition to the platelets, the white blood cells (WBC) composition may also be analyzed, as the concentration of these cells is also an important factor in tissue healing [11].



Prediction and Modulation of Platelet Recovery by Discontinuous Centrifugation of Whole Blood for the Preparation of Pure Platelet-Rich Plasma

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- José Fábio S.D. Lana
- Ana Amélia Rodrigues
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Prediction and Modulation of Platelet Recovery by Discontinuous Centrifugation of Whole Blood for the Preparation of Pure Platelet-Rich Plasma

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Abstract

The aim of this study was to describe the behavior of the separation of red blood cells (RBCs) by discontinuous centrifugation (DC) of whole blood to modulate and control the platelet recovery in the preparation of pure platelet-rich plasma (P-PRP). P-PRP is a platelet-rich plasma (PRP) in which the white blood cell layer is not included. To achieve this goal, an analytical model was derived that takes into account the packing of RBCs and predicts the behavior of platelet and plasma recovery efficiencies (PiPRE) based on the volume of whole blood, the hematocrit, and the volume of supernatant, as a function of the operating variables: centrifugal acceleration, and time. The model was derived from the basic equation of DC, which originates from the equilibrium balance of forces on a particle, and included the addition of one factor that corrected the terminal velocity of RBCs and was also correlated to the PiPRE in the supernatant. This factor was the ratio between the fractional volume concentrations of plasma and RBCs in the centrifugation pellet after centrifugation. The model was validated and the variability of the data was determined using experimental data from 10 healthy donors in the age range of 25–35 years. The predicted behavior for the packing of RBCs and the PiPRE was consistent with the behavior seen in the experimental data. Thus, the PiPRE could be modulated and controlled through centrifugal acceleration, time, and hematocrit. Use of this model based on a physical description of events is the first step of a reliable standardization of PRP preparations.

Key words: biomaterials; bioprocessing; regeneration; tissue engineering; wounds

Introduction

Platelet-rich plasma (PRP) is defined as an autologous preparation from whole blood (WB), in which platelets are concentrated in a small fraction of plasma. This broad definition is considered to be the consensus definition by the International Olympic Committee in sports medicine.¹

Platelets are rich in growth factors, which are critical for tissue regeneration.² Specifically, growth factors are released from activated platelets at sites of injury; the amount and activity of the growth factors depend on the recovery and preservation of platelets during PRP preparation.³

In general, PRP preparation is a sequential three-step process that involves blood collection, centrifugation to separate and concentrate the platelets, and activation of the platelets. Accordingly, PRP quality and efficiency is highly dependent

on the protocol used for its preparation.^{4,5,6} There are a multitude of PRP preparation protocols in the literature, which differ in terms of the conditions used in the preparation steps, such as centrifugal acceleration and time, the number of centrifugation steps, the type of anticoagulant, and the type of platelet agonist.^{7–11}

Due to this variation, it is difficult to compare the biological effects that are reported in different studies, even for a specific use, which can lead to doubts that compromise the credibility of PRP-based therapies.¹²

For the preparation of PRP, blood collection must be performed without trauma to the vessel wall to ensure the integrity of the platelets. Centrifugation is the first step in PRP preparation, which requires the recovery of a large number of intact platelets. Thus, both platelet activation and the final properties of the PRP preparation are influenced by the centrifugation step.

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