REVISTA BRASILEIRA DE REUMATOLOGIA

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Review article

Platelet-rich plasma for osteoarthritis treatment

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ARTICLE INFO

Article history:
Received 3 January 2014
Accepted 11 January 2015
Available online 5 August 2015

Keywords:
Platelet-rich plasma
Cartilage
Osteoarthritis

ABSTRACT

We conducted a comprehensive and systematic search of the literature on the use of platelet-rich plasma (PRP) in the treatment of osteoarthritis, using the Medline, Lilacs, Cochrane and SciELO databases, from May 2012 to October 2013.

A total of 23 studies were selected, with nine being controlled trials and, of these, seven randomized, which included 725 patients. In this series, the group receiving PRP showed improvement in pain and joint function compared to placebo and hyaluronic acid. The response lasted up to two years and was better in milder cases.

However it was found that there is no standardization in the PRP production method, neither in the number, timing, and volume of applications. Furthermore, the populations studied were not clearly described in many studies. Thus, these results should be analyzed with caution, and further studies with more standardized methods would be necessary for a more consistent conclusion about the PRP role in osteoarthritis.

Plasma rico em plaquetas no tratamento da osteoartrite

Palavras-chave:
Plasma rico em plaquetas
Cartilagem
Osteoartrite

RESUMO

Fez-se uma pesquisa abrangente e sistemática da literatura sobre o uso de plasma rico em plaquetas (PRP) no tratamento da osteoartrite nas bases de dados do Medline, Lilacs, Cochrane e SciELO, de maio de 2012 a outubro de 2013.

Foram selecionados 23 estudos, entre eles nove ensaios controlados e, desses, sete randomizados, os quais incluíram 725 pacientes. Nessa casuística, o grupo que recebeu PRP apresentou melhoria na dor e na função articular quando comparado ao que recebeu placebo e ácido hialurônico. A resposta durou até dois anos e foi melhor nos casos mais leves.

Entretanto, verificou-se que não há uma padronização no método de obtenção do PRP, bem como no número, intervalo e volume de aplicações. Além disso, as populações estudadas

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http://dx.doi.org/10.1016/j.rbre.2015.07.002

também não foram claramente descritas em muitos estudos. Desse modo, esses resultados devem ser analisados com cautela e seriam necessários novos estudos com métodos mais padronizados para uma conclusão mais consistente sobre o papel do PRP na osteoartrite.

Introduction

Although osteoarthritis (OA) is one of the most prevalent musculoskeletal diseases in the world, its treatment is still relatively limited.[1] The Osteoarthritis Research Society International notes that there is little evidence that the currently used drugs have effective action against the progression of the disease.[2]

A relatively new strategy for the treatment of OA is the use of cell elements and biomediators of tissue response. In this context, the platelet-rich plasma (PRP) has been configured as a perspective for improving clinical and structural outcomes by delivering a high concentration of growth factors that mediate cartilage healing and remodeling. Its potential has been shown in vitro and in vivo studies, however its real efficacy in OA is not well established.[3]

Thus, this study has the purpose to present some technical aspects for obtaining PRP, possible mechanisms of action and a review of its use in knee osteoarthritis.

Methods

We conducted a comprehensive and systematic literature search using MEDLINE, LILACS, Cochrane and SciELO databases, from May 2012 to October 2013. The key words used were "platelet-rich plasma," "platelet-rich growth factor", "osteoarthritis", "hip", "knee", "ankle", "human" and "cartilage". The studies found in the initial search were reviewed and additional references were also evaluated and included where relevant. The search was limited to studies performed in humans. The selected articles were read in full by two reviewers for analysis of their methods and their limitations. Disagreements were discussed for a consensus, with the mediation of a third author.

The quality of the studies analyzed was initially classified according to randomization. Then we proceeded to the evaluation of the following items: type of control group (active controller – hyaluronic acid – or placebo), double-blind evaluation (with description of SHAM procedure), number of treated patients, definition of radiographic and level of pain in the inclusion criteria, definition of exclusion criteria, description of blinding and randomization process, intention to treat analysis, assessment tools (whether including OMERACT criteria or not), description of the process to obtain PRP, platelet concentration, volume injected, guided-injection performance, number of injections in the treated and control groups, and report of adverse events.

A total of 23 studies (Fig. 1 and Tables 1 and 2) were selected, with nine being controlled trials, and of these, seven randomized, which included 725 patients. In this review some results of other 13 non-controlled studies, and also a retrospective cohort were also listed.

Mechanism of action of PRP

When PRP is injected into the injured site, platelets are activated by endogenous thrombin and/or intra-articular collagen.[4] Once activated, there is secretion of growth factors by degranulation of the α-granules.[5] Among secreted substances we can find: platelet-derived growth factor (PDGF), interleukin-1 receptor antagonist (IL-1RA), soluble receptor of tumor necrosis factor α (TNF-RI), transforming growth factor β (TGF-β), platelet factor 4 (PF4), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), insulin-like growth factor (IGF), osteocalcin (Oc), osteonectin (On), fibrinogen, vitronectin, fibronectin and thrombospondin-1 (TSP-1).[6]

Many of these mediators act as anti-catabolic and anti-inflammatory agents. The antagonist of IL-1 receptor inhibits activation of NFκB gene, cytokine involved in apoptosis and inflammation process.[4,7] Moreover, the soluble receptors of the tumor necrosis factor bind to TNF-α, preventing its interaction with cellular receptors and its pro-inflammatory signaling. TGF-β1 also acts as a factor inhibiting cartilage degradation, regulating and enhancing gene expression of tissue inhibitors of metalloproteinases (TIMP-1).[8] Other factors such as IGF-1, PDGF and TGF-β1 favor the stabilization of cartilage by controlling the metabolic functions of chondrocytes and subchondral bone, maintaining the homeostasis between the synthesis and degradation of proteoglycans, and stimulating the proliferation of chondrocytes.[9,10] It was also found that platelet growth factors stimulate synovial fibroblasts to synthesize hyaluronic acid.[9] These mechanisms are illustrated in Fig. 2.

Technical aspects for obtainment of platelet-rich plasma

PRP is obtained by centrifuging the autologous venous blood, causing a high concentration of platelets in a small volume of plasma.[11] There is no standardization regarding the speed, duration and number of centrifugations needed, neither which layer exactly is removed from the precipitate after this process.[3]

After the separation of the blood component rich in platelets, platelet activation can be stimulated artificially. The most commonly used activator is calcium chloride, which stimulates the production of thrombin, leading to release of growth factors. Other activators described are bovine thrombin and type I collagen. It is believed that the latter leads to a more gradual and durable release of the platelet granules, in