

Blood-Derived Biological Therapies in the Management of Osteoarthritis

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Abstract

Osteoarthritis (OA) is a progressive and multifactorial joint disease characterized by cartilage degeneration, subchondral bone remodeling, osteophyte formation, and synovial inflammation. OA is now understood to be a dynamic disease fueled by inflammatory mediators, catabolic enzymes, and cellular death, rather than a straightforward “wear and tear” ailment. These processes affect the synovium, joint capsule, and periarticular tissues in addition to speeding up the breakdown of cartilage, which eventually results in pain, stiffness, and impaired function. Traditional treatment approaches continue to be primarily palliative, providing brief respite without altering the course of the illness. Regenerative methods are becoming more and more popular as viable substitutes for both human and veterinary patients in recent years.

Biological products produced from blood, including autologous conditioned serum (ACS), autologous protein solution (APS), platelet-rich plasma (PRP), and platelet-rich fibrin (PRF), have shown promising outcomes. In order to promote chondrocyte activity, extracellular matrix formation, angiogenesis, and mesenchymal stem cell activation, PRP and PRF mainly work by supplying platelets, growth factors, and cytokines. ACS and APS, on the other hand, reduce pain and restore joint homeostasis by targeting inflammatory pathways, namely by regulation of interleukin-1 receptor antagonist (IL-1Ra). According to preclinical and clinical research, these products may help with both structural and symptom alleviation, particularly in cases of early to moderate OA.

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Notwithstanding encouraging results, variations in product composition, treatment regimens, and preparation techniques restrict standardization and make cross-study comparisons more difficult. Nonetheless, blood-derived products provide OA patients enhanced function and quality of life by combining regeneration potential with symptom control, making them a valuable biological therapy.

1. Introduction

Degeneration of articular cartilage, changes in subchondral bone, the production of osteophytes, muscular weakening, and inflammation of the synovial membrane are the hallmarks of osteoarthritis (OA), a chronic and progressive illness. Although it has often been referred to be a “wear and tear” disorder, new research has shown that inflammatory processes are crucial to its emergence. In addition to cartilage, OA is a complicated disease that also affects the joint capsule, synovial membrane, subchondral bone, and surrounding supporting tissues such ligaments and muscles. By sensitizing nociceptive neurons or activating high-threshold receptors, inflammatory mediators fuel pain and accelerate the course of disease (Bilge et al., 2018; Choi et al., 2019). The primary regulators of matrix production are matrix metalloproteinases (MMPs) and their inhibitors (TIMPs), which are composed of synovial cells, chondrocytes, ligamentocytes, and leukocytes. Nuclear factor kappa B (NF- κ B), transforming growth factor- β (TGF- β), cyclooxygenase-2 (COX-2), prostaglandin E2 (PGE2), interleukin-1 β (IL-1 β), tumor necrosis factor- α (TNF- α), MMP-13, and inducible nitric oxide synthase (iNOS) are important molecular mediators in the pathogenesis of OA. High levels of IL-1 β and TNF- α are present in cartilage, synovial fluid, and the synovium. They promote the release of prostaglandins and matrix-degrading enzymes, increase matrix degradation, and induce chondrocyte death. Additionally, they encourage fibroblasts to produce type I and III collagen (Janusz et al., 2001; Pelletier et al., 2001; Choi et al., 2019; Lee et al., 2020).

Clinically, middle-aged to older, large-breed, and obese dogs are more likely to have OA. Other significant risk factors include trauma, dysplasias, and developmental abnormalities. Instead of overt clinical indications, OA in cats typically manifests more discreetly, with behavioral changes, hidden lameness, or decreased activity. The impact of OA on joint function and quality of life is highlighted by its progressive nature and the scarcity of effective treatments. Thus, in both human and veterinary orthopedics, new biological therapeutic techniques that combine regeneration support

with symptomatic alleviation have drawn more attention (Goldring, 2000; Notoya et al., 2000; Aigner et al., 2002; Cope et al., 2019).

2. REGENERATIVE TREATMENT APPROACHES

Regenerative medicine aims to restore damaged tissue to its original state while reducing pain and inflammation and improving cartilage function in OA patients. This approach is especially relevant where conventional therapies provide only symptomatic control. Blood-derived biological products represent one of the most widely used and increasingly validated strategies in OA management. These products include platelet-rich plasma (PRP), platelet-rich fibrin (PRF), autologous conditioned serum (ACS), and autologous protein solution (APS) (Baltzer et al., 2009; Zhang et al., 2016; Li et al., 2017; Camargo Garbin & Morris, 2021; Sahin & Yesil, 2023; Gupta, 2024).

PRP is an autologous product obtained from whole blood with a high platelet concentration. It delivers platelets along with their stored growth factors and cytokines, which stimulate tissue regeneration, reduce inflammation, and create a favorable microenvironment for stem cells. The most important growth factors in PRP include platelet-derived growth factor (PDGF), transforming growth factor beta (TGF- β), vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), and epidermal growth factor (EGF). PDGF promotes chondrocyte and fibroblast proliferation; TGF- β regulates collagen synthesis and cell differentiation; VEGF and bFGF stimulate angiogenesis and tissue nutrition. Through these combined effects, PRP enhances cartilage metabolism, reduces extracellular matrix (ECM) degradation, and modulates intra-articular inflammation (Jang et al., 2013; O'Connell et al., 2019; Filardo et al., 2021).

Clinically, intra-articular PRP injections have been shown to promote cartilage regeneration, reduce pain, and improve functional outcomes in OA, particularly in the stifle joint. Literature suggests that PRP provides superior results compared to hyaluronic acid (HA) and placebo injections, especially in mild to moderate stages of OA, with prolonged symptomatic relief. However, PRP efficacy depends on platelet and leukocyte concentration, activation method, dosage, and number of injections. Classification systems such as PAW (platelet, activation, white blood cells) and DEPA (dose, efficiency, purity, activation) have therefore been proposed to allow better comparison and standardization of products (DeLong et al., 2012; Osterman et al., 2015; Magalon et al., 2016; Meheux et al., 2016).

PRF, a second-generation platelet concentrate, shares many biological properties with PRP but provides a slower and more controlled release of platelets, leukocytes, and growth factors within a fibrin matrix. PRF enhances mesenchymal stem cell (MSC) activation, cell migration, proliferation, inflammation modulation, and cartilage regeneration. PRF membranes entrap cells in a fibrin network and allow gradual release of growth factors. Preclinical and clinical studies have shown that PRF can reduce pain, improve joint function, and support cartilage regeneration. Since PRF is prepared without anticoagulants, it maintains a natural release profile of growth factors; however, its leukocyte content may have variable pro- and anti-inflammatory effects depending on the tissue context (Lo Monaco et al., 2020; Nicola, 2020; Işık et al., 2022).

Autologous conditioned serum (ACS) and autologous protein solution (APS) were developed primarily to target joint inflammation. ACS is produced by monocyte activation, leading to increased levels of interleukin-1 receptor antagonist (IL-1Ra), which counteracts inflammation. Clinical studies have shown that ACS improves pain and function in moderate knee OA, with benefits lasting up to two years. APS, on the other hand, offers the advantage of single-session preparation and increases the IL-1Ra/IL-1 ratio to reduce inflammation. Both ACS and APS aim to modulate symptoms, support anabolic processes within the joint, and restore homeostasis. Nevertheless, biological variability, cytokine profile differences, and lack of standardization remain limiting factors for optimizing efficacy (Baltzer et al., 2009; O'Connell et al., 2019; Camargo Garbin & Morris, 2021; Sahin & Yesil, 2023; Gupta, 2024).

3. DISCUSSION AND CLINICAL PERSPECTIVES

Blood-derived biological products provide effective therapeutic options in OA by reducing pain and inflammation while improving joint function. PRP and PRF mainly promote cartilage regeneration through stem cell activation and growth factor release, whereas ACS and APS focus on modulating inflammation to provide symptomatic relief. Among these, PRP has shown the strongest evidence, particularly in mild and moderate OA, offering functional improvement and long-term pain reduction. PRF contributes through controlled growth factor release and MSC activation, while ACS and APS help restore homeostasis by suppressing inflammatory cascades (Baltzer et al., 2009; Zhang et al., 2016; Li et al., 2017; Nicola, 2020; Sahin & Yesil, 2023).

However, the lack of randomized controlled trials, differences in preparation methods, and the diverse makeup of these products limit their uniformity in clinical practice. Disease stage, dosage, application frequency, and methodology all affect efficacy. According to recent meta-analyses and systematic reviews, PRP works better than HA and corticosteroid injections, especially when it comes to reducing pain and improving function in knee OA. As potential biological agents, PRF, ACS, and APS also seem to have positive effects in early to moderate OA (Jang et al., 2013; Nicola, 2020; Filardo et al., 2021; Işık et al., 2022).

Overall, blood-derived products represent an important therapeutic strategy for OA, addressing both symptomatic relief and regenerative potential. Future studies should focus on standardization, long-term outcomes, and optimized treatment protocols to enhance their clinical utility. Particularly in early stages of OA, these therapies may support functional recovery, improve quality of life, and offer a biological alternative to conventional symptomatic treatments (Baltzer et al., 2009; DeLong et al., 2012; Zhang et al., 2016; Otahal et al., 2020).

4. CONCLUSION

Because of its progressive nature, intricate pathophysiology, and scarcity of available treatments, osteoarthritis continues to pose a significant problem in both human and veterinary medicine. Blood-derived biological agents that combine symptomatic treatment with regeneration potential, like PRP, PRF, ACS, and APS, offer intriguing substitutes. ACS and APS control inflammatory pathways to reestablish joint homeostasis, whereas PRP and PRF promote tissue repair by growth factor release and stem cell activation. Their effectiveness in lowering pain and enhancing function is currently supported by research, but widespread clinical use is still significantly hampered by variations in preparation techniques and a lack of standardization. Future studies should concentrate on developing clinical use guidelines, elucidating long-term results, and streamlining processes. Overall, these therapies represent an important step toward biological and regenerative strategies that can enhance quality of life and functional recovery, particularly in early to moderate stages of OA.

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