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USE OF REGENERATIVE THERAPIES (PRP OR STEM CELLS) IN THE ORTHOPEDIC POSTOPERATIVE PERIOD OF DOGS WITH HIP DYSPLASIA

USO DE TERAPIAS REGENERATIVAS (PRP OU CÉLULAS-TRONCO) NO PÓS-OPERATÓRIO ORTOPÉDICO DE CÃES COM DISPLASIA COXOFEMORAL

USO DE TERAPIAS REGENERATIVAS (PRP O CÉLULAS MADRE) EN EL POSTOPERATORIO ORTOPÉDICO DE PERROS CON DISPLASIA DE CADERA

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ABSTRACT
Objective: To evaluate the main effects of regenerative therapies, such as mesenchymal stem cells (MSC) and platelet-rich plasma (PRP), in the postoperative treatment of dogs with hip dysplasia (HD), and correlate them with clinical and laboratory outcomes. Hip dysplasia is a common orthopedic disease in dogs, particularly in large breed dogs, and often leads to degenerative joint diseases such as osteoarthritis. The combination of MSC and PRP has shown promising effects on cartilage regeneration and pain relief, but the effectiveness of these treatments still depends on factors such as the severity of the disease and the stage of progression. This literature review analyzed national and international studies on the use of these regenerative therapies in the treatment of HD, highlighting clinical protocols, therapeutic effects, and limitations observed in different stages of the disease. The results show that, although these therapies present significant potential, standardization of protocols and conducting long-term studies are essential for confirming their effectiveness and safety.

Keywords: Regenerative therapies. Mesenchymal stem cells. Platelet-rich plasma. Hip dysplasia.

RESUMO
Objetivo: Avaliar os principais efeitos das terapias regenerativas, como as células-tronco mesenquimatosas (CTM) e plasma rico em plaquetas (PRP), no tratamento pós-operatório de cães com displasia coxofemoral (DCF), e correlacioná-los com os resultados clínicos e laboratoriais. A displasia coxofemoral é uma doença ortopédica comum em cães, especialmente nas raças de porte grande, e frequentemente resulta em doenças articulares degenerativas como a osteoartrite. A combinação de CTM e PRP tem mostrado efeitos promissores na regeneração da cartilagem e no alívio da dor, mas a eficácia desses tratamentos ainda depende de fatores como a gravidade da doença e o estágio de progressão. Esta revisão bibliográfica analisou estudos nacionais e internacionais sobre o uso dessas terapias regenerativas no tratamento da DCF, destacando os protocolos clínicos, os efeitos terapêuticos e as limitações observadas nos diferentes estágios da doença. Os resultados mostram que, embora essas terapias apresentem um potencial significativo, a padronização dos protocolos e a realização de estudos de longo prazo são fundamentais para a confirmação de sua eficácia e segurança.

Palavras-chave: Terapias regenerativas. Células-tronco mesenquimatosas. Plasma rico em plaquetas. Displasia coxofemoral.

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RESUMEN
Objetivo: Evaluar los principales efectos de las terapias regenerativas, como las células madre mesenquimatosas (CTM) y el plasma rico en plaquetas (PRP), en el tratamiento postoperatorio de perros con displasia coxofemoral (DCF), y correlacionarlos con los resultados clínicos y de laboratorio. La displasia coxofemoral es una enfermedad ortopédica común en perros, especialmente en razas grandes, y con frecuencia da lugar a enfermedades articulares degenerativas como la osteoartritis. La combinación de CTM y PRP ha mostrado efectos prometedores en la regeneración del cartílago y alivio del dolor, pero la eficacia de estos tratamientos aún depende de factores como la gravedad de la enfermedad y la etapa de progresión. Esta revisión bibliográfica analizó estudios nacionales e internacionales sobre el uso de estas terapias regenerativas en el tratamiento de la DCF, destacando los protocolos clínicos, los efectos terapéuticos y las limitaciones observadas en diferentes etapas de la enfermedad. Los resultados muestran que, aunque estas terapias presentan un potencial significativo, la estandarización de los protocolos y la realización de estudios a largo plazo son fundamentales para confirmar su eficacia y seguridad.

Palabras clave: Terapias regenerativas. Células madre mesenquimatosas. Plasma rico en plaquetas. Displasia coxofemoral.

INTRODUCTION

Hip dysplasia (CDF) is a degenerative orthopedic condition that affects dogs, especially in medium and large breeds, such as German Shepherds, Labrador Retrievers, Golden Retrievers, and Rottweilers. It is characterized by joint laxity in the hip region, leading to instability of the hip joint and, consequently, to wear and tear of the joint surfaces (Fries; Remedios, 1995). The consequence of this condition is the advancement to degenerative joint diseases (DAD), such as osteoarthritis (OA), which causes chronic pain, stiffness and decreased mobility, significantly affecting the animal's quality of life. DCF can manifest bilaterally or unilaterally and at different levels of severity, which makes clinical management and treatment selection a challenge for veterinarians (Ginja et al., 2010).

Therapy for DCF combines conservative and surgical methods, varying according to the severity of the condition and the patient's age. Conservative strategies involve the use of anti-inflammatory medications, physical exercise, and weight control. On the other hand, surgical interventions involve procedures such as triple pelvic osteotomy, intertrochanteric osteotomy, hip arthroplasty, or colocephalectomy (Schachner; Lopez, 2015). However, even with the alternatives available, there is no universally accepted "gold" standard, and the search for more efficient and less invasive alternative therapies persists as an important topic in veterinary research.

In recent years, cell therapy, focused on the use of mesenchymal stem cells (MSC), has emerged as a promising strategy for the treatment of degenerative joint diseases, such as DCF. Stem cells have the ability to repair injured cartilage and reduce inflammation, in addition to having immunomodulatory properties that can aid in the functional recovery of damaged joints (Whitworth; Banks, 2014; Black et al., 2007). MSCs can be obtained from various sources, such as bone marrow and adipose tissue, presenting excellent results in tissue regeneration in experimental and clinical models (Volk; Theoret, 2013).

In addition to stem cells, platelet-rich plasma (PRP), which contains a high concentration of growth factors, has been used to promote tissue regeneration and accelerate postoperative recovery. PRP has been shown to be effective in reducing pain and improving the healing of damaged tissues in a variety of contexts, including veterinary orthopedic treatments (Vilar et al., 2014). When combined with mesenchymal stem cells, PRP has the ability to intensify regenerative effects, favoring a more agile

and efficient recovery in dogs that have undergone surgery to treat DCF (Marx et al., 2014).

The application of regenerative therapies in the management of DCF has shown promising results, however, greater standardization of treatment protocols is still needed, as well as long-term studies that allow a better understanding of the long-term effects and efficacy of these approaches. This study aims to discuss the potential benefits of mesenchymal stem cells and PRP in the postoperative treatment of dogs with DCF, based on recent clinical studies, and to explore how these therapies can complement or even replace traditional approaches in managing this debilitating condition.

METHODOLOGY

To carry out this study, a systematic literature review of scientific articles, dissertations and relevant publications on the use of regenerative therapies, such as mesenchymal stem cells and platelet-rich plasma in the postoperative treatment of dogs with DCF, was conducted. The search for sources was carried out in the scientific databases PubMed, Google Scholar and Scopus, with emphasis on publications from the last 20 years, in order to gather the most current studies on the subject. The inclusion criteria were: clinical articles, case studies, systematic reviews and clinical trials that discuss the effects of regenerative therapies in dogs with DCF. The data collected were analyzed to identify the main findings on the efficacy of MSC and PRP, the protocols used, the post-treatment results, and the limitations of these treatments. The studies were evaluated based on the methodological quality and relevance of the results presented.

RESULTS AND DISCUSSION

The use of regenerative therapies, such as MSC and PRP, in the treatment of dogs with hip dysplasia has shown significant results in pain relief, improvement in joint functionality and postoperative recovery. However, the effects of these therapies can vary depending on the stage of the disease, the technique applied, and the individual response of the animals.

EFFECTS OF STEM CELLS IN THE TREATMENT OF HIP DYSPLASIA

MSCs have been widely investigated and used in regenerative therapies due to their ability to differentiate into various cell types, such as cartilage, bone and muscle. With regard to DCF, MSC therapy has shown notable advantages in the recovery of damaged articular cartilage, in addition to reducing inflammation and favoring the recovery of affected tissues (Whitworth; Banks, 2014).

Several studies, such as those conducted by Black et al. (2007) and Vilar et al. (2014), showed that the intra-articular implementation of MSC can lead to a notable improvement in clinical parameters, such as decreased claudication and increased range of motion. This happens because of the ability of MSCs to transform into cartilage cells, contributing to the recovery of joint integrity and reducing stress on injured joints.

In the research conducted at the Veterinary Hospital of the Federal Rural University of Pernambuco (HV-UFRPE), it was observed that dogs with DCT treated with adipose-derived stem cells (AD-CTM) had a remarkable clinical evolution. Mobility analysis indicated a decrease in lameness rates at days 60 and 90 after stem cell injection. Significant improvement in pain parameters and functional capacity was also observed, with dogs demonstrating a greater willingness to walk and run after treatment. These findings are in line with those of other researchers, such as Whitworth and Banks (2014), who underscore the ability of MSCs to relieve pain and regain joint function in dogs with osteoarthritis and other degenerative joint conditions.

In addition to the results already mentioned, more recent studies reinforce the potential of mesenchymal stem cells (MSC) in the treatment of DCF. Pinna et al. (2022) demonstrated that the intra-articular application of MSCs derived from adipose tissue, in combination with PRP, promoted significant improvement in joint function and pain reduction in treated dogs. Ferris et al. (2023) also reported the reduction of inflammatory mediators in the synovial fluid of these animals, suggesting a relevant immunomodulatory effect. Another important factor observed by Lopes et al. (2021) was the greater viability and clinical efficacy of MSCs of adipose origin compared to those derived from bone marrow, pointing to a trend in the use of this cellular source.

However, it is important to highlight that the efficacy of MSCs can be influenced by the severity of the disease. In early and moderate stages of DCF, stem cell therapy has shown faster and more significant results. In the more advanced stages, such as in cases of severe osteoarthritis, cartilage regeneration may be more limited, and the

response to treatment may be slower. These findings reinforce the need for a careful evaluation of the stage of the disease before opting for MSC therapy (Vilar et al., 2014; Whitworth & Banks, 2014).

COMBINING PRP AND STEM CELL THERAPY

The combination of MSC and PRP is a promising strategy to treat DCF, as both contain growth factors that can enhance tissue regeneration and accelerate the recovery process. PRP stimulates collagen creation and joint cell regeneration, as well as decreasing inflammation and enhancing the recovery of injured tissues. When associated with MSCs, PRP has the ability to generate a synergistic effect, accelerating joint recovery and favoring faster relief from inflammation (Volk; Theoret, 2013).

In a study conducted by Vilar et al. (2014), the combination of AD-CTM and PRP showed notable advantages in dogs with severe osteoarthritis in the hip joints. The findings indicated that dogs submitted to the combination of PRP and MSC had a considerable decrease in lameness and an increase in range of motion compared to dogs in the control group. In addition, the combined use of PRP and MSC proved to be efficient in improving joint function, relieving pain and improving the mobility of dogs with DCF. These results corroborate the findings of Marx et al. (2014), which indicate that PRP can be an effective complementary therapy in regenerative treatments, particularly in joint conditions such as DCF (Vilar et al., 2014; Marx et al., 2014).

Additional studies, such as those by Kim et al. (2021) and Harman et al. (2022), reinforce the beneficial effects of the association between MSC and PRP in the management of DCF. The authors highlight the reduction of pain, the improvement of range of motion and the functional recovery of the treated animals. Chandrashekaraiah et al. (2023) also point out that the combination of stem cells with biomaterials, such as scaffoldings, may represent a promising alternative to enhance regenerative effects and improve clinical response in more advanced cases of DCF.

Although the initial results are quite promising, the combination of PRP and MSC still needs more studies to optimize the application protocols and better understand the long-term effects. The variability in the results can be influenced by the PRP preparation technique, the dose, and the form of application of the stem cells, which reinforces the need for standardization in clinical studies to ensure the efficacy and safety of these therapies (Vilar et al., 2014).

CHALLENGES AND LIMITATIONS

Although several studies have shown positive results, there are significant restrictions on the application of regenerative therapies in the treatment of hip dysplasia. The main constraint is the variation in response to treatment, which can be affected by elements such as the age of the animal, the stage of the disease, the method of administration and the origin of the stem cells. Despite the remarkable benefits of stem cell and PRP treatments, total regeneration of articular cartilage is still a challenge, particularly in the more advanced stages of DCF, where significant degenerative changes in the joint are already observed (Rivière et al., 2005; Volz et al., 2018).

In the early and moderate stages of DCF, the effects of regenerative therapies are faster and more visible, however, the response in more advanced stages still needs a deeper understanding. Although promising, cartilage regeneration is restricted by the level of existing joint wear. Research shows that cartilage in more advanced stages of DCF, already severely damaged, does not respond adequately to cellular treatments. This emphasizes the importance of early diagnosis and intervention in the early stages of the disease (Evans et al., 2012; Misumi et al., 2004).

Another critical point is the requirement for more extensive research, with larger samples and clearly established application protocols. Although initial studies point to good treatment results, it is essential to constantly monitor the effectiveness and safety of regenerative therapies. The lack of uniformity in treatment protocols and evaluation methods complicates the comparison of the results of different studies, making it crucial to carry out randomized controlled studies to define precise guidelines for the implementation of these therapies in veterinary clinical practice (Filaro et al., 2016; Whitworth et al., 2017). In addition, the paucity of data on the long-term effects and possible side effects of regenerative therapies implies the need for a cautious and well-planned approach to their clinical implementation.

Although the initial results are encouraging, recent literature reinforces the need for greater standardization of application protocols, including dose, frequency, and method of administration. The lack of uniformity between studies makes it difficult to compare results and define clinical guidelines (Kim et al., 2021; Harman et al., 2022). In addition, the incorporation of biomaterials, although promising, requires further evaluations regarding the safety and efficacy of these combinations (Chandrashekaraiah et al., 2023). It is essential that there is standardization of

treatment protocols and the use of consistent application methods to maximize the results of regenerative therapies. The diversity in treatment responses, added to the lack of consensus on the optimal dose, number of applications, and combined use with other approaches, still prevents these therapies from consolidating themselves as a common option in the treatment of DCF (Fitzpatrick et al., 2014; Fazzio et al., 2019).

FINAL CONSIDERATIONS

The use of regenerative therapies, such as mesenchymal stem cells and platelet-rich plasma, in the treatment of dogs with hip dysplasia, has shown promising results, especially in reducing pain, improving joint functionality, and accelerating postoperative recovery. However, the effectiveness of these therapies may be influenced by the severity of the disease and the stage at which treatment is initiated. While initial results are encouraging, more research is needed to standardize application protocols, better understand long-term effects, and ensure the safety of therapies. The combination of CTM and PRP emerges as a synergistic approach with great potential, but the variability in results and the lack of standardization highlight the need for more randomized controlled trials to establish clear guidelines in veterinary clinical practice.

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