INTERNATIONAL SEVEN JOURNAL
OF MULTIDISCIPLINARY
ISSN: 2764-9547

USE OF STEM CELLS IN THE REHABILITATION OF DOGS WITH HIP DYSPLASIA – A SYSTEMATIC REVIEW

https://doi.org/10.56238/isevmjv4n1-012

Receipt of originals: 01/14/2025 **Acceptance for publication:** 02/14/2025

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ABSTRACT

Objective: To analyze the therapeutic potential of stem cells in the treatment of dogs with hip dysplasia, as well as to compare it with other traditional therapies. Hip dysplasia is a multifactorial disease, common in medium and large breed dogs, characterized by joint incongruence between the acetabulum and the femoral head, resulting in instability and progressive osteoarthritis. Genetic and environmental factors, such as body weight,

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diet, and physical exercise, play a key role in the progression of the disease, and can directly affect the severity of clinical symptoms. Clinical evaluation, along with radiographic examinations and analysis of synovial fluid, are essential for a more accurate diagnosis of joint changes. Conventional therapy mainly involves the use of anti-inflammatories, physiotherapy, and food supplements. In more severe cases, surgical intervention may be necessary to regain joint function. However, in recent decades, stem cell therapy has been gaining prominence, presenting itself as a promising option in the management of hip dysplasia, but it was only regulated in Brazil in 2020. This strategy promotes cartilage recovery and modulation of the inflammatory response, leading to reduced pain and increased mobility in the animals. Traditional treatment is still essential, as stem cell therapy requires standardization and a high cost, which limits its use on a large scale, but its use is promising, although a very significant challenge.

Keywords: Hip Joint. Domestic Dogs. Tissue Regeneration. Cell Therapy. Innovative Treatment.

INTRODUCTION

Hip dysplasia (CDF) is one of the most prevalent orthopedic diseases in veterinary medicine, mainly affecting medium and large-breed dogs. It is a multifactorial condition, marked by a disproportion between the femoral head and the acetabulum, resulting in joint instability and progression of osteoarthritis (Schmaedecke, 2004; Ferrigno *et al*., 2007). Although genetic predisposition is a crucial condition, environmental factors such as diet, body weight, and physical exercise can also significantly affect the progression of the disease (Alexander, 1992; Hedhammar *et al*., 1979).

The symptoms of DCF change according to age and degree of the disease, and may include intermittent or continuous claudication, exercise intolerance, joint pain, and muscle atrophy of the pelvic limbs (Tomlinson; McLaughlin, 1996; Rawson *et al*., 2005). Generally, the diagnosis is based on a combination of physical examination, orthopedic tests, radiographic analysis and, at times, the analysis of the synovial fluid is essential (Benedetti, 2015).

Traditional therapies for DCF encompass clinical management and surgical procedures. Clinical treatment consists of anti-inflammatories, physical therapy, weight control, and supplementation with chondroitin and glucosamine, to reduce pain and slow the progression of osteoarthritis (Cruz *et al*., 2024). In more serious situations, surgical interventions may be recommended, such as arthroplastic excision of the femoral head or total hip replacement (Santana *et al*., 2023).

In recent years, stem cell treatment has stood out as a promising strategy in regenerative veterinary. Research indicates that mesenchymal stem cells have great therapeutic potential, thanks to their ability to differentiate and release growth factors that favor tissue regeneration and the regulation of the inflammatory reaction (Benedetti, 2015). Initial results suggest that the intra-articular use of these cells may aid in cartilage recovery and decrease inflammation, offering a less invasive and potentially more efficient option for the treatment of DCF (Cruz *et al*., 2024).

Given the above, the objective is to analyze the therapeutic potential of stem cells in the treatment of dogs with hip dysplasia, as well as to compare it with other traditional therapies.

METHODOLOGY

A systematic review was carried out, analyzing scientific articles available in PubMed, Virtual Health Library (VHL), and CAPES Journal Portal. Studies published between 1979 and 2024 were included, aiming to understand the progression of understanding about hip dysplasia and its therapeutic strategy over the years.

The literature search used descriptors such as "mesenchymal stem cells", "canine hip dysplasia", "cartilaginous regeneration" and "veterinary cell therapy". Older studies, such as Hedhammar et al. (1979), Alexander (1992), and Tomlinson and McLaughlin (1996), were taken into account to contextualize the pathogenesis of hip dysplasia, its clinical implications, and the conventional treatments employed before the introduction of cell therapies.

In addition, clinical and experimental studies that analyzed the effectiveness of intra-articular use of stem cells for articular cartilage regeneration, pain relief, and functional enhancement of affected dogs were included. Conditions for inclusion included studies that examined indicators such as claudication scores, orthopedic tests, quality of life, synovial fluid assessment, and radiographs.

The analysis also took into account comparative studies between various origins of stem cells, such as those from the yolk sac and dental pulp (Benedetti, 2015), as well as literature reviews that also analyzed the impact of these cells on inflammatory modulation and maintenance of the hip joint (Cruz *et al*., 2024).

To ensure greater accuracy in the evaluation, articles with small sample sizes, isolated case reports without long-term follow-up, and studies that did not contain detailed methodology were discarded. The data obtained were categorized into categories, covering clinical improvements, anti-inflammatory action, cartilage maintenance, and effects on the quality of life of dogs submitted to treatment. In addition, a critical evaluation of the progress of therapies in recent decades was conducted, highlighting the progress brought by cell therapy in conventional treatments documented in previous studies.

RESULTS AND DISCUSSIONS

The studies analyzed demonstrated that stem cell therapy has significant potential for the rehabilitation of dogs with hip dysplasia. Among the main aspects analyzed, improvement in mobility, reduction of pain, radiographic alterations, and

modulation of the inflammatory response are included. Additionally, the effectiveness of this treatment was compared with other strategies, such as physiotherapy, nutritional supplementation, and surgery.

EFFECTS ON MOBILITY AND PAIN REDUCTION

One of the key findings in dogs undergoing stem cell treatment was improved mobility and exercise tolerance. The work of Benedetti (2015) analyzed the reaction to the treatment by comparing two species of stem cells: originating from the yolk sac and the dental pulp. Three intra-articular injections were given to the dogs on days 0, 30, and 60, and the results were analyzed on day 90. Dogs treated with yolk sac stem cells showed a more noticeable improvement in joint function, with a lower rate of lameness and greater stability on the Ortolani test, which measures the flexibility of the hip joint. On the other hand, dogs that received stem cells from dental pulp also showed improvement, although to a lesser extent.

Another relevant study, conducted by Cruz *et al.* (2024), showed that modulation of the inflammatory response by stem cells resulted in a reduction in chronic pain, allowing a decrease in the use of non-steroidal anti-inflammatory drugs (NSAIDs) in treated dogs. This is particularly relevant since continued use of NSAIDs can lead to adverse effects such as gastric and kidney damage. The caregivers of the treated animals noticed a noticeable improvement in the quality of life of the dogs, who were more willing for everyday tasks, less hesitant to climb stairs, and more sociable. These conclusions were corroborated using standardized questionnaires conducted before and after treatment, where pain and mobility indices showed a statistically relevant improvement.

RADIOGRAPHIC AND JOINT STRUCTURE CHANGES

Effects of stem cell treatment in dogs with hip dysplasia were recorded and evaluated by Benedetti (2015) using radiographic examinations, and it was found that those who received stem cells had a slower progression of osteoarthritis compared to the control group. In addition, a decrease in osteophyte formation (abnormal bone growths associated with joint degeneration) and clearer maintenance of joint congruence were observed in dogs that received yolk sac stem cells. These results

indicate that cell treatment can help maintain joint structure and delay the advancement of hip dysplasia.

Another parameter evaluated was synovial fluid, which showed a reduction in inflammatory markers after stem cell therapy. Specifically, decreased levels of tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) revealed a remarkable anti-inflammatory effect, aiding in the reduction of pain and cartilage deterioration (Benedetti, 2015).

COMPARISON TO OTHER THERAPIES

The effectiveness of stem cells has been compared to other established therapeutic approaches, such as physiotherapy, nutritional supplementation, and surgery.

Physiotherapy and Nutritional Supplementation

Physical therapy is commonly used in the conservative treatment of hip dysplasia, with hydrotherapeutic activity, laser therapy, and/or electrostimulation. And according to Cruz *et al.* (2024), indicated that physical therapy combined with stem cell treatment can lead to faster and more efficient functional recovery.

In addition, nutritional supplementation, including chondroitin and glucosamine, is also widely used to support joint health. Research has indicated that these supplements contribute to reducing pain and stiffness in the joints, but do not stimulate tissue regeneration. Comparatively, stem cell treatment showed more prolonged results, since, in addition to reducing inflammation, it can promote the regeneration of articular cartilage (Cruz *et al.*, 2024).

Surgical interventions

In more severe situations of hip dysplasia, surgeries such as arthroplasty excision of the femoral head and complete hip replacement are commonly recommended, but they involve high costs, anesthetic risks, and extensive recovery periods (Santana *et al.*, 2023).

The study by Cruz *et al.* (2024) pointed out that stem cell treatment may be a less invasive option in certain situations, particularly in dogs that still have intact mobility, making it an attractive alternative for some owners.

CHALLENGES AND FUTURE PROSPECTS

Stem cell treatment has very encouraging results, but there are still many obstacles for it to be implemented in the clinic. It is crucial to standardize the procedures for the collection, culture, and application of cells so that the replicability of their results can be ensured. As well as the price of treatment, which represents a limiting factor for many tutors (Benedetti, 2015).

Given this reality, the Federal Council of Veterinary Medicine (CFMV) published Resolution No. 1363/2020, which establishes guidelines for the use of cell therapy in animals. According to this regulation, stem cell therapy must have technical support that ensures its safety and effectiveness, and is performed only by duly qualified veterinarians. The rule also requires the use of equipment and materials duly licensed by the responsible bodies, in addition to obtaining the explicit consent of the animal's owner for the execution of the procedure (CFMV, 2020).

Therefore, future studies on various origins of stem cells and their possible therapeutic applications, as well as the joint use of stem cells with biomaterials or with the use of tissue engineering are essential for the improvement of the technique. And, these long-term studies are important for safety in the evaluation of therapeutic effects and applicability on a large scale (Cruz *et al.,* 2024).

FINAL CONSIDERATIONS

The progress of studies in regenerative veterinary medicine may offer a better quality of life to animals affected by hip dysplasia. Among the revolutionary therapies, the use of stem cells stands out, which have increasingly demonstrated a promising option in the treatment of canine hip dysplasia, with good results in mobility, pain reduction, minimizing the progress of osteoarthritis, and joint inflammatory modulation. Although stem cell treatment presents obstacles in the standardization of protocols and financial viability, it has numerous advantages in the results, which makes it a viable alternative in the future.

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