An evaluation of the effectiveness of Equine allogenic chondrogenic-induced mesenchymal stem cells in treating osteoarthritis

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Abstract

One of the main causes of lameness and failure in equine athletes is joint disease, with Osteoarthritis (OA) accounting for 60% of cases (Baccarin et al., 2022). OA is potentially career-ending and life-threatening, creating significant demand from equestrian athletes and owners for research into effective treatments to prolong performance. As there is no cure for OA, a multimodal treatment approach is recommended.

This study investigates regenerative medicine as a viable treatment for equine osteoarthritis, aiming to extend high-performance careers and improve overall equine health. A secondary SWiM analysis of two studies compared AAEP lameness scores between MSC-treated and control horses. Hedges' g was applied to evaluate the magnitude of MSC therapy effectiveness in reducing lameness.
Results showed a mean AAEP score reduction of 1.3 points in Study 1 and 3.2 points in Study 2, indicating clinically meaningful improvements (Hedges' g 6.34–6.54). These findings suggest MSCs may significantly reduce lameness and support prolonged athletic careers. However, further research with larger sample sizes is needed to validate these promising results.

Introduction

Osteoarthritis (OA) is the progressive destruction of articular cartilage with associated changes in bone and soft tissues, leading to pain, reduced mobility, and lameness in performance horses. Cartilage consists of chondrocytes and an extracellular matrix (ECM) composed of collagens, proteoglycans, and structural proteins that maintain joint integrity (Baccarin et al., 2022). Pathogenesis begins with injury or pathology in cartilage, subchondral bone, or soft tissues, leading to synovitis, capsulitis, and progressive degradation (McIlwraith et al., 2016).

Current treatments, including NaPPS, NSAIDs, and supplements such as 4CYTE™, focus on symptom relief and slowing degeneration but do not reverse cartilage damage. NaPPS has shown disease-modifying properties, while MSC therapy has demonstrated greater potential by promoting cartilage regeneration and modulating inflammation, reducing AAEP lameness scores by 1–3 points (Longhini et al., 2019).

Mesenchymal stem cells (MSCs) are stromal cells capable of self-renewal and multilineage differentiation, commonly derived from bone marrow or blood. They are administered intra-articularly, migrating to damaged sites to support repair through paracrine effects, including immunomodulation, anti-apoptosis, angiogenesis, and anti-scarring (da Silva Meirelles et al., 2009b; Harman et al., 2021).

Clinical outcomes vary due to small sample sizes, MSC source, and inconsistent protocols, highlighting the need for standardised approaches and long-term studies. Lameness, a key clinical sign of OA, is used as the primary outcome measure to evaluate MSC therapy effectiveness.

Figure 1 Fetlock joint.

Grade	Criteria
0	Lameness not perceptible under any circumstances
1	Lameness that is difficult to observe and is not consistently apparent, regardless of circumstances
2	Lameness that is difficult to observe at a walk or when trotting in a straight line, but consistently apparent under certain circumstances
3	Lameness is consistently observable at a trot under all circumstances
4	Lameness is obvious at a walk

Figure 2. AAEP lameness scale.

Methods and Materials

This study was conducted as a secondary review of literature analysing the effects of mesenchymal stem cell (MSC) therapy on equine osteoarthritis (OA). A systematic PubMed search ('equine' AND 'mesenchymal stem cells' AND ('degenerative joint disease' OR 'osteoarthritis')) identified 95 studies. Screening followed PRISMA guidelines, with irrelevant studies excluded, duplicates removed, and only clinical trials retained. Inclusion criteria required primary lameness data, randomized blinded designs, and adherence to ethical standards. Two studies met all criteria.

AAEP lameness scores were extracted into Excel, with means and standard deviations recorded from tables or estimated from figures. Effect sizes were calculated using Cohen's d and converted to Hedges' g to account for small sample sizes. Variance, standard error, and 95% confidence intervals were computed. Due to the small number of studies (k = 2), narrative synthesis following SWiM guidelines and sensitivity analysis (leave-one-out and ±0.2 AAEP adjustment) assessed robustness and reliability.

Results

Both studies investigated the effect of MSC therapy on AAEP lameness scores in horses with fetlock OA. Study 1 included 75 horses (50 IVP, 25 CTRL) over 18 weeks. Mean improvement was 1.8 (IVP) versus 0.44 (CTRL), producing a large Hedges' g value (6.34) with a CI of 5.21–7.46, indicating high precision and low variability (0.33). Study 2 involved 12 horses (6 IVP, 6 CTRL) over 6 weeks. Mean improvement was 2.2 (IVP) versus –1.33 (CTRL), resulting in a Hedges' g of 6.54 with a CI of 3.69–9.38, indicating lower precision and higher variability (2.1).

Pooled results showed a large effect in favour of MSC therapy. Sensitivity analysis confirmed robustness across several checks. Leave-one-out re-pooling demonstrated that removing either study still resulted in a very large pooled effect, confirming findings were not dependent on a single dataset. Extraction uncertainty analysis adjusted AAEP means by ±0.2 points to account for possible digitisation errors; the effect size decreased slightly under conservative assumptions but remained large, with 95% CI excluding zero. Under optimistic adjustments, effect size increased further. Sensitivity analysis therefore showed that conclusions were consistent across different analytical scenarios and resistant to small variations in data extraction.
MSC therapy demonstrated a significant positive impact on AAEP lameness scores; however, unusually high effect sizes, small samples, and potential conflicts of interest indicate caution in interpretation.

Excluded	Pooled g	SE	95% CI low	95% CI high
Study 1	6.595211	1.583722	3.491117	9.699305
Study 2	6.337488	0.578873	5.202897	7.47208

(figure 5, table displaying re-pooling effects)

Scenario	Pooled g	SE	95% CI low	95% CI high
Baseline	6.368	0.544	5.302	7.433
Conservative (IVP -0.2; CTRL +0.2)	4.594	0.424	3.763	5.425
Optimistic (IVP +0.2; CTRL -0.2)	8.075	0.667	6.769	9.382

(figure 6, table displaying sensitivity scenarios.)

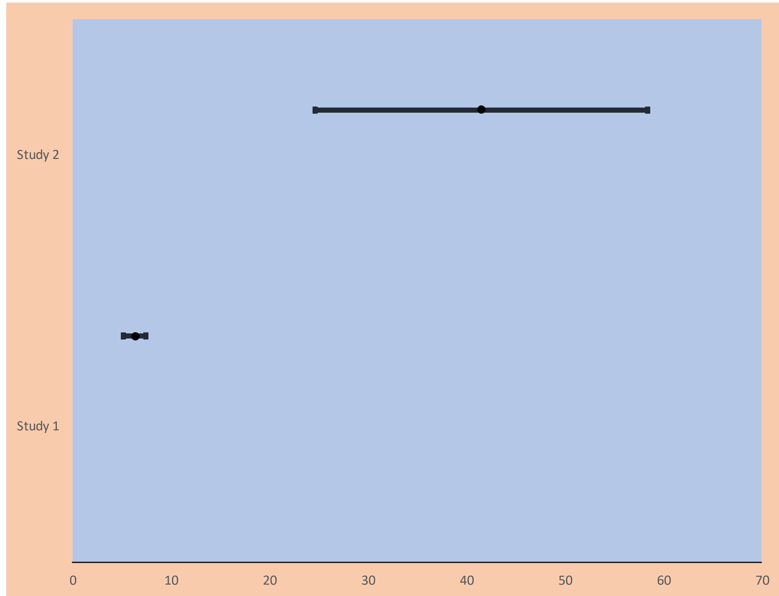

Chart 1. Forest plot displaying hedges g value and CI values for each study

Quantitative synthesis

Study ID	Time (weeks)	Outcome	Mean change (MSC)	SD change (MSC)	n MSC	Mean change (CTRL)	SD change (CTRL)	n CTRL
Study 1	18	AAEP	1.8	0.24	50	0.44	-0.14	25
Study 2		AAEP	2.2	0.69	6	1.33	-0.11	6

Study ID	SD_ Pooled	d (cohens d)	J (hedges correlation factor)	Hedge's g	Variance of hedges g	Standard error of hedges g	CI low	CI high
Study 1	0.212383731	6.40350366	0.98969072	6.33748816	0.32822068	0.57290547	5.21459344	7.46038287
Study 2	0.494064773	7.08409138	0.92307692	6.53916127	2.10577833	1.45113002	3.69494644	9.38337611

(figure 3, table displaying meta data)

Discussion

The use of mesenchymal stem cells (MSC) in treating equine osteoarthritis showed greater efficacy than saline controls, supporting the study hypothesis. Effectiveness was quantified using Hedges' g, selected over Cohen's d due to small sample sizes, providing less biased estimates and enabling comparison across studies. A SWiM approach was adopted due to limited studies (k = 2) and design differences, using effect sizes, confidence intervals, and a forest plot for structured narrative synthesis.

Hedges' g values were exceptionally large (6.34; 6.54), with Study 1 demonstrating greater precision (CI 5.21–7.46) than Study 2 (CI 3.69–9.38), which had wider intervals due to its smaller cohort. Reliability is weakened by small sample sizes, short follow-up, and methodological inconsistencies. Potential bias from industry funding may have inflated effect sizes. Despite strong therapeutic indications, limitations in design, reproducibility, and generalisability highlight the need for larger, standardised, and independent trials.

Conclusions

The secondary review supports initial findings that mesenchymal stem cell (MSC) therapy may be an effective treatment for improving AAEP lameness scores in horses with osteoarthritis (OA) in the fetlock joint, confirming the research question. Study 1 showed a mean reduction of 1.3 points and Study 2 showed 3.2 points, indicating clinically meaningful improvements in joint function and pain. These results suggest MSC therapy holds therapeutic potential for equine joint rehabilitation and return to work. However, small sample sizes, short follow-up periods, and procedural risks highlight the need for caution and further investigation. Future research should focus on larger, blinded, multi-centre trials with standardised outcome measures, extended follow-up, and cost-effectiveness analysis to ensure broader accessibility. Despite limitations, findings are relevant to the equine community and suggest MSC therapy may significantly reduce lameness and prolong horse careers when applied under controlled clinical conditions.

Contact

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