





The Knee

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Review

The efficacy of intra-articular injections in the treatment of knee osteoarthritis: A network meta-analysis of randomized controlled trials

Utkarsh Anil, Danielle H. Markus  , Eoghan T. Hurley, Amit K. Manjunath, Michael J. Alaia, Kirk A. Campbell, Laith M. Jazrawi, Eric J. Strauss

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Abstract

Purpose

Osteoarthritis (OA) is a debilitating joint disease characterized by progressive loss of articular cartilage. Intra-articular injections are a mainstay of nonoperative treatment, however, there is controversy as to the optimal injectable for these patients. The purpose of the current study is to perform a network meta-analysis of the randomized control trials in the literature to ascertain whether there is a superior injectable nonoperative treatment for knee OA.

Methods

The literature search was conducted based on the PRISMA guidelines. Randomized control trials (RCTs) evaluating intra-articular injectables in osteoarthritic knees were included. Data was extracted and Visual Analogue Scale (VAS) scores and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores, where available were analyzed at 1, 3, 6 and 12 months. Clinical outcomes were compared using a frequentist approach to network meta-analysis, with statistical analysis performed using R. The treatment options were ranked using the P-Score.

Results

Seventy-nine RCTs with 8761 patients were included in this review. Intra-articular injectables evaluated included autologous conditioned serum (ACS), bone marrow aspirate concentrate (BMAC), botulinum toxin, corticosteroids (CS), hyaluronic acid (HA), mesenchymal stem cells (MSC), ozone, saline placebo, platelet-rich plasma (PRP), plasma rich in growth factor (PRGF), and stromal vascular fraction (SVF). At 4–6 weeks

and 3 months of follow-up, the treatment with the highest P-Score for WOMAC score was high molecular weight (HMW) HA+CS [P-Score=0.9500 and 8503, respectively]. At 6-months follow-up, the treatment with the highest P-Score for WOMAC score was PRP [P-Score=0.7676]. At all post-injection time points, the treatment with the highest P-Score for VAS score [P-Score Range=0.8631–9927] and Womac score at 12 Months [P-Score=0.9044] was SVF.

Conclusions

The current evidence shows that SVF injections result in the greatest improvement in pain and functional outcomes in patients with knee OA at up to 1 year of follow-up.

Introduction

Osteoarthritis (OA) is a debilitating joint disease affecting 30 million people in the United State alone, imparting substantial morbidity including disability, reduction in quality of life, and financial burden [1], [2]. The knee is the most common site of OA, comprising 80% of the case load globally [3]. Orthopedic surgeons have consequently sought to refine current treatment paradigms in order to improve patient outcomes. Intra-articular (IA) injections remain a central component in nonoperative treatment modalities for OA, as they present a low risk of harm while providing short-term pain reduction and improved joint function [4], [5], [6], [7].

Several types of IA injections exist, including corticosteroids (CS), platelet rich plasma (PRP), hyaluronic acid (HA), botulinum toxin type A, autologous conditioned serum (ACS), and stromal vascular fraction (SVF). However, discerning the optimal management for symptomatic OA remains a challenge despite a vast amount of literature on the topic [8], [9]. Existing studies are heterogenous, comparing different combinations of treatment modalities at varying time points, which can at times conclude in conflicting results. Furthermore, a recent network meta-analysis [10] pooled varying subtypes of PRP/HA injections with dissimilar biological properties, which may impact the outcomes reported and thus lead to inaccurate results. Additionally, other network meta-analyses exist but have limited their scope to only PRP, HA and CS, failing to include other available therapies.

The purpose of the current study is to perform a network meta-analysis of the randomized control trials in the literature to ascertain whether there is a superior injectable nonoperative treatment for knee OA. Our hypothesis was that orthobiologic therapies would prove superior to other intra-articular injectables in the treatment of knee OA.

Section snippets

Study selection

Two independent reviewers performed the literature search based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [11]. The search results were reviewed, and if any discrepancies existed, a third author reconciliated. All search results were evaluated by title and abstract, and any studies potentially included were then reviewed in full. Additionally, references of all included studies were then screen manually for any additional articles that may...

Literature search

The initial literature search resulted in 5594 total studies. Once duplicates were removed and articles were screened by title and abstract, 177 studies were included, and full texts were assessed for eligibility. Ultimately, 79 studies with 8761 patients met inclusion and exclusion criteria (Figure 1)....

Patient demographics

There were 79 RCTs with a total of 8,761 patients. The mean age of included patients was 61.1, the majority of patients were female (64.4%), and the follow-up ranged from 4-weeks to 24-months....

Discussion

The most important finding of this study was that SVF resulted in the highest P-Score for VAS score at all time points, indicating that this had the greatest effect on pain post-injection at all time points. Furthermore, SVF had the highest WOMAC score at 12-months post-injection indicating that these patients also had the highest functional outcome scores following treatment. However, it is still worth noting that the majority of intra-articular injections had higher P-Scores than the saline...

Limitations

As a systematic review, a major limiting factor is the lack of available data between the included studies. Similarly, discrepancies exist in reported outcome measures as follow-up was obtained at various points during the post-operative period. In the included pooled analyses, the standardization of reporting limited our analysis. Thus, some intra-articular injections could not be added to comparisons at certain time points. However, we mitigated the heterogeneity by including random effects...

Conclusion

The current evidence shows that SVF injections result in the greatest improvement in pain and functional outcomes in patients with knee OA at up to 1-year follow-up....

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper....

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...Dual therapy demonstrated improved WOMAC functional scores and VAS pain scores compared to PRP alone.³¹ Network meta-analysis by Anil et al., also showed combination injections of high molecular weight HA with PRP, both leukocyte rich and leukocyte poor, demonstrated repeated benefits compared to single therapy and control for up to 12 months.¹⁴ Other modalities such as cell-based therapies have been used in many fields within orthopaedic surgery such as spinal fusions and nonunion surgeries....

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