

# Efficacy of Intra-articular Mesenchymal Stem Cell Injections Compared to Intra-articular Corticosteroids in Pain Control for Osteoarthritis of the Knee



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## Abstract

Many adults suffering with knee pain due to osteoarthritis (OA) rely on intra-articular corticosteroids for pain management. Mesenchymal Stem Cells (MSC) intra-articular injections have emerged as an alternative treatment that may have less side effects and may alter disease progression. This review of literature seeks to compare efficacy of pain control of MSC injections compared to standard of care. More research is required however intra-articular MSC injections show statistically significant reductions in pain similar to corticosteroid injections.

## Introduction

### Overview:

- Chronic degenerative condition due to loss of articular cartilage
- Risk Factors: genetics, female sex, obesity, joint injury
- Pain, stiffness, loss of function → decreased mobility
- In the USA 30.8 million adults are affected by OA
  - by 2013 knee OA = \$27 billion in annual health care expenditure

### Treatments:

- first line: exercise, weight loss, NSAIDs
- intra-articular corticosteroid injections may be used for short term pain control
  - many patients eventually require knee arthroplasty
- MSC intra-articular injections are being investigated as alternative
  - may reduce pain and regenerate structure

## Methods

A literature search was conducted through PubMed, Clinical Key, and Google Scholar in October 2018 through April 2020. Eight articles consisting of randomized controlled trials were selected based on their relevance to research question, publication dates, interventions, and outcome measurements.

### ➤ Exclusion Criteria:

- Systematic reviews or meta-analysis
- Trials performed on animals
- Trials performed on joints other than the knee
- Studies investigating alternative interventions
- Studies investigating conditions other than OA
  - ACL tear, Rheumatoid Arthritis

## Results

1. Emadedin M, Labibzadeh N, et al. (2018)
  - RCT of 43 participants designed to compare single injection of autologous bone-marrow derived MSC to saline placebo to treat knee OA, follow up over 6 months
2. Song Y, Du H, Dai C, et al. (2018)
  - RCT of 18 participants designed to compare low, mid range, and high doses of human adipose derived MSC for OA of the knee with two injections and long term follow up to 96 weeks
3. Vega A, Martin-Ferrero MA, Del Canto F, et al. (2015)
  - RCT of 30 participants comparing allogeneic bone marrow MSC injection to hyaluronic acid (placebo) with injection on day 1 and follow up to 12 months
4. Khalifeh SS, Forogh B, Ahmadbeigi N, et al. (2018)
  - RCT of 20 participants designed to compare intra-articular injections of allogeneic placental MSCs with saline (placebo) with one injection and follow up to 24 weeks
5. Freitag J, Bates D, Wickham J, et al. (2019)
  - RCT of 30 participants comparing autologous adipose derived MSC injections for knee OA with conservative treatment using two injections at day one and six months with follow up through 12 months
6. McAlindon TE, LaValley MP, Harvey WF, et al. (2017)
  - RCT of 140 participants designed to compare triamcinolone injection and placebo every 12 weeks for two years to evaluate pain and cartilage volume in patients with knee OA, follow up to 27 months
7. Bodick N, Lufkin J, Willwerth C, et al (2015)
  - RCT of 228 participants comparing extended-release triamcinolone acetate with immediate release with injection on day 1 and follow up to 85 days
8. Shrestha R, Shrestha R, Thapa S, et al. (2018)
  - RCT of 117 participants investigating intra-articular triamcinolone injections compared to saline (placebo) for knee OA in a community setting

Study	WOMAC	KOOS	Pain Rating	Quality of Life	Function Tests	Cartilage change on MRI
1 (MSC)	SS	NA	NS	NA	SS	NA
2 (MSC)	SS	NA	SS	SS	NA	SS
3 (MSC)	SS	NA	SS	NS	SS	SS
4 (MSC)	NA	SS	NS	NA	SS	SS
5 (MSC)	SS	SS	SS	SS	NA	SS
6 (CS)	NS	NA	NS	NA	NS	SS
7 (CS)	SS	NA	SS	NA	NA	NA
8 (CS)	SS	SS	SS	NA	NA	NA

WOMAC = Western Ontario and McMaster Osteoarthritis Index; KOOS = knee osteoarthritis outcomes score; MSC = mesenchymal stem cells; CS = corticosteroids; SS = statistically significant; NS = not significant; NA = not applicable

## Discussion

**Both MSC and Corticosteroids showed statistically significant improvements in pain in most of the studies, suggesting that MSCs may be as efficacious at controlling pain.**

### Strengths:

- Corticosteroid sample sizes sufficient
- All RCT + adequate blinding → mitigation of bias/confounders
- Similar age ranges and KL grades
- Consistent corticosteroid dose across studies
- most studies use saline as placebo
- p value across studies was <0.05
- most studies utilized WOMAC and/or KOOS, pain rating scales

### Limitations:

- MSC sample sizes too small
- inconsistency in dose and source of MSCs across studies
- inconsistent treatment regimen and follow up
- no direct comparison of corticosteroids and MSC injections

### Future Research:

- Larger sample sizes of MSCs
- Determine optimal dosing and source of MSCs
- long term studies utilizing multiple injections, longer follow up
- direct comparison on MSC and corticosteroids

## Conclusion

The results of the study indicate that intra-articular MSC injections have the potential to become a widely utilized treatment for knee OA, similar to how corticosteroids are used today. An additional benefit is that they may reverse the disease process as seen by articular cartilage regeneration on MRI. More research is necessary.

At this time MSC injections may be an option for people with allergies to corticosteroids, or those with pain refractory to steroids. It also may be worth exploring for those who are not candidates for knee replacement surgery. Important factors to consider are availability and cost.

Overall this review shows that the novel treatment has merit, but in order to answer the question posed a direct comparison of MSC injections and corticosteroid injections in patients with knee OA is required.

## Reference List

1. Emadedin M, Labibzadeh N, et al. Intra-articular implantation of autologous bone-marrow derived mesenchymal stromal cells to treat knee osteoarthritis: a randomized, triple-blind, placebo-controlled phase ½ clinical trial. *Cytotherapy*. 2018; 20(10):1238-1246
2. Song Y, Du H, Dai C, et al. Human adipose-derived mesenchymal stem cells for osteoarthritis: a pilot study with long term follow up and repeated injections. *Regen Med*. 2018; 13(3):295-307. doi:10.2217/rme-2017-0152
3. Vega A, Martin-Ferrero MA, Del Canto F, et al. Treatment of knee osteoarthritis with allogeneic bone marrow mesenchymal stem cells: a randomized controlled trial. *Transplantation*. 2015; 99(8); 1681-90.
4. Khalifeh SS, Forogh B, Ahmadbeigi N, et al. Safety and efficacy of allogenic placental mesenchymal stem cells for treating knee osteoarthritis: a pilot study [published online ahead of print December 3, 2018]. *Cytotherapy*. Doi: 10.1016/j.jcyt.2018.11.003
5. Freitag J, Bates D, Wickham J, et al. Adipose-derived mesenchymal stem cell therapy in the treatment of knee osteoarthritis: a randomized controlled trial [published online ahead of print February 14, 2019]. *Regenerative Medicine*. DOI: 10.2217/rme-2018-0161
6. McAlindon TE, LaValley MP, Harvey WF, et al. Effect of intra-articular triamcinolone vs saline on knee cartilage volume and pain in patients with knee osteoarthritis: a randomized clinical trial. *JAMA*. 2017; 317(19):1967-1975. doi:10.1001/jama.2017.5283.
7. Bodick N, Lufkin J, Willwerth C, et al. An intra-articular, extended-release formulation of triamcinolone acetone prolongs and amplifies analgesic effect in patient with osteoarthritis of the knee: a randomized clinical trial. *JBJS*. 2015; 97(11): 877-888. doi:10.2106/JBJS.N.00918
8. Shrestha R, Shrestha R, Thapa S, et al. Clinical outcome following intra-articular triamcinolone injection in osteoarthritic knee at the community: a randomized double blind placebo controlled trial. *Kathmandu Univ Med J*. 2018; 62(2):175-80.