The Effectiveness and Safety of Intra-Articular Injection Using Collagen in Knee Osteoarthritis: Systematic Review

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OBJECTIVES

Knee osteoarthritis (KOA) is a chronic disease that causes pain and worsens not only articular function, but also the patient's quality of life (QoL). Collagen for intra-articular injection, such as atelocollagen and polymerized collagen, features low immunogenicity. Previous studies reported that it could help improve symptoms of KOA. The aim of this systematic review was to evaluate the effectiveness and safety of intra-articular injection using collagen in KOA with Kellgren-Lawrence grade 1-3.

METHODS

We searched Ovid-MEDLINE, Ovid-EMBASE, Cochrane library and five Korean databases on 26 November 2020. The risk of bias was assessed by Scottish Intercollegiate Guidelines Network methodology checklist.

PICO

- **Patient**: Knee osteoarthritis (Kellgren-Lawrence grade 1-3)
- **Intervention**: Intra-articular injection using collagen
- **Comparators**
  - Intra-articular injection using Hyaluronic Acid
  - Intra-articular injection using Steroid
  - Intra-articular injection using Sodium Polynucleotide
  - Sham control
- **Outcomes**
  - Procedure-related adverse events
  - Improvement of knee articular or physical function
  - Patient satisfaction and quality of life

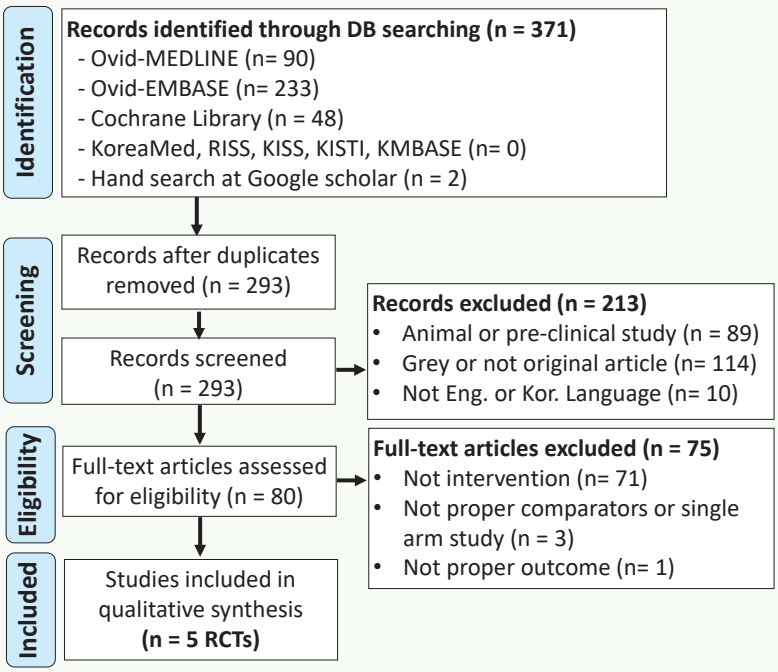

Fig. PRISMA Flow Diagram

RESULTS

Of the total 373 articles retrieved, 5 RCT studies were selected. Two articles were compared with hyaluronic acid (HA) and three were compared with sham control.
There was no significant difference observed between the collagen and hyaluronic acid groups in terms of the degree of pain improvement measured by VAS and the usage of analgesics. Articular function, assessed by Lequesne knee index (LKI) and international knee documentation committee (IKDC), showed no significant differences in both groups.
Three studies compared collagen with sham control using polyvinyl-pyrrolidone (PVP) or normal saline. In two out of the three studies, significant reductions in pain and improvements in articular function were reported in the collagen group compared to the PVP group.
Among the five articles reporting QoL and patient satisfaction, one study reported significantly higher satisfaction with collagen compared to normal saline, and two studies reported more positive results with collagen than PVP. All studies reported pain lasting less than 24 hours and only mild adverse events.

CONCLUSIONS

The evidence showed that intra-articular injection using collagen is safe and effective for relieving pain and improving articular function in KOA. The New Health Technology Assessment Committee determined intra-articular injection using collagen in KOA with Kellgren-Lawrence grade 1-3 to a safe and effective technique, and announced through the Korean Ministry of Health and Welfare bulletin No. 2021-115 (12 April 2021).

Selected Studies

1. Lee HS, Oh KJ, Moon YW, In Y, Lee HJ, Kwon SY. Intra-articular Injection of Type I Atelocollagen to Alleviate Knee Pain: a Double-Blind, Randomized Controlled Trial. Cartilage. 2019:1-9.
2. Martin Martin LS, Massafra U, Bizzi E, Migliore A. A double blind randomized active-controlled clinical trial on the intra-articular use of Md-Knee versus sodium hyaluronate in patients with knee osteoarthritis ("Joint"). BMC Musculoskelet Disord. 2016;17(94):1-8.
3. Arteaga-Solis JR, Negrete-Corona J, Chavez-Hinojosa E, Diaz-Martinez B. [Effectiveness of two intraarticular drugs in patients with knee arthrosis. Polymerized collagen versus hylan]. Acta Ortop Mex. 2014;28(3):164-7.
4. Furuzawa-Carballeda J, Lima G, Llorente L, Nunez-Alvarez C, Ruiz-Ordaz BH, Echevarria-Zuno S, et al. Polymerized-type I collagen downregulates inflammation and improves clinical outcomes in patients with symptomatic knee osteoarthritis following arthroscopic lavage: A randomized, double-blind, and placebo-controlled clinical trial. Scientific World Journal. 2012:1-11.
5. Furuzawa-Carballeda J, Munoz-Chable OA, Maclas-Hernandez SI, Agualimpia-Janning A. Effect of polymerized-type i collagen in knee osteoarthritis. II. in vivo study. Eur J Clin Invest. 2009;39(7):598-606.

This study was supported by the National Evidence-based Healthcare Collaborating Agency (NECA), New Health Technology Assessment Committee and the Korean Ministry of Health and Welfare (HTA-2021-24).

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