

An Observational Prospective Study Of Long-Term Effects Of Intra-Articular Injection Of Il-1 Ra(Interleukin-1 Receptor Antagonist) Autologous Conditioned Serum In Patients With Early Primary Osteoarthritis Of Knee.

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Abstract

Background: Osteoarthritis (OA) of the knee is a common degenerative joint disorder associated with pain, stiffness, and progressive functional limitation. Interleukin-1 (IL-1) plays an important role in the inflammatory and catabolic processes involved in osteoarthritis. Autologous conditioned serum (ACS), enriched with interleukin-1 receptor antagonist (IL-1Ra), has been proposed as a biological treatment aimed at reducing IL-1-mediated inflammation and improving clinical symptoms.

Aim: To evaluate the long-term clinical outcomes of intra-articular injection of interleukin-1 receptor antagonist-enriched autologous conditioned serum in patients with early primary osteoarthritis of the knee.

Methods: This prospective observational study was conducted in the Department of Orthopaedics, Noble Hospital, Pune, from December 2022 to December 2025. Thirty consecutive patients with early primary knee osteoarthritis (Kellgren-Lawrence grade 1 or 2) were included. All patients received a single intra-articular injection of IL-1Ra-enriched autologous conditioned serum through a superolateral approach. Clinical outcomes were assessed using the Visual Analogue Scale (VAS) for pain and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at baseline, 1 week, 4 weeks, 6 months, and 12 months following injection.

Results: The study included 30 patients with a mean age of 58.4 ± 6.7 years; 23 (76.7%) were female and 7 (23.3%) were male. Eleven patients (36.7%) had Kellgren-Lawrence grade 1 and 19 (63.3%) had grade 2 osteoarthritis. The mean VAS score decreased from 6.50 ± 0.63 at baseline to 2.08 ± 0.93 at 1 week, 2.52 ± 1.13 at 4 weeks, 2.97 ± 1.33 at 6 months, and 3.80 ± 1.51 at 12 months. The mean WOMAC score decreased from 70.13 ± 6.00 at baseline to 24.54 ± 2.10 at 1 week, 31.75 ± 7.33 at 4 weeks, 36.99 ± 10.31 at 6 months, and 48.34 ± 7.20 at 12 months. The thesis reported statistically

significant improvement in both VAS and WOMAC scores throughout follow-up ($p < 0.01$). At 12 months, improvement from baseline was 29.3% for VAS and 33.8% for WOMAC. Two patients (6.7%) developed swelling and two (6.7%) reported local-site pain; no complications were recorded in 26 patients (86.7%).

Conclusion: A single intra-articular injection of IL-1Ra-enriched autologous conditioned serum was associated with improvement in pain and functional outcome measures over 12 months in patients with early primary knee osteoarthritis. The greatest improvement was observed during the early follow-up period, with beneficial effects persisting at 12 months. These findings support further controlled studies with larger sample sizes and appropriate comparative designs to establish the clinical efficacy and long-term role of autologous conditioned serum in early knee osteoarthritis.

Keywords: Knee osteoarthritis; Autologous conditioned serum; Interleukin-1 receptor antagonist; IL-1Ra; Intra-articular injection; VAS; WOMAC

1. Introduction

Knee osteoarthritis is a common chronic disorder characterized by pain, impaired function, cartilage loss, subchondral bone remodeling, osteophyte formation, and synovial inflammation. It is associated with considerable individual and societal burden because of its chronic course and progressive limitation of activity [1–5].

Early osteoarthritis has attracted increasing attention because identification and treatment at an earlier stage may provide an opportunity to improve symptoms before advanced structural changes develop [2]. Conventional management includes pharmacological and non-pharmacological measures, but long-term symptomatic treatment may be limited by adverse effects and does not necessarily address the inflammatory pathways involved in disease progression [5].

Interleukin-1 is one of the inflammatory mediators implicated in cartilage catabolism. IL-1 signaling can stimulate matrix-degrading enzymes and other inflammatory mediators while reducing synthesis of cartilage matrix components. Interleukin-1 receptor antagonist (IL-1Ra) is an endogenous inhibitor of IL-1 signaling [5,6].

Autologous conditioned serum is prepared from the patient's own blood under conditions intended to increase anti-inflammatory mediators, including IL-1Ra, and has consequently been investigated as an orthobiologic treatment for symptomatic knee osteoarthritis. Experimental and clinical studies have reported improvements in pain and function following ACS or IL-1-targeted treatment [7–12]. More recent systematic reviews have reported potential symptomatic benefits while emphasizing heterogeneity and limitations in the available evidence [13,14].

The present hospital-based prospective observational study was undertaken to observe the long-term effects of a single intra-articular injection of IL-1Ra-enriched autologous conditioned serum in patients with early primary osteoarthritis of the knee, using VAS and WOMAC scores and recording complications during 12 months of follow-up.

Aim

To observe the long-term effects of intra-articular knee injection of IL-1 Ra (Interleukin-1 Receptor Antagonist) - Autologous Conditioned Serum in patients with early primary Osteoarthritis of knee.

2. Objectives

To study long-term effects of intra-articular knee injection of Autologous Conditioned Serum.

To study clinical improvement with Visual Analogue Scale (VAS) and Western Ontario and McMaster Universities Arthritis Index (WOMAC).

To draw a conclusion regarding whether Autologous Conditioned Serum injections are effective in long term symptomatic relief or not.

3. Materials and Methods**Study design and setting**

This was a hospital-based observational prospective study conducted in the Department of Orthopaedics, Noble Hospital, Pune. The study period was December 2022 to December 2025. The study was commenced after approval from the institutional ethical committee, and written informed consent was obtained from each patient before the injection process.

Study population and sample size

Patients with early primary osteoarthritis of the knee attending the outpatient department of Noble Hospital, Pune, were considered for inclusion. Consecutive non-probability sampling was followed. A total of 30 cases of early primary osteoarthritis of the knee, defined as Kellgren-Lawrence grade 1 or 2, were included after informed consent.

Inclusion criteria

- Either gender with age >18 years.
- Patients with early primary osteoarthritis (Kellgren-Lawrence grade 1 and 2).
- Patients willing to give written informed consent and follow study-related procedures.

Exclusion criteria

- Kellgren-Lawrence grade 3 and 4 osteoarthritis of the knee.
- Patients with knee deformity, paralytic conditions, poliomyelitis, or previous significant injuries to the knee.
- Age >65 years or <18 years.
- Patients with overlying skin infection over the knee.
- Patients with chronic systemic medical diseases including chronic kidney disease, congestive heart disease, or chronic liver disease.

Intervention and injection technique

All cases received a single intra-articular injection of IL-1Ra (interleukin-1 receptor antagonist)-autologous conditioned serum. The injection was performed through the superolateral approach at the junction of the superior and lateral margins of the patella. An 18-gauge needle was used and angled downwards and medially into the joint space. All injections were prepared and administered by the primary investigator under the guidance of a senior consultant.

Safety measures

- Complete pre-procedure clinical examination and diagnostic work-up was performed for selection of appropriate patients.
- Intra-articular injection was administered under aseptic conditions.

Outcome measures and follow-up

Pain was assessed using the Visual Analogue Scale (VAS). Knee-related symptoms and function were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), comprising pain, stiffness, and physical-function domains. Assessments were performed at baseline and at 1 week, 4 weeks, 6 months, and 12 months. Complications during follow-up were recorded.

4. Results

Baseline characteristics

Characteristic	Result
Sample size	30
Mean age	58.4 ± 6.7 years
Female sex	23 (76.7%)
Male sex	7 (23.3%)
Kellgren-Lawrence grade 1	11 (36.7%)
Kellgren-Lawrence grade 2	19 (63.3%)
Right knee	16 (53.3%)
Left knee	14 (46.7%)
Mean symptom duration	3.7 years
Hypertension	14 (46.7%)
Diabetes mellitus	6 (20.0%)

The cohort consisted predominantly of women. Twenty-four participants (80.0%) had symptoms for 1–5 years, 2 (6.7%) for ≤1 year, and 4 (13.3%) for >5 years. Hypertension was the most frequently recorded comorbidity, followed by diabetes mellitus.

Pain outcome

Time point	VAS, mean ± SD	Reported p value
Baseline	6.50 ± 0.63	—
1 week	2.08 ± 0.93	<0.01
4 weeks	2.52 ± 1.13	<0.01
6 months	2.97 ± 1.33	<0.01
12 months	3.80 ± 1.51	<0.01

Mean VAS improved markedly after treatment and remained below baseline through 12 months. The thesis reports a 29.3% improvement from baseline at 12 months.

Functional outcome

Time point	WOMAC, mean ± SD	Reported p value
Baseline	70.13 ± 6.00	—
1 week	24.54 ± 2.10	<0.01

4 weeks	31.75 ± 7.33	<0.01
6 months	36.99 ± 10.31	<0.01
12 months	48.34 ± 7.20	<0.01

WOMAC improved substantially at 1 week and remained below the baseline value throughout follow-up. The thesis reports a 33.8% improvement from baseline at 12 months.

Safety

Recorded complication	n (%)
Swelling	2 (6.7%)
Local-site pain	2 (6.7%)
No recorded complication	26 (86.7%)

No major complication was reported in the study dataset. Local pain and swelling were each recorded in two participants.

5. Discussion

The present prospective observational study evaluated a single intra-articular IL-1Ra-enriched ACS injection in 30 patients with early primary knee osteoarthritis and followed clinical outcomes for 12 months. Both pain and WOMAC scores improved after treatment, with mean values remaining better than baseline at the end of follow-up.

The early reduction in VAS and WOMAC scores was most pronounced at 1 week, followed by partial worsening over subsequent months while remaining improved relative to baseline. This pattern indicates an observed symptomatic improvement in this cohort. However, because there was no untreated or comparator group, the study design does not permit attribution of the observed changes specifically to ACS.

The findings are directionally consistent with previous investigations cited in the thesis. Chevalier et al. reported that intra-articular IL-1Ra was well tolerated and investigated clinical outcomes in patients with painful knee osteoarthritis [9]. Yang et al. reported clinical benefits of autologous IL-1Ra compared with placebo in a randomized controlled study [10]. Studies evaluating ACS/Orthokine have also reported improvements in pain and function [8,11,12]. More recent systematic reviews have suggested possible symptomatic benefits of anti-IL-1 therapeutics while emphasizing heterogeneity and limitations in the available evidence [13,14].

The safety profile observed in the present cohort was favorable, with local pain and swelling each occurring in 6.7% of participants and no recorded major adverse event. These findings should nevertheless be interpreted cautiously because the sample size was small and uncommon complications may not be detected in a cohort of this size.

Importantly, the present study evaluated symptomatic and functional outcomes only. It did not include a structural imaging endpoint or a control group and therefore cannot establish a disease-modifying or cartilage-protective effect.

6. Strengths and Limitations

Strengths of the study include prospective follow-up, standardized patient-reported outcome measures, inclusion of an early knee osteoarthritis population, and follow-up extending to 12 months. Important limitations include the small sample size, single-center design, absence of a control or comparator group, non-randomized sampling, and reliance on patient-reported outcomes without structural imaging endpoints.

7. Conclusion

In this prospective observational cohort of patients with early primary knee osteoarthritis, a single intra-articular injection of IL-1Ra-enriched autologous conditioned serum was associated with improvement in pain and WOMAC scores that persisted relative to baseline through 12 months. Few local adverse events were recorded. These findings support further investigation but do not establish efficacy or disease modification because of the absence of a control group and the small sample size.

8. Declarations

Ethics approval and consent to participate

The study was commenced after approval from the institutional ethical committee and that written informed consent was obtained from each participant.

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