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Research Article

# Comparison of Efficacy and Safety of Intra-Articular Injection of Dexmedetomidine and Triamcinolone in Improving Knee Pain and Function in Patients with Primary Knee Osteoarthritis

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**ABSTRACT**

**Background:** With the increasing prevalence of knee osteoarthritis, providing treatment solutions was on the agenda of research teams. Therefore, the present study was conducted to compare the efficacy and safety of intra-articular injection of Dexmedetomidine and Triamcinolone in improving knee pain and function in patients with primary knee osteoarthritis.

**Methods:** To carry out the current clinical trial study, all patients with knee osteoarthritis referred to Imam Hossein Hospital in Tehran were included within one year. Eligible patients were randomly divided into two groups: (D) Dexmedetomidine and (T) Triamcinolone. After registering the patients' demographic information, the Knee Injury and Osteoarthritis Outcome Score (KOOS) was used to evaluate the treatment process of the patients in two groups. VAS was used to measure the patient's pain level in three periods before the injection, one month and three months after the last injection. Data were recorded in a pre-designed questionnaire and analyzed using the SPSS 20.0 statistical program.

**Results:** The pain, symptoms, sports-recreational performance, and knee-related quality of life three months after the procedure showed a statistically significant difference between the dexmedetomidine and the triamcinolone groups (P value <0.05).

**Conclusion:** The overall results show that patients with primary knee osteoarthritis who received dexmedetomidine had reduced pain and required fewer analgesics than those who received triamcinolone.

## Introduction

Osteoarthritis of the knee is one of the most prevalent and crippling chronic pain diseases [1-2]. The pathophysiology of this painful disease is poorly understood, and the current intervention strategy for treating knee osteoarthritis pain cannot provide satisfactory pain relief [3-4]. It is demonstrated that intra-articular injections of opioids, α2-adrenergic agonists, and local anesthetics can effectively manage postoperative joint pain [5-7].

Dexmedetomidine is regarded as a complete agonist of the alpha-2 receptor, resulting in analgesia, sympatholysis, and drowsiness. Although the exact mechanism underlying the analgesic action of intra-articular dexmethomidine injection is unknown, it bears similarities to the clonidine mechanism. Studies on the use of intra-articular dexmedetomidine for acute pain are now more numerous than those on chronic conditions such as osteoarthritis [8-9]. However, some research

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indicates that this method's analgesia is superior to other recommended ways, and its adverse effects, like bradycardia and hypotension, are reduced [10].

On the other hand, it was demonstrated that injecting 20 μg/kg of dexmedetomidine intraperitoneally decreased the inflammatory pain in rats with monoarthritis, indicating that dexmedetomidine helps lower arthritis pain [11]. However, the function and mode of action of dexmedetomidine in the management of osteoarthritis are yet unknown based on research done on arthritic rats. So, this research aimed to evaluate the safety and effectiveness of intra-articular injections of two medications, triamcinolone and dexmedetomidine, in reducing knee pain and function in individuals with primary osteoarthritis of the knee.

## Methods

### Ethics committee's approval

The present study was designed and implemented as a double-blind, randomized clinical trial. For this purpose, after obtaining the code of ethics from the ethics committee in biomedical research of Shahid Beheshti University of Medical Sciences in Tehran (IR.SBMU.RETECH.REC.1402.267) and the RCT code from the Iranian clinical trial system (IRCT20130518013364N11), the patient recruitment process was carried out at Imam Hossein Hospital in Tehran.

### Samples and the study method

Patients with knee osteoarthritis referred to Imam Hossein Hospital for one year were included in the study. Among them, 60 patients based on inclusion criteria (age>40 years, pain caused by osteoarthritis >3 months, findings confirming osteoarthritis based on American College of Rheumatology (ACR) criteria) and exclusion criteria (history of knee surgery, history lower limb deformity and contracture, suffering from neuromuscular disease of the lower limb, acute lumbar pathology, steroid injection in the last two months, history of inflammatory rheumatoid arthritis, infection, diabetes, pregnancy, BMI >35, suffering from knee deviation (varus or valgus greater than five degrees)), suffering from radio-collar knee pain, those who have used anticoagulant medications, those who have had post-traumatic arthritis, intra-articular injections <11 months, allergic to any of the medications, suffering from systemic or psychiatric diseases, severe osteoarthritis > grade more than III, suffering from hepatitis, AIDS, cytomegalovirus, syphilis, osteomyelitis, substance abuse, and alcohol) were evaluated in the form of this scientific plan after obtaining informed consent.

The mentioned patients were divided into two groups using a random block method ((D) Dexmedetomidine and (T) Triamcinolone).

The treatment team, implementation method and tools used were the same for all patients in both groups. Therefore, all patients were made to lie supine throughout the surgery, and the landmark of the injection location was identified. The patient's knee was flexed 30-45 degrees on the lateral side of the knee. Following disinfecting the injection site with povidone-iodine solution, needle number 27 was used to inject two millilitres of 2% lidocaine solution, numbing the skin and joint surface for a painless needle entry. Then, with a 20-gauge needle and guided by ultrasound, an injection was performed in the intra-articular space of the knee. Ultrasound guidance (Site Site, PICO. probe Convex 3-7, Linear 5-12) was administered to ensure needle accuracy and intra-articular injection of triamcinolone/dexmedetomidine.

In group (D), using a 20-gauge needle, 1 ml of 1% lidocaine and dexmedetomidine at the rate of 1 μg/kg were injected under ultrasound guidance.

In group (T), using a 20-gauge needle, 1 ml or 40 mg of triamcinolone plus 2 ml of 2% lidocaine were injected under ultrasound guidance.

The treatment team, implementation method and tools used were the same for all patients in both groups.

### Data collection

The patient and the pain specialist physician filled out pre-made information forms and Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaires, which were used to gather data. The patient completed the KOOS questionnaire twice before treatment began and three months after the last injection. It consisted of five items covering pain, symptoms, daily activities, sports and recreational performance, and quality of life related to the knee. Responses were recorded on a 4-point Likert scale (0–4). The VAS (0–10) was used to quantify the patients' pain level. The sign provides a pain score, and the patients were requested to complete it before treatment, one month, and three months after the final injection. If a problem arose, the kind of problem was also noted. It should be mentioned that throughout the study period, the patients did not take steroids, antidepressants, or sedatives.

### Statistical analysis

The information needed for the experiments was recorded using the information in the patient's file and the information obtained from the follow-up and interview and the patient's visit in pre-prepared information sheets. In order to examine the experimental results, SPSS 20.0 (Chicago, IL, USA) was used. The significant differences between the means were ascertained using the t-test analysis (P value <0.05).

## Results

Sixty-seven participants responded to the survey between 20 September 2022 and 20 September 2023, of whom 60 (89.55%) with an average age of 51.01±6.89 years provided complete data on variables included in the present analyses. According to the results in (Table 1), 44 (73.33%) of all individuals were men, and 16 (26.66%) were women (Figure 1).

Based on the results in (Table 2), pain level based on the KOOS questionnaire three months after the procedure (P value<0.001), symptoms score based on the KOOS questionnaire three months after the procedure (P value=0.026), sport-recreational performance based on the KOOS questionnaire three months after the procedure (P value=0.002), and knee-related quality of life score based on the KOOS questionnaire three months after the procedure (P value<0.001) are significant differences in the two groups.

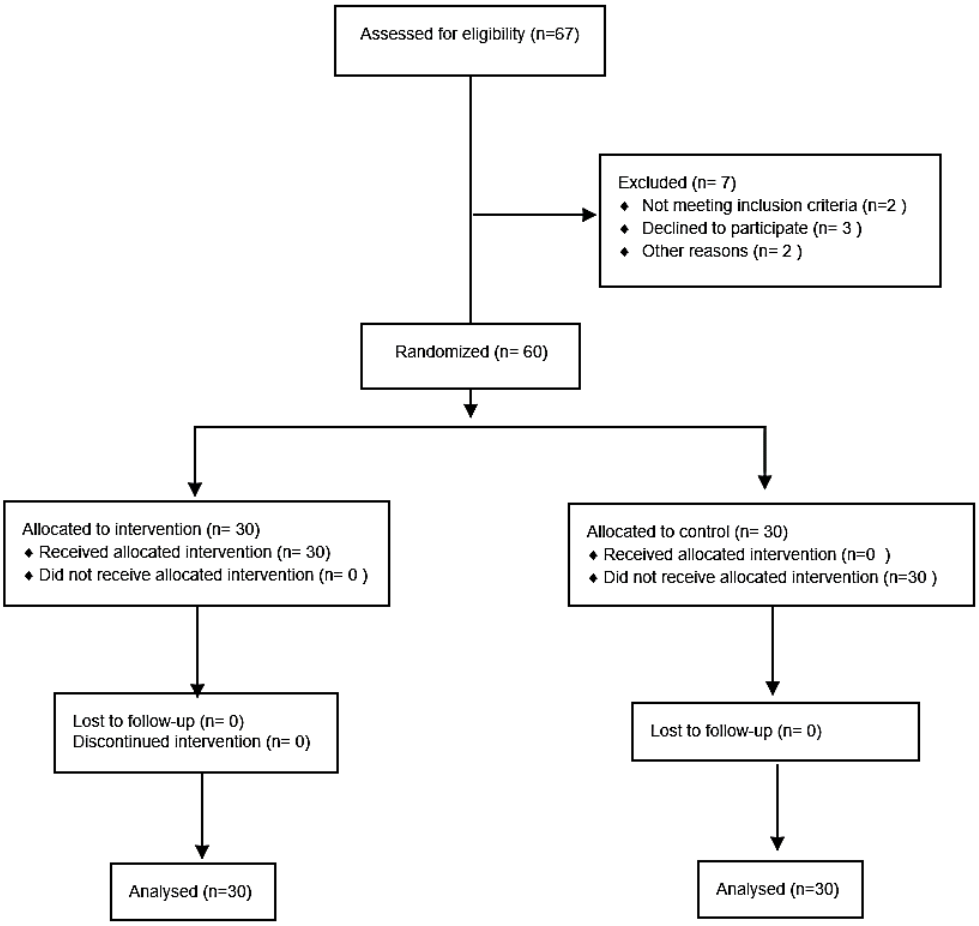


**Figure 1- Flowchart of patients with osteoarthritis participating in the study**

**Table 1- Demographic information and patient records**

| Indexes | Mean | | N (%) |
|---|---|---|---|
| Age | | 51.01±6.89 | - |
| Sex | Male | - | 44 (73.33%) |
| | Female | - | 16 (26.66%) |
| Side effects before treatment | | - | 0 (0.0%) |
| | Hematoma at the injection site | - | 5 (8.3%) |
| Side effects in the first month | Swelling at the injection site | - | 4 (6.7%) |
| | Neurological complications | - | 3 (5.0%) |
| | Hematoma at the injection site | - | 2(3.3%) |
| Side effects in the third month | Swelling at the injection site | - | 4(6.7%) |
| | Neurological complications | - | 2(3.3%) |

**Table 2- The results of the effect of dexmedetomidine and triamcinolone injection on improving knee function in patients with primary knee osteoarthritis.**

| INDEX | Dex Group | Tri Group | P value |
|---|---|---|---|
| VAS, before the procedure | 2.80 ± 1.24 | 3.40 ± 1.06 | 0.049 |
| VAS, one month after the procedure | 4.00 ± 1.14 | 4.23 ± 1.22 | 0.449 |
| VAS, three months after the procedure | 2.43 ± 0.81 | 2.53 ± 0.68 | 0.609 |
| Pain score based on the KOOS questionnaire, before the procedure | 3.90 ± 1.53 | 4.50 ± 1.38 | 0.118 |
| Symptoms score based on the KOOS questionnaire, before the procedure | 2.23 ± 0.77 | 3.13 ± 0.73 | 0.000 |
| Score of daily activities based on the KOOS questionnaire, before the procedure | 12.76 ± 4.11 | 12.63 ± 3.70 | 0.896 |
| Sports-recreational performance based on the KOOS questionnaire, before the procedure | 2.36 ± 0.66 | 2.96 ± 0.80 | 0.003 |
| knee-related quality of life score based the KOOS questionnaire, before the procedure | 2.00 ± 0.74 | 2.56 ± 0.89 | 0.010 |
| Pain score based on the KOOS questionnaire, one month after the procedure | 2.63±1.27 | 3.06±1.00 | 0.097 |
| Symptoms score based on the KOOS questionnaire, one month after the procedure | 2.23±0.71 | 2.47±0.68 | 0.052 |
| Score of daily activities based on the KOOS questionnaire, one month after the procedure | 10.36±3.79 | 10.03±3.86 | 0.764 |
| Sports-recreational performance based on the KOOS questionnaire, one month after the procedure | 1.89±0.61 | 2.00±0.69 | 0.53 |
| knee-related quality of life score based the KOOS questionnaire, one month after the procedure | 1.98±0.71 | 2.23±0.86 | 0.51 |
| Pain score based on the KOOS questionnaire, three months after the procedure | 1.93 ± 0.90 | 2.86 ± 1.04 | 0.000* |
| Symptoms score based on the KOOS questionnaire, three months after the procedure | 1.46 ± 0.81 | 2.00 ± 0.98 | 0.026* |
| Score of daily activities based on the KOOS questionnaire, three months after the procedure | 8.10 ± 3.87 | 8.16 ± 3.60 | 0.945 |
| Sports-recreational performance based on the KOOS questionnaire, three months after the procedure | 1.26 ± 0.73 | 1.86 ± 0.73 | 0.002* |
| knee-related quality of life score based the KOOS questionnaire, three months after the procedure | 1.40 ± 0.77 | 2.20 ± 0.80 | 0.000* |
| BMI | 24.69 ± 3.47 | 25.38 ± 2.52 | 0.379 |

*Significance at a difference level of less than 5%.

## Discussion

Until now there is no critical evaluation of international guidelines comprehensively presented for treatment based on intra-articular injection of dexmedetomidine in knee osteoarthritis [12]. Therefore, in this study, the benefits of dexmedetomidine as an adjuvant drug in combination with local anesthetic in creating and prolonging analgesia were investigated.

As we know, BMI is one of the risk factors of knee Osteoarthritis and in this study, the amount of BMI in both groups was almost the same and there were no significant differences.

According to our results, three months after the procedure, there was a significant difference between the dexmedetomidine group and triamcinolone group regarding pain level (based on the KOOS questionnaire), and the dexmedetomidine group experienced less pain.

A similar study investigated the effect of intra-articular injection of dexmethomidine in rat osteoarthritis and showed that dexmethomidine with a dose of 1 and 3 μg/kg significantly reduced knee pain. Histological analysis of dexmethomidine does not cause synovial membrane damage. α-TNF level showed a significant decrease in the dexmethomidine injection group with a dose of 3 μg/kg after 28 days. In addition, they proved the dexmedetomidine's ability to reduce rat pain by clinical parameters of osteoarthritis, while no anti-inflammatory effect was observed, as evidenced by histological evaluation [13]. Nesioonpour et al., in a similar study, showed that dexmedetomidine injection significantly reduced postoperative pain and analgesic consumption while delaying the time to request the first dose of analgesic [14].

The side effects of dexmedetomidine have been discussed a lot by several studies. Akça et al. concluded that in a placebo-controlled in vivo trial, intra-articular use of dexmedetomidine seemed safe according to the histopathological parameters [15]. In our study, we also did not observe severe complications in patients. However, one month after dexmedetomidine injection, 5

people (8.3 %) experienced hematoma, 4 people (6.7 %) had swelling, and 3 people (5.0 %) reported neurological complications such as relative numbness and tingling at the injection site. Three months after the treatment, 2 people (3.3 %) reported hematoma, 4 people (6.7 percent) experienced swelling at the injection site, and 2 people (3.3%) had relative numbness and tingling at the injection site.

The analgesic impact of intra-articular dexmedetomidine injection has been demonstrated in arthroscopic procedures [15]. Dexmedetomidine has been shown in numerous randomized controlled trials (RCTs) to prolong the analgesic effect during knee arthroscopy, notably lowering the pain score and postoperative diclofenac sodium consumption [16-18]. However, other research has produced inconsistent findings [19]. According to rat research, dexmedetomidine inhibits the NF-κB pathway via the α2A -AR subtype, which lowers the inflammatory factor [20]. So, since chronic and degenerative osteoarthritis is an inflammatory disease that gradually destroys knee cartilage and causes secondary inflammation of the synovial membrane, it can be said that the use of dexmedetomidine can play a positive role in reducing the pain caused by this disease.

## Conclusion

According to the general findings of our study, the injection of dexmedetomidine made patients experience less pain compared to the triamcinolone treatment. Therefore, these results can point to the better effect of dexmedetomidine in improving knee pain and function in patients with primary knee osteoarthritis. However, it is recommended that research be conducted on the long-term side effects of dexmedetomidine in larger statistical communities.

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