RESEARCH ARTICLE

# Effect of Intra-articular Dexmedetomidine on Postoperative Pain after Knee Arthroscopic Surgery

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*Received: 18 December 2020* *Accepted: 15 April 2021*

## Abstract

**Background:** This study aimed to prevent and control the pain after arthroscopy that leads to patient satisfaction, rehabilitation, and return to normal life as soon as possible. It is hypothesized that there is no difference between intra-articular injection of dexmedetomidine and placebo after knee arthroscopy regarding pain level.

**Methods:** This double-blind randomized clinical trial was conducted on 70 patients aged 18-60 years who were candidates for elective knee arthroscopic surgery with the American Society of Anesthesiologists Classification I-II. All patients underwent spinal anesthesia equally and were randomly divided into two groups of 35 cases per group. The drug group (D) received 2 µg/kg dexmedetomidine with 0.9% normal saline reached to a volume of 20 ml, and 20 ml of 0.9% normal saline was injected into the knee joint through the cannular sheath in the control group (C). Postoperative pain intensity was recorded 1, 2, 4, 8, 16, 24 h after injection using the Visual Analogue Scale. The time of requesting the first analgesic and the amount of analgesics consumed were recorded after 24 h.

**Results:** There was no significant difference between the two groups in terms of age, height, weight, duration of spinal anesthesia, and duration of surgery ($P>0.05$). In group D, there was a decrease in postoperative pain, a decrease in the amount of analgesic consumed, and an increase in the time of the first analgesic request, compared to group C ($P<0.05$).

**Conclusion:** This study showed that intra-articular injection of dexmedetomidine relieved postoperative pain, reduced analgesic consumption, and increased the time of first analgesic request after knee arthroscopy.

**Level of evidence:** I

**Keywords:** Arthroscopy, Dexmedetomidine, Pain

## Introduction

Prevention and control of pain after surgery is one of the most important factors influencing the outcome of surgery. Proper management of postoperative pain requires finding pain pathology, pain reduction methods, and patient-related factors, such as anxiety, depression, and psychosis (1). A number of physiological responses to acute pain and stress are triggered by the activation of the neuroendocrine and increased sympathetic tone. Pain causes tachycardia, immune suppression, hypercoagulopathy, stable catabolism, and other changes (2). Postoperative pain prolongs hospital stays, patient dissatisfaction, and even delays in postoperative rehabilitation, as well as returns to normal life (3). Acute pain can also become chronic pain, and pain control techniques include regional and systemic methods. Among them are opioids and non-opioids, non-steroidal anti-inflammatory drugs (NSAIDs) (e.g., aspirin and acetaminophen), gabapentinoids, anticonvulsants, ketamine, and $\alpha_2$ agonists (e.g., clonidine and dexmedetomidine).

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Anti-inflammatory medications, such as dexamethasone can provide good analgesia in the immediate postoperative period (4). Arthroscopic surgery is one of the most common practices in orthopedic surgery. Following arthroscopy, the stimulation of the nerve endings in the synovial tissue, anterior fat, and joint capsule causes pain (5). Continuous epidural analgesia, femoral nerve blockade, patient-controlled analgesia, and intra-articular injection of analgesics are various techniques of analgesia to control postoperative knee arthroscopy pain. Local anesthesia is directly affected at the site of intervention, which reduces the side effects of systemic drug action (6).

The injection of various intra-articular drugs, such as local anesthetics (lidocaine and bupivacaine), opioids (morphine and fentanyl), α2 agonists (clonidine and dexmedetomidine), magnesium, ketorolac, tramadol, and neostigmine can provide adequate analgesia after surgery created (7). Dexmedetomidine is a selective α2-adrenergic agonist with anti-anxiety effects. Intravenous injection has sedative, anxiolytic, analgesic, anti-hypertensive, and sympatholytic properties (8). Various methods, such as intravenous, intra-articular, and neuraxial injections are used to induce anesthesia (9). New research suggests the use of intra-articular pain control techniques to reduce the side effects of other methods, such as nausea, vomiting, drowsiness, heartburn, urinary retention, restlessness, and decreased respiratory function (10). It is hypothesized that there is no difference between intra-articular injection of dexmedetomidine and placebo after knee arthroscopy regarding the pain level.

## Materials and Methods

This prospective double-blind study was performed on 70 male patients who were candidates for anterior cruciate ligament (ACL) reconstruction by knee arthroscopy in 2019 and referred to the clinic of Shohadaye Naft Hospital, Sousangerd, Iran. Written consent was obtained from all patients to participate in the study. The inclusion criteria were patients with the American Society of Anesthesiologists Classification I-II and age range from 18 to 60 years. On the other hand, the patients with kidney failure, liver failure, valvular and ischemic heart disease (identified by patient history, physical examination, electrocardiogram, and echocardiography), high blood pressure, diabetes, history of infection and malignancy, history of coagulation diseases, and drug allergies, as well as drug users, and those who consumed NSAIDs and analgesics 24 h before surgery were excluded from the study. It is worth mentioning that the patients were randomly divided into the two groups of drug (D) and control (C) (35 cases per group) based on an online research randomizer (http://www.randomizer.org). The obtained codes were placed in secure envelopes and given to a person who was unaware of the purpose of the study.

In the preoperative visit, the research procedure and objectives, as well as the Visual Analogue Scale (VAS) scoring (from 0 painless to 10 maximum pain) were explained to the patients and their families. In the operating room, a safe intravenous route was taken with the angiocatheter number 18 and hydrated with 8 ml/kg lactated ringer solution. Electrocardiographic monitoring, heart rate, pulse oximetry, and a non-invasive barometer was performed for the patients. All patients were placed in a sitting position, and after skin preparation and under sterile conditions, the intervertebral space was blocked with 15 mg of 0.5% hyperbaric bupivacaine (Mylan Pharmaceuticals Inc., PA, USA) in the L3-L4 or L4-L5 with a Quincke needle (25-G) in the midline of the spine. Sensory block was assessed by examining the pinprick sense with a needle (25-G) along the axillary midline every 2 min. Motion block was assessed by examining with a Bromage Scale. Surgery was allowed to begin when the level of the sensory block reached L1, and a motor block was established (Bromage Scale≥2). Arthroscopic ACL reconstruction with hamstring tendon autograft was performed using anteromedial and anterolateral portals. Fifteen minutes before opening the tourniquet, the surgeon injected 2 μg/kg dexmedetomidine (Elixir, Iran) with 0.9% normal saline reached to a volume of 20 ml in group D and 20 ml 0.9% normal saline into the knee joint in group C without knowing its contents. The sterile injection was performed through a cannula sheet into the intra-articular space of the knee. The incisions were then sutured, and the knee was flexed and extended three times to help distribute the drug to the entire joint space [Figure1]. In the case of bradycardia (HR<60), 0.5 mg of atropine was injected intravenously. Hypotension (MAP less than 20% of baseline) was treated with 5 mg ephedrine intravenously. Postoperative pain intensity 1, 2, 4, 8, 16, 24 h after injection was recorded using the VAS. In the case of VAS≥3, the patient was injected intravenously with 0.3 mg/kg of meperidine and repeated if necessary. In the study, when the movement block was destroyed (Bromage Scale=0), the time was considered zero, and the patient was transferred from the post-anesthesia care unit to the floor. The time of the first analgesic request and the total amount of analgesic consumed were recorded 24 h after surgery. The questionnaires were completed by an anesthesia resident who did not know the patients' groups. In this study, no patient was excluded from the study.

**Figure 1. Intra-articular injection**

### *Sample size calculation*

The sample size was estimated at 35 patients considering alpha=0.05 and beta=0.2 using the data from a study by Alipour et al. based on the following formula (9):

$$n = \frac{(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2 (s_1{}^2 + s_2{}^2)}{(\bar{x}_1 - \bar{x}_2)^2}$$

The data were analyzed in SPSS software (version 23) (SPSS, Chicago, II, USA) using mean±SD, frequency, and percentage for descriptive data. To compare the data in the two groups, the t-test and Mann-Whitney test were used for the normal and abnormal (and ranked) distributions of the data, respectively. Moreover, repeated-measures ANOVA was employed to compare the two groups. A *P-value* less than 0.05 was considered statistically significant.

## Results

There was no significant difference between the groups in terms of age, height, weight, as well as the duration of spinal anesthesia and surgery (*P>0.05*) [Table 1]. VAS at all postoperative hours was lower in group D, compared to group C, which was significant (*P<0.05*) [Table 2]. Moreover, the time of receiving the first analgesia in group D was longer, and the amount of analgesic consumption in group D was less than that in group C. This difference was also significant (*P<0.001*) [Table 3]. The patients did not experience the side effects of dexmedetomidine, such as hypotension and bradycardia.

**Table 1. Demographic characteristics of the patients, time of spinal anesthesia, and time of surgery***

| Groups | Age (y) | Height (cm) | Weight (kg) | Time of spinal anesthesia (min) | Time of Surgery (min) |
|---|---|---|---|---|---|
| Control | 26.91±4.9 | 178±4.47 | 74.22±4.4 | 130.85±23.4 | 87.57±14.16 |
| Drug | 27.88±5.4 | 178.25±4.7 | 72.51±12.42 | 114±8.97 | 80.71±9.4 |
| *P-value*** | 0.43 | 0.85 | 0.46 | 0.58 | 0.59 |

*Values are expressed as mean±SD
** *P<0.05* shows significant differences between groups

**Table 2. Postoperative pain severity based on Visual Analogue Scale***

| Groups | Visual Analogue Scale | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0 H | 1 H | 2 H | 4 H | 8 H | 16 H | 24 H |
| Control | 1.45±0.65 | 2.2±0.63 | 4.17±1.31 | 5.54±1.48 | 6.31±2.09 | 6.17±1.56 | 5.25±1.46 |
| Drug | 1.25±0.5 | 1.68±0.58 | 2.62±.68 | 3.2±1.36 | 4.05±1.79 | 3.77±1.57 | 3.4±1.55 |
| *P-value*** | 0.001 | 0.001 | 0.001 | 0.021 | 0.002 | 0.001 | 0.001 |

*Values are expressed as mean±SD
** Significant differences between groups (*P<0.05*)

**Table 3. Total Dose of Meperidine consumption in the first 24 h after the operation and time to first analgesic request***

| Groups | Meperidine equivalents 0-24 h (mg) | Time to first analgesic request (min) |
|---|---|---|
| Control | 125.82±1.62 | 65.9±1.82 |
| Drug | 76.31±1.12 | 142.85±1.62 |
| *P-value*** | 0.001 | 0.001 |

*Values are expressed as mean±SD
** Significant differences between groups (*P<0.05*)

## Discussion

This study was performed on 70 patients who were candidates for knee arthroscopy. After arthroscopy, dexmedetomidine was injected in group D, and group C received normal saline intra-articularly. The results of this study showed that intra-articular administration of dexmedetomidine reduced pain after knee arthroscopy due to the fact that the two groups were similar in type of surgery and anesthesia and only differed in terms of dexmedetomidine and placebo. The reduction in pain,

the decrease in the need for analgesic in the first 24 h after surgery, as well as the increase in the time to first analgesic request, are probably due to the intra-articular administration of dexmedetomidine. A study by Davi et al. in 2018 evaluated the effect of intra-articular injection of bupivacaine alone versus bupivacaine with dexmedetomidine or magnesium sulfate on analgesia after knee arthroscopy.

The patients were divided into three groups. The first (B) and second groups (M) received 20 ml bupivacaine 0.25% and 20 ml bupivacaine 0.25% with 10 mg/kg magnesium sulfate, respectively. Moreover, 20 ml bupivacaine 0.25% was injected with 0.5 μg/kg dexmedetomidine to the third group (D). They concluded that the duration of analgesia was longer in groups D and M, compared to group B (*P<0.05*). The results of this study are similar to the findings of our study, despite the fact that in this study, a lower dose of dexmedetomidine was used as an adjuvant drug (11). Ismail et al. in 2017 concluded that the intra-articular injection of 1μg/kg dexmedetomidine and 2.5 mg bupivacaine 0.25% was effective in relieving pain after knee arthroscopy and reducing the need for meperidine after surgery (*P<0.05*). The results of this study with a lower dose of dexmedetomidine as an adjuvant are similar to the findings of our study (12).

A study by Moeen et al. in 2017 evaluated the effect of intra-articular injection of dexamethasone or dexmedetomidine with bupivacaine on analgesia after knee arthroscopy surgery. They divided the patients into three groups. The first group was injected with 18 mg bupivacaine 0.25% with 8 mg dexamethasone, and the second group received the same amount of bupivacaine with 1 μg/kg dexmedetomidine. Following that, the same amount of bupivacaine with 2 ml of normal saline was injected in the knee joint of the third group. The researchers revealed a decrease in the VAS scores in the first and second groups, compared to the third group (P<0.05). There was no significant difference between the first and second groups in this regard. The results of this study with a lower dose of dexmedetomidine as an adjuvant are similar to the findings of our study (13). Li et al. in 2017 in a systematic review and meta-analysis reviewed five studies (18mL ropivacaine, dexmedetomidine 2 μg/kg versus intra-articular ropivacaine [20mL]; intra-articular 100μg [1mL] of dexmedetomidine added to 19 mL of 0.25% ropivacaine versus intra-articular 19 mL of 0.25% ropivacaine and 1mL of isotonic saline; intra-articular 1μg/kg dexmedetomidine and isotonic saline versus intra-articular 25mL isotonic saline; dexmedetomidine 1μg/kg intravenously for 10min, followed by dexmedetomidine 0.3μg/kg for 50 min versus 2g of propacetamol; and buccal dexmedetomidine 2.5μg/kg versus buccal 0.9% NaCl 2mL).

They concluded that intra- articular injection of dexmedetomidine was effective in reducing knee pain after arthroscopy (*P<0.05*). Although dexmedetomidine was compared in different doses with other drugs in this study, the results of this study are similar to the findings of our study (14). A study by Anarwal et al. in 2017 evaluated the analgesic effect of morphine or dexmedetomidine in combination with intra-articular levobupivacaine on knee arthroscopy surgery. The patients were divided into three groups. The first (M) and second (D) groups received 18 ml of levobupivacaine 0.25% with 8 mg of morphine and the same amount of levobupivacaine with 100 μg dexmedetomidine, respectively. Moreover, the third group (C) received 2 ml of isotonic saline. They concluded that the total analgesia received during the 24 h after surgery was lower in group M, compared to the other groups (P<0.05). The results of this study are different from the findings of our study due to the use of different doses of dexmedetomidine along with other drugs (7). Elbadawy et al. in 2015 compared the effect of intra-articular injections of ketamine and dexmedetomidine on knee arthroscopy. In the B/D and B/K groups, 25 ml bupivacaine 0.25% with 1μg/kg dexmedetomidine and 25 ml bupivacaine 0.25% with 1 mg/kg ketamine were injected, respectively. On the other hand, group B received only 25 ml bupivacaine 0.25% intra-articularly. The researchers found that in the B/D group, postoperative analgesia and total analgesia were less, and the time for requesting the first analgesia was longer, compared to the other two groups (P<0.05). In this study, lower dose of dexmedetomidine was used as an adjuvant (15).

The role of intra-articular dexmedetomidine in enhancing quality, duration of postoperative analgesia, and reducing opioid use has been observed. The mechanism of intra-articular dexmedetomidine is not well understood. However, it may be similar to the effect of clonidine on α2-adrenergic presynaptic receptors, which inhibit the release of norepinephrine in the peripheral nociceptor of afferents. In addition, it causes analgesia by inhibiting the transmission of nociceptive stimulation in the posterior horn of the spinal cord. Another mechanism of clonidine as a local anesthetic is the inhibition of nerve impulses of Aδ and C fibers. This analgesic effect is a combination of the effect of narcotics and stimulation of enkephalin-like substances in the environment (12, 15). Articular absorption of the drug is increased by using a tourniquet. In our study, after injecting an intra-articular drug, the tourniquet remained inflated for 15 min. Factors related to the severity of pain after knee surgery include some surgical injury, residual analgesic effects at surgery, and sensitivity of methods used to record postoperative pain (16). Due to this, all patients had a uniform surgical injury (arthroscopy in which the meniscus was removed). The duration of surgery and the surgical team were almost the same. The analgesic technique was the same in all patients.

In addition, all patients were hospitalized and monitored during the study period to accurately record the pain rating and the amount of analgesia required after surgery. Due to the fact that various anesthesia methods have been used to perform knee arthroscopy, the analgesic method with intra-articular injection of dexmedetomidine is considered an easy and effective method that can ultimately make knee arthroscopy less invasive, with a minimum length of hospital stay. However, it is very helpful and necessary to conduct more extensive studies and compare other anesthesia methods with each

other to determine the advantages and disadvantages of intra-articular injection of dexmedetomidine in knee arthroscopy. Moreover, it is of importance to consider other determinants, such as different combinations and doses of different anesthetics. One of the limitations of our study was the lack of measurement of plasma levels of dexmedetomidine and its relationship with clinical findings in patients, which may explain its local efficacy.

Based on the findings of this study, intra-articular injection of dexmedetomidine can be recommended for analgesia after knee arthroscopy, which increases the time of receiving the first analgesic and reduces the analgesic consumption of patients. Furthermore, 2 µg/kg dexmedetomidine can be safe and effective in causing analgesia.

***Authers'Contribution:*** Study concept and design: Sholeh Nesioonpour, Hooman Pedram, and Sara Poursalehan. Analysis and interpretation of data: Sholeh Nesioonpour and Yasaman Esfahanian. Manuscript preparation: Ahmad Reza Mohtadi, Mohsen Savaie, Ali Ghomeishi, and Yasaman Esfahanian. Collection of data: Yasaman Esfahanian. Critical revision: Sholeh Nesioonpour and Yasaman Esfahanian.

***Confilict of Interests:*** The authers declare there was no conflict of interest.

***Ethical Considerations:*** http://ethics.research.ac.ir/IR.AJUMS.REC.1398.771.

***Funding/Support:*** This article is the result of the thesis of Dr. Yasman Esfahanian (IR.AJUMS.REC.1398.771), (IRCT20200205046390N1).The financial support was provided by Ahvaz Jundishapur University of Medical Sciences,Vise Chancellor for Research and Technology.

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## References

1. Sapola J, Smith C, Brandt C. Postoperative pain control. Surgical clinics. 2015; 95(2): 301-318.
2. Vincet J, Abraham E, Kochanek P, Moore F, Fink M. Text book of critical care; 7nd ed. Canada: Elsevier; 2017. P 25-35.
3. Chen X, Mou X, He Z, Zhu Y. The effect of midazolam on pain control after knee arthroscopy: a systematic review and meta-analysis. Journal of orthopaedic surgery and research. 2017;12(1):1-6.
4. Miller R, Cohen N, Eriksson L, Flesher L, Leslie K, Wiener-Kronish J. Miller's Anesthesia. 9nd ed. Canada: Elsevier; 2020. P 661-689.
5. Wang X, Way G, Lie C, Cain D. Effectiveness of intra-particular ozone injections on out come of post-arthroscopic surgery knee osteoarthritis. Experimental and therapeutic medicine. 2018; 15(6):5323-5329.
6. Weiker G, Kuivila T, Pippinger C. Serum lidocaine and bupivacaine levels in local technique knee arthroscopy. Am J sports med. 1991;19:499-502.
7. Agarwal R, Rayal Y, Chopra G, Agrawal A. Analgesic effect of intra-articular morphine or dexmedetomidine added with levobupivacaine in arthroscopic knee surgeries. Journal of clinical & diagnostic research. 2017;11(4):uc13-uc15.
8. Al- Metwalli RR, Mowafi HA, Ismail SA, Al- Ghamdi AM, Shafi MA, El- Saleh AR. Effect of intra- articular dexmedetomidine on postoperative analgesia after arthroscopic knee surgery. British journal of anesthesia. 2008;101(3):395-9.
9. Alipour R, Tabari M, Farhadi R, Makhmalbaf H, Salehi M, Moosavitekye M. Effect of dexmedetomidine on postoperative pain in knee arthroscopic surgery. The archives of bone and joint surgery. 2014;2(1):52-56.
10. Jung H, Seo K, Kang J, Jeong J, Kim Y, Han N. Optimal dose of perineural dexmedetomidine for interscalene branchial plexus block to control postoperative pain in patients undergoing arthroscopic shoulder surgery. Medicine. 2018;97(16):e0440.
11. Devi M, Gupta S, Amaravathi R, Udupa S, Hegde A, Ghosh S. Comparison of efficacy of intra arthicular plain bupivacaine with adjuvants (dexmedetomidine and magnesium sulfate) for postoperative analgesia in arthroscopic knee surgeries. Anesthesia Essays and Researches. 2018;12(4):848-854.
12. Ismail E, Saged J, Bakri M, Mahfouz R. Comparison of intrathecal versus intra-articular dexmedetomidine as an adjuvant to bupivacaine on postoperative pain following knee arthroscopy. The korean journal of pain. 2017;30(2):134-141.
13. Moeen S, Ramadan I, Elkady H. Dexamethasone and dexmedetomidine as an adjuvant to intraarticular bupivacaine for postoperative pain relief in knee arthroscopic surgery. Pain physician journal. 2017;20:671-680.
14. Li C, Qu J. Efficacy of dexmedetonidine for pain management in knee arthroscopy. Medicine. 2017;96(43):7938.

15. Elbadawy A, Salama A, Mohammad M. Comparative study of intra-articular Dexmedetomidine versus Ketamine as adjuvant analgesics after knee arthroscopy. Egyption journal of anesthesia. 2015;31:4.
16. Mosavi Tekye S, Sharifian Attar A, Aghaee R. Comparison of analgesic effect of intravenous Sufentanil and intra-articular injection of Sufentanil and Sufentanil plus Methylprednisolone after arthroscopic knee surgery. Iranian society of anesthesiology and critical care. 2006;53:2.