

# Analgesic Effect of Intra-articular Morphine or Dexmedetomidine Added with Levobupivacaine in Arthroscopic Knee Surgeries - A Comparative Evaluation

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## ABSTRACT

**Introduction:** Knee arthroscopy is associated with variable amount of postoperative pain. In an attempt to improve postoperative analgesia, intra-articular injection of local anaesthetic in combination with other agent have been studied. However, the best combination is not known.

**Aim:** To compare the analgesic efficacy of intra-articular injection of morphine and dexmedetomidine when added with levobupivacaine in arthroscopic knee surgeries.

**Materials and Methods:** Seventy eight patients, scheduled to undergo elective arthroscopic procedure under spinal anaesthesia were recruited for the study. All the patients received 18 ml of 0.25% levobupivacaine however in addition to this Group M patients received 8 mg (2 ml) morphine, Group D patients received 100µg (2 ml) of dexmedetomidine while Group C patients received 2 ml of isotonic saline intra-

articularly. Postoperatively the intensity of pain was assessed using Numerical Rating Scale (NRS). Rescue analgesia was given at NRS  $\geq$  4. The duration of analgesia and total diclofenac consumption was noted.

**Results:** The mean duration of analgesia was longest in Group M (576.20 $\pm$ 67.09 minutes) followed by Group D (460.93 $\pm$ 38.95 minutes) and Group C (370.27 $\pm$ 58.80 minutes) statistically this difference was found to be highly significant (p-value < 0.001). Total consumption of diclofenac in 24 hours was found lowest in group M (86.25 $\pm$ 27.48 mg) followed by group D (110.87 $\pm$ 44.48 mg) and group C (141.35 $\pm$ 44.13 mg) this difference was found to be highly significant (p-value < 0.001).

**Conclusion:** Morphine when added with levobupivacaine in patients undergoing arthroscopic knee surgery improves the quality and prolongs the duration of postoperative analgesia.

**Keywords:** Anaesthetic technique, Diclofenac sodium, Postoperative analgesia, Synergistic effect

## INTRODUCTION

Knee arthroscopy is one of the most common minimal invasive procedures performed for establishing the diagnosis and treatment of various internal structures of knee. However, it is usually associated with variable amount of postoperative pain [1]. Adequate pain relief is a key factor in reducing the morbidity and improving the overall patient satisfaction.

In previous studies intra-articular local anaesthetic agents have been used either alone [2-5] or in combination with other agent however, it was observed that use of combination of drug is better than single drug for prevention of postoperative pain [6-9]. Though, the combination of drugs provides synergistic effect and reduces the side effect compared to high dose of single drug [10] still the best combination is not known.

We therefore planned this study with an aim to investigate the effect on durations of analgesia using intra-articular levobupivacaine alone, levobupivacaine in combination either with dexmedetomidine or with morphine following arthroscopic knee surgery.

## MATERIALS AND METHODS

This double-blind randomized controlled study was conducted in the Department of Anaesthesia, Himalayan Institute of Medical Sciences, SRH University, Dehradun, Uttarakhand, India from January 2015 to December 2015. After approval from institutional ethical committee, the written informed consent was obtained from all the patients. Total 81 patients aged between 18 and 65 years of either sex, ASA I or II, undergoing elective arthroscopic procedure such as removal of loose body, diagnostic purposes, repair of

ruptured ligaments, partial or total meniscectomy etc., under spinal anaesthesia were included in the study.

Patients who refused for participation or with history of diabetes, hepatic, renal or cardiopulmonary abnormality, coagulopathy and long term analgesic therapy were excluded from the study. Patients were also excluded if there was any contraindication to spinal anaesthesia as well as contraindication to study drugs such as levobupivacaine, dexmedetomidine and morphine. Patients were randomly assigned to one of the three groups using computer-generated random numbers comprising of 27 patients in each group.

On preoperative visit after thorough preanaesthetic check up and explaining the procedure, the patient were taught to interpret the NRS. All eligible patients were kept fasting for six hours prior to surgery and were given tablet alprazolam 0.25 mg orally a night before and two hours prior to surgery. In the operating room, standard monitoring such as Electrocardiograph (ECG), noninvasive blood pressure (systolic, diastolic, and mean) and pulse oximetry (SpO<sub>2</sub>) were established and baseline value was recorded and noted.

As per hospital protocol the anaesthetic technique was standardized for all patients. Lumbar puncture was performed with patient in sitting position at L3-4/L4-5 inter vertebral space through median approach using 25-gauge spinal needle. Total 3 ml of 0.5% hyperbaric bupivacaine was given and patient was kept in supine position. After achieving the adequate block, the arthroscopy was allowed to perform. Prefilled syringes (20 ml) prepared with levobupivacaine plus morphine or levobupivacaine

plus dexmedetomidine or levobupivacaine plus saline and were kept in number coded under aseptic precaution. At the end of the surgical procedure, intra-articular solutions was injected into the knee joint through the cannular sheath after withdrawal of camera by the orthopaedic surgeon before the arthroscope was removed. Group M received 18 ml 0.25% levobupivacaine plus 2 ml (8 mg) morphine; group D received 18 ml of 0.25% levobupivacaine plus 2 ml (100 µg) dexmedetomidine while group C received 18 ml of 0.25% levobupivacaine plus 2 ml of 0.9% saline. During post anaesthesia care, the intensity of pain was assessed using NRS till it reached  $\geq 4$  and the total duration of analgesia was noted. Diclofenac sodium (75 mg) was administered intravenously as rescue analgesic if NRS pain score of 4 or more was recorded and was repeated every eight hourly if required. The duration to the first analgesic requirement and the total diclofenac consumption during first 24 hours after operation were also recorded.

## STATISTICAL ANALYSIS

Previous studies [2,4,7] were taken into account to calculate the sample size. The primary outcome of variable in the study was the duration of analgesia assuming the difference in period of analgesia between the groups as approximately four hours, and considering large effects in groups. Using a two tail value with  $\alpha$  of 5% and  $\beta$  of 80%, we needed 23 subjects in each of the three groups. However, considering the possible drop out we have included 81 patients (27 in each group).

The data was analysed statistically using Software Microsoft Office Excel 2010 and SPSS IBM version 22. Quantitative data was expressed as mean and standard deviation while qualitative data was expressed in terms of range or frequencies and percentages. The means of the continuous variables were compared between the three groups by using One-way Analysis of Variance (ANOVA). Haemodynamic changes were compared with the help of repeated measure ANOVA using Tukey's correction. The p-value  $< 0.05$  was considered significant and p-value  $< 0.001$  was considered as highly significant.

## RESULTS

Total of 81 patients were recruited however, one patient from group C and two patients from group M were excluded from the study as the effect of subarachnoid block was not adequate and the anaesthesia was therefore supplemented with general anaesthesia, total 78 patients met the inclusion criteria. There were no significant differences between the three groups regarding the demographic data such as age, sex, weight, ASA physical status, duration of surgery and tourniquet time [Table/Fig-1].

The mean duration of analgesia (duration between the intra-articular injection of the study drug and the first postoperative analgesic request i.e., NRS 4) was longest in Group M (576.20 $\pm$ 67.09 minutes) followed by Group D (460.93 $\pm$ 38.95 minutes) and Group C

Variables	Group M (n=25)	Group D (n=27)	Group C (n=26)	p-value
Age in Years (Mean $\pm$ SD)	32.28 $\pm$ 9.44	28.59 $\pm$ 11.13	32.77 $\pm$ 11.80	0.324 <sup>†</sup>
Sex M:F	14:11	21:6	22:4	0.056*
ASA I:II	22:3	24:3	24:2	0.865*
Weight in Kg (Mean $\pm$ SD)	56.80 $\pm$ 7.79	59.63 $\pm$ 9.50	61.46 $\pm$ 6.26	0.118 <sup>†</sup>
Duration of Surgery in min (Mean $\pm$ SD)	78.32 $\pm$ 41.09	76.81 $\pm$ 39.26	87.27 $\pm$ 40.63	0.600 <sup>®</sup>
Tourniquet Time (min) Mean $\pm$ SD	92.58 $\pm$ 37.72	81.56 $\pm$ 38.02	82.60 $\pm$ 41.41	0.533 <sup>®</sup>

[Table/Fig-1]: Demographic profile of three groups.

<sup>†</sup> ANOVA, \*Chi square, <sup>®</sup> ANOVA with post-hoc Tukey's or Tamhane Test

(370.27 $\pm$ 58.80 minutes) statistically this difference was found to be highly significant (p-value = 0.0008). Total consumption of diclofenac in 24 hours was found lowest in group M (86.25 $\pm$ 27.48 mg) followed by group D (110.87 $\pm$ 44.48 mg) and group C (141.35 $\pm$ 44.13 mg) this difference was found to be highly significant (p-value = 0.0009) [Table/Fig-2].

Variables	Group M (n=25)	Group D (n=27)	Group C (n=26)	p-value
Time to reach NRS 4 (min) Mean $\pm$ SD	576.20 $\pm$ 67.09	460.93 $\pm$ 38.95	370.27 $\pm$ 58.80	0.0008*
Dose of diclofenac (mg) Mean $\pm$ SD	86.25 $\pm$ 27.48	110.87 $\pm$ 44.48	141.35 $\pm$ 44.13	0.0009*

[Table/Fig-2]: Time to reach NRS 4 and consumption of diclofenac in 24 hours postoperative.

p-value  $< 0.001$  \* Highly significant

Complications such as hypotension, hypertension, bradycardia, nausea, vomiting, hypoxia, headache or any other complication was found in none of the patient in any group. Though sedation was found in two of the group D and one patient of the group M, however clinically and statistically it was found to be insignificant.

## DISCUSSION

The role of knee arthroscopy is well established; however knee arthroscopy is associated with variable amount of pain. Therefore, appropriate assessment of pain and its management plays an important role in overall patient satisfaction. In this study, we used NRS for assessment of pain as it is sensitive and also able to differentiate the sex while measuring pain intensity [11].

In this study, there were no significant differences between the groups in terms of demographic profile such as age, gender, weight and the duration of surgery. The variables such as the type of surgery, type of knee disorder, dose and volume and kinds of analgesic used and their combinations can influence the pain [7]. However, in our study all three groups were similar regarding these variables.

We observed that addition of morphine (8 mg) with levobupivacaine for intra-articular injection significantly prolonged the postoperative analgesia when compared with addition of dexmedetomidine (100 µg) or the addition of saline. Intra-articular injections of local anaesthetics however provide faster onset of anaesthesia and analgesia but this anaesthesia and analgesia usually last for limited period of time [12]. As postoperative pain after arthroscopy originate in joints therefore it is logical to administer peripherally acting agents to the damaged area [13]. Morphine was found to be a good analgesic when given intra-articularly, Beyaz SG et al., concluded that 5 mg intra-articular morphine was as effective as 40 mg intra-articular triamcinolone [9]. The analgesic efficacy of intra-articular morphine, levobupivacaine and dexmedetomidine has been proven in previous studies [14-17]. We also observed that total analgesic requirement during 24 hours postoperatively was significantly lower in morphine group as compared to dexmedetomidine and saline group.

Longer duration of postoperative analgesia and lesser requirement of rescue analgesia in intra-articular drug administration may be due to slower rate of absorption through poorly vascular intra-articular surface. Though, the exact mechanism of analgesic and anti-inflammatory effect of intra-articular morphine is not yet known. Probably the activation of opioids receptors of peripheral nerve terminals may be responsible for this [18-20]. This fact is supported by the study of Brandsson S et al., they suggested that the effect of analgesics and narcotics on the joint is due to the existence of peripheral mechanism in the joint, which reduces the pain without significant systemic effect [21]. Intra-articular morphine may have some anti-inflammatory actions. In chronic arthritis patients, intra-articular morphine injection provides analgesia, equivalent

to dexamethasone [22] and triamcinolone [9]. It has also been demonstrated that local opioid-dependent analgesic actions are more pronounced in inflamed tissues than non inflamed tissues [23].

In terms of postoperative analgesia and analgesic requirement we found that dexmedetomidine was found superior to saline group. Though the exact mechanism of analgesia for intra-articular dexmedetomidine is unclear but it might be same as with intra-articular clonidine [24]. The possibility of analgesic action by direct local action and a central analgesic action resulting from systemic absorption cannot be ruled out. Previous studies [14,16] also supported that intra-articular dexmedetomidine enhances the postoperative analgesia after arthroscopic knee surgery.

Though our study was not aimed at mechanism of prolong analgesia of the particular drug however longest duration of postoperative analgesia in our morphine group may be contributed because of the reason explained in above studies as well as intra-articular drug administered may get slower rate of absorption through poorly vascular intra-articular surface and remains at the injected site for longer duration however slower systemic absorption leading to prolong analgesia cannot be excluded.

We have observed that two patients in dexmedetomidine group and one patient in morphine group had sedation but it was found clinically insignificant, otherwise no other complication has been found in any of the groups.

## LIMITATION

The limitations of present study were; in our study the systemic controls of the drug used were not taken secondly; the plasma concentrations of analgesics used were not measured.

## CONCLUSION

We conclude that decreasing postoperative pain and increasing comfort is one of the main challenges in modern medicine. Effective pain treatment should decrease postoperative hospitalization and allow for early rehabilitation hence addition of morphine with levobupivacaine for intra-articular injection in arthroscopic surgery results in prolong and better analgesia during postoperative period and also decreases the requirement of rescue analgesic without any unwanted side effects.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Oct 26, 2016**  
Date of Peer Review: **Dec 03, 2016**  
Date of Acceptance: **Dec 11, 2016**  
Date of Publishing: **Apr 01, 2017**