Comparative Study of Intra-articular Dexmedetomidine Versus Ketamine as an Adjuvant Analgesic after Arthroscopy

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Abstract

Background: The primary aim of this study was to evaluate the analgesic effect and safety of intra-articular Dexmedetomidine versus Ketamine in patients undergoing knee arthroscopic surgeries.
Material and Methods: A total of 100 patients were allocated into two equal groups (n= 50 in each group) using random numbers, in an allocation ratio of 1:1. Syringes were labelled either D (dexmedetomidine) or K (ketamine) and study drugs were injected via intra-articular route after completion of knee arthroscopy. Analgesic effect of study drugs was compared using VAS score at 6 hrs, 12 hrs and 24 hrs. Safety of study drugs was compared using mean HR, mean BP and adverse events observed. **Results**: Lower VAS score, increased time for first rescue analgesic requirement and decreased need for postoperative analgesics were observed in the dexmedetomidine group as compared to ketamine group. Mean HR and Mean BP were lower in patients receiving dexmedetomine compared to those receiving ketamine. Hypotension was detected in 2 patients receiving dexmedetomedine while 1 patient on ketamine developed delirium. **Conclusion**: Intra-articular use of dexmedetomidine is superior to ketamine for post-operative analgesia without significant adverse effects.
Key words: Knee arthroscopy, Intra-articular Dexmedetomidine, Intra-articular Ketamine

Introduction

Arthroscopy is one of the day care procedures which may be diagnostic or therapeutic.[1]Knee arthroscopy is a well established minimally invasive procedure. Arthroscopic Surgeries are often associated with considerable degree of post operative pain usually caused by stimulation of the synovial tissue free nerve endings, anterior fat pad and capsule of the joint by either surgical excision or resection.[2,3] Postoperative pain control is very important for early rehabilitation and short term hospitals stay.[4] It can prevent complications like thromboembolism, myocardial ischemia, atelectasis etc.There are various routes and drugs which can be used to provide analgesia in arthroscopic surgeries during post operative period. Inta-articular route can be used for local deposition of drug at knee joint; which is likely to cause minimum alteration in physiology. Intra-articular route of drug administration targets peripheral receptors, is site specific and is an effective modality for postoperative analgesia.[5] Intraarticular bupivacaine is the most preferred local anaesthetic with or without adjuvant for post arthroscopic pain relief.[6] Dexmedetomidine is a potent and highly selective adreno-receptor agonist.[7,8] It has sedative- hypnotic , anxiolytic, analgesic, anaesthetic and sympatholytic effects.[9] Ketamine act as an anaesthetic substance with analgesic property.[10] It has been found to interact with a number of receptors such as NMDA and opioid receptors.[11,12] NMDA

receptors located in peripheral somatic and visceral pain pathways play important role in nociception. These have been found to exist in joints as well.[13]

Currently, data regarding intra-articular use of dexmedetomidine and ketamine following arthroscopy in Indian population is limited. Hence, the present study was conducted to compare the effectiveness and safety of dexmedetomidine and ketamine for post-operative analgesia in patients undergoing Knee arthroscopic surgery.

Materials & Methods

After obtaining approval from the Institutional Ethics Committee (Ref no 102/2018 dated 14/12/2019), written informed consent was obtained from participants fulfilling selection criteria. Patients having American society of Anaesthesiologist (ASA) physical status up to III, of both genders undergoing arthroscopic surgeries under SA were enrolled in the study. Patients having ASA grade IV and V and patients with altered coagulation profile were excluded. All patients were explained about the study procedure and perioperative course during preoperative visit on the day before the surgery. A total of 100 patients were allocated into two equal groups (n= 50 in each group) using random numbers, in an allocation ratio of 1:1. Syringes filled with study drugs were labelled either D or K [D for Dexmedetomidine (1µg/kg) + Inj. NS 20 ml] and K for [Inj. Ketamine (1mg/kg) + inj. NS 20 ml]. Both study drugs were in the Government supply. In pre-operative assessment; patient's general examination, systemic examination and all required investigations (Hb%, complete blood count, random blood sugar, blood urea, serum creatinine, liver function test, ECG and chest X-ray) were performed a day before the surgery. Patients were advised to remain nil by mouth (NBM) for 6-8 hours before the surgery.

Preparations in operation theatre:

- Baseline vitals: ECG, Pulse, Blood pressure, Oxygen saturation, Temperature
- Monitoring: ECG, Non invasive blood pressure, Oxygen saturation, Temperature
- Securing an intravenous line with 18 or 20 gauge intravenous cannula and starting i.v. fluids. Pre-loading was done with crystalloids 15-20 ml/kg of body wt.
- Premedication: Inj. Ondansetron 0.1mg/kg IV 10 minutes prior to anaesthesia.
- Spinal Anaesthesia: Under all aseptic and antiseptic precautions, subarachnoid block was administered with inj. Bupivacaine 0.5% (heavy) 3 ml in the sitting position using a 23-gauge Quincke spinal needle positioned at the L3-L4 interspace. Patients were immediately turned to the supine position. Onset and level of sensory and motor blocks were recorded. Sensory level was checked with pin prick method and was achieved between T8 to T10 segments. A pneumatic thigh tourniquet was applied on the lower limb to be operated with an inflation pressure of 250-350 mm Hg maintained throughout the surgery.
- Intra-operative blood pressure, heart rate, oxygen saturation, ECG and respiratory rate were monitored till the completion of surgery.
- Intraarticular analgesia:

  Group D (n=50): Inj. Dexmedetomidine (1µg/kg) + Inj. NS 20 ml

  Group K (n=50): Inj. Ketamine(1mg/kg) + inj. NS 20ml

Study drug either from group D or K was administered via intra-articular route in an aseptic manner by the operating surgeon through trocar after completion of surgery. Tourniquet was deflated after 10 minutes of administration of study drug. Total duration of surgery and time of intra-articular injection was noted.

- Postoperative period: Patients were monitored in the recovery room for Pulse, Blood pressure (SBP, DBP) and oxygen saturation. Pain assessment was performed using Visual Analogue Scale (VAS) with a score of 0 to 10 (0= No Pain, 10 = Worst Possible Pain) at 1 hr, 2 hrs, 4 hrs , 6 hrs, 8 hrs, 12 hrs, 16 hrs, 20 hrs and 24 hrs. Rescue analgesic in the form of Inj. Diclofenac sodium 75mg IV was administered as and when VAS score was ≥ 4 and the time for the same was noted. Total number of dosages needed during the 24 hrs period was noted. Duration of analgesia was calculated from the time of intra-articular deposition of the study drug till the requirement of first dose of rescue analgesic. Efficacy of study drug was determined using VAS score, the duration of analgesia and total no. of doses of rescue analgesics required during 24 hrs.

Also, recovery time from spinal anaesthesia, in terms of wearing off motor and sensory effects was noted. Heart rate and systolic blood pressure were monitored and recorded at the above-mentioned intervals up to 24 hrs. Patients were monitored to detect any adverse reactions during the post-operative period e.g. hypotension, bradycardia, vomiting etc.

Data analysis: Continuous variables were expressed as Mean ±SD, while categorical variables were expressed in numbers and percentages. Difference in mean score of various parameters was assessed using student's t- test. *P*< 0.05 was considered as significant.

Results

Demographic data

Of the 100 patients enrolled, 70 were men and 30 were women. A total of 39 men were in group D and 31 in group K, while a total of 11 women were present in group D and 19 in group K **(figures 1& 2)**. Mean age of patients in both groups (33.06 ± 11.44 in group D and 33.26 ± 11.47 in group K) was found to be similar (P=0.46). There was a preponderance of male patients in our study.

Figure 1: Age and gender distribution in patients receiving intr-articular dexmedetomidine (n=50)

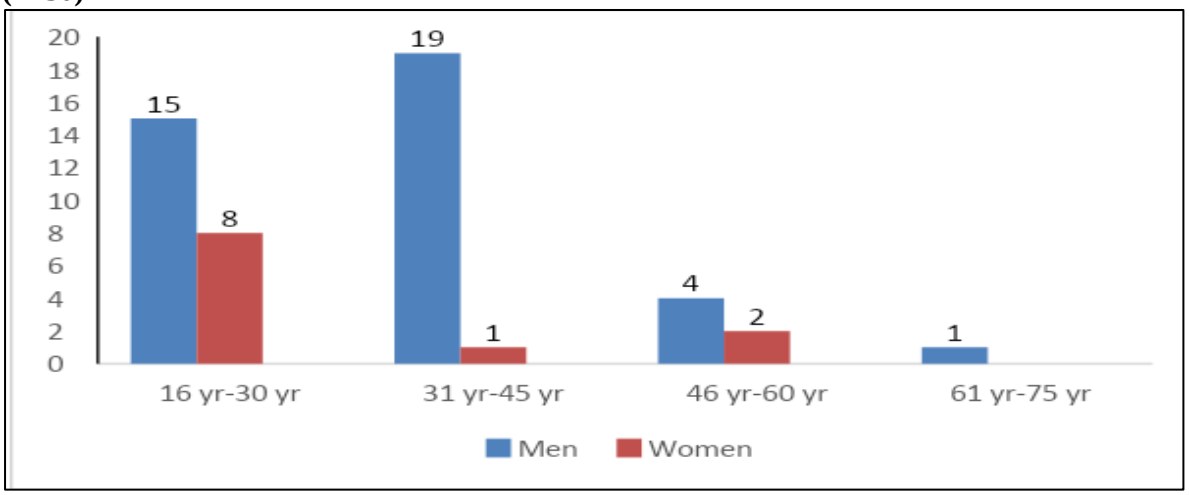
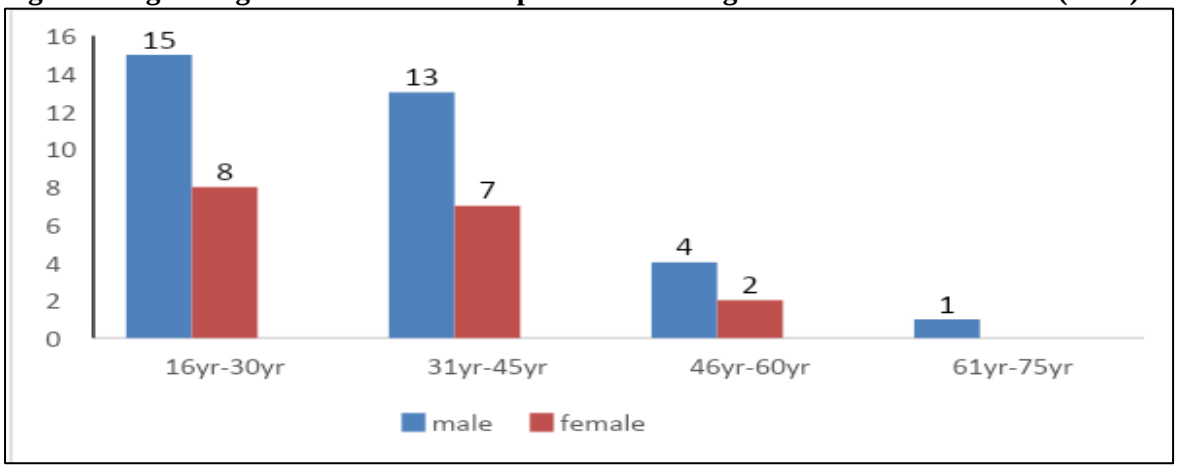


Figure 2: Age and gender distribution in patients receiving intra-articular ketamine (n=50)



At 6 hrs in Group D, 42 patients had VAS score 0 and 8 patients had VAS score 1, whereas in Group K; 1 patient had VAS score 0, 20 patients had VAS score 1, 28 patients had VAS score 2, and 1 patient had VAS score 3. The VAS score of Group D (0.16 ± 0.14) was significantly less as compared to Group K (1.58 ± 0.33) at 6 hours following surgery.

At 12 hrs in Group D, 6 patients had VAS score 0, 31 patients had VAS score 1 and 13 patients had VAS score 2, where as in Group K, 18 patient had VAS score 2 and 32 patients had VAS score 3. The VAS score of Group D (1.14 ± 0.37) was significantly less as compared to Group K (2.86 ± 0.98) at 12 hours following surgery.

At 24 hrs in Group D, 7 patients had VAS score 0, 16 patients had VAS score 1, 18 patients had VAS score 2 and 9 patients had VAS score 3, whereas in Group K; 3 patient had VAS score 1, 16 patients had VAS score 2, 19 patients had VAS score 3, 9 patient had VAS score 4 and 3 patients had VAS score 5. The difference in mean VAS score in both groups at 24 hours was not significant (Table 1). Two patients received rescue analgesic in group D while 5 patients received rescue analgesic in group K. Average duration of analgesia was longer (12.24 hrs) in Dexmedetomidine group compared to 9.71hrs in Ketamine group among patients receiving rescue analgesic.

Table 1: Visual Analogue Scale (VAS) score in patients receiving Intra-articular Dexmedetomidine or Ketamine at 6 hours, 12 hours and 24 hours post surgery

VAS score in study groups (Mean±SD)			
Time (Hrs) since surgery	Group D	Group K	*P* value
6	0.16±0.14	1.58±0.33	<0.001
12	1.14±0.37	2.64±0.98	<0.001
24	2.58±0.90	2.86±0.98	0.15

Table 2. Comparison of heart rate (Mean ± SD) at 6 hours, 12 hours and 24 hours following surgery in patients receiving intra-articular dexmedetomidine or ketamine

Time (Hrs)	**Group D**	**Group K**	***P* value**
6	79.2±5.24	82.55±4.23	0.000366
12	80.94±5.30	83.55±4.61	0.0052
24	80.48±4.84	83.02±5.03	0.006

A statistically significant difference was observed in mean HR in both groups post operatively at 6 hrs, 12 hrs and 24 hrs with group D showing lower mean HR. (P value <0.05 in all).

Table 3. Comparison of mean blood pressure (Mean ± SD) at 6 hours, 12 hours and 24 hours following surgery in patients receiving intra-articular dexmedetomidine or ketamine

Time (Hrs)	**Group D**	**Group K**	**P value**
6	73.88±2.57	83.59±4.00	0.00001
12	84.42±2.87	82.84±5.28	0.4234
24	75.28±3.85	83.12±4.79	0.00001

Mean blood pressure was comparable in both groups at 12 hours post operatively, but a statistically significant difference was observed at 6 hrs and 24 hours with group D showing lower mean BP.

Table 4. Post operative complications observed in patients receiving intra-articular dexmedetomidine and ketamine

Postoperative complication	**Group D**	**Group K**
Hypotension	2	0
Delirium	0	1
Bradycardia	0	0
Convulsion	0	0
Respiratory depression	0	0
Nausea / vomiting	0	0

A total of 3 patients developed complications in the post-operative period with two patients developing hypotension in group D, which was managed with IV fluids. One patient in group K developed delirium, which recovered without any intervention within 30 mins.

Discussion

The most feared aspect for a patient undergoing any surgery is the excruciating post-surgical pain. Pain after knee arthroscopy surgery is caused by irritation of free nerve endings of the synovial tissue, anterior fat pad and joint capsule. Arthroscopic procedures of the knee are performed on outpatient basis, so there is a risk of failure to control postsurgical pain which causes unnecessary suffering, delayed recovery, prolonged hospitalization and increased financial burden to the patient and the hospital. In an attempt to address post-operative pain, anaesthesiologists have tried various evidence based modalities of postoperative pain management.

Good postoperative pain management brings the most gratifying smile on the patient's face in addition to other benefits like attenuation of the neuro-endocrine stress response, reduction of postoperative pulmonary and cardiac complications, an opportunity to institute early physiotherapy and early mobilization. Knee arthroscopy patients require a highly effective peri-operative analgesic regimen with minimal side effects, which can be easily managed away from the hospital or surgical centre. Arthroscopic surgery allows intra-articular orthopedic procedures to be performed with less trauma to surrounding normal soft tissues than is the case for open surgery. In an attempt to improve fast rehabilitation after arthroscopic knee surgery, research has been directed toward newer techniques for postoperative analgesia. More recently, it has been demonstrated to reduce postoperative analgesic requirements.

In the present study, an identical distribution of patients of both groups was observed in terms of mean age. There was a preponderance of male patients in our study. Oza et al. in a study conducted in 2018 reported similar demographic data with male preponderance.[8]

Our study included two groups: Group D (Dexmedetomidine) and Group K (Ketamine). A total of 100 patients were included in the study and randomly allocated into two groups using random numbers. Study drugs were administered intra-articularly just after the completion of arthroscopy. Post-operative analgesia was assessed using VAS score. Also, changes in hemodynamic parameters were noted.

Patients in group D demonstrated a lower mean VAS score at 6 hours and 12 hours as compared to group K. This suggested better pain control in patients receiving dexmedetomidine as compared to those receiving ketamine. Difference in VAS score in study groups at 24 hours was not found to be significant, suggesting a comparable effect at 24 hours. More number of patients demonstrated VAS score 0 to 2 in patients receiving dexmedetomidine at all time intervals as compared to group K. Thus, overall better pain control was observed in patients receiving intra-articular dexmedetomidine as compared to ketamine.

According to our observation, patients in dexmedetomidine group required first analgesic at an average post-operative period of 12.2 hrs while patients in ketamine Group (group K) required the same at an average duration of 9.71 hrs. This suggested that intra-articular dexmedetomidine provided longer duration of analgesia than Ketamine. ELbadawy AM et al. in a study in 2015 noted that intra-articular dexmedetomidine is associated with significantly lower VAS scores and longer time to first analgesic request with reduced analgesic use as compared to ketamine,[5] similar to the present study.

In the present study, postoperative hemodynamics in the form of heart rate and mean blood pressure were recorded at specified intervals. Mean HR was increased more in group K as compared to group D at all time intervals while mean BP was more in group K as compared to group D at 6 and 24 hours. ELbadawy AM et al found similar results regarding hemodynamic variations in both groups.[1] This suggested that dexmedetomidine is more cardiostable than ketamine, when used via intra-articular route for post-operative analgesia.

During the post-operative period; complications were observed in few patients (3%) only. None of the patients in both groups developed nausea, vomiting, respiratory depression, bradycardia or convulsions. However, two patients from Group D developed hypotension which was treated with IV fluids and one patient from Group K developed delirium which subsided without any intervention. Hence, both the drugs were well tolerated in the study population.

Limitations

The study was open label in nature which could have influenced the pain assessment. All the patients were given spinal anesthesia as per the routine protocol of our institute. However, neuroaxial block can affect the pain scores in the early post-operative time. Use of general anaesthesia with endotracheal intubation with short acting anaesthetic agents (Propofol, fentanyl,sevoflurane and N_2O), which allows patients to regain full conciousness within 30 mins after recovery from anaesthesia could have been better. These were the limitations of the present study.

Conclusion

Intraarticular use of dexmedetomidine provides superior postoperative analgesia as compared to ketamine in patients undergoing knee arthroscopy.

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