Indian Journal of Clinical Anaesthesia 2019;6(4):570–575

Content available at: iponlinejournal.com

Indian Journal of Clinical Anaesthesia

Journal homepage: www.innovativepublication.com

Original Research Article

Comparison of postoperative analgesia after intraarticular injection of two different doses of morphine (5 mg) and Morphine (10 mg) with 0.5% bupivacaine in arthroscopic knee surgery : Randomized, double blinded prospective study

Geetha Acharya[1], Sumedha Mehta[1,*]

[1]*Dept. of Anesthesia, Smt Kashibai Navle Medical College and General Hospital, Pune, Maharashtra, India*

ARTICLE INFO

Article history:
Received 06-08-2019
Accepted 30-08-2019
Available online 20-11-2019

Keywords:
Arthroscopy
Morphine
Postoperative
Analgesia
Bupivacaine
Intraarticular

ABSTRACT

Introduction and Aims: Pain relief after knee arthroscopy is preferred for early recovery and mobility. We aim to compare effectiveness and safety of different doses of morphine 5mg and 10mg combined with 0.5% bupivacaine given intra- articularly after knee arthroscopy for postoperative analgesia.

Materials and Methods: This prospective, double blind study was done in 80 patients of either sex, undergoing elective diagnostic / therapeutic arthroscopic knee surgery under spinal anesthesia. Patients were randomly allocated to two groups. 20 ml of 0.5% Bupivacaine with 5 mg, 10 mg morphine as additive were injected intra-articularly in Group 1 and Group 2 respectively. Postoperative analgesia was assessed by Visual Analogue Scale at the 1st, 2nd, 4th, 6th, 12th, 18th and 24th after surgery. Time of the first request of rescue analgesia when VAS>4, total rescue analgesic consumption and any side effects in first 24 hour postoperatively was recorded.

Results: Time of first postoperative rescue analgesic was significantly longer in Group 2 (464.88 $\pm$ 25.00 min) compared to Group 1 (442.75 $\pm$ 39.79 min). Post-operative VAS score was significantly lower at 6th, 8th, 12th and 24th hour in Group 2. Total dose of analgesic used in 24 hours in Group 2 was significantly lower than Group 1. Few side effects noted in both groups were comparable.

Conclusion: We conclude that intraarticular dose of 10mg Morphine is better than 5mg Morphine with 20 ml of 0.5% Bupivacaine as it provides better postoperative analgesia with longer duration and minimal side effects.

1. Introduction

Arthroscopic knee surgery is a commonly performed orthopaedic procedure which is accompanied by variable degree of postoperative pain. Solheim et al.[1] in their study found that 67% of patients who underwent knee arthroscopy under general anaesthesia complained of moderate to severe pain within first postoperative hour. Therefore, management of postoperative pain has become essential factor to improve patient rehabilitation, convalescence and overall patient satisfaction after the arthroscopic procedure. The advantages of adequate postoperative pain control are decrease in stress response to surgery, early ambulation, shorter hospital stay and cost effectiveness. Routine established methods to provide analgesia are systemic analgesics like Non-steroidal anti- inflammatory drugs (NSAIDs) which include paracetamol, diclofenac, ketorolac etc. and opioids mainly like morphine, fentanyl and tramadol. Regional and local methods to provide analgesia include peripheral nerve blocks like lumbar plexus block, femoral nerve block and intra-articular injection of morphine, tramadol and local anaesthetics.[2–4] The intra-articular (IA) route for providing postoperative pain relief with morphine after arthroscopic knee procedure became prevalent after a pivotal study done by Stein and associates in 1991. The routine use of morphine for post-operative analgesia is not preferred due to the complications associated with it such as drowsiness,

* *Corresponding author*.
E-mail address: drsumedhamehta1@gmail.com (S. Mehta).

https://doi.org/10.18231/j.ijca.2019.111

respiratory depression, pruritus and urinary retention. Stein et al. found IA morphine results in pain relief through its action on peripheral opioid receptors present in knee joint and with no major side effects.[5] Morphine exerts analgesic effect by acting on local opioid receptors, has anti-inflammatory effect on joints and is not associated with chondrotoxicity.[6] Various doses of morphine and bupivacaine are used in literature.[7–9] There are few study investigating the efficacy of higher doses of intraarticular morphine combined with 0.5% bupivacaine for pain relief in arthroscopic knee surgery. We hypothesized that higher dose of intraarticular morphine and bupivacaine, will result in increase in duration of effective analgesia with reduction in analgesic requirement. In order to investigate the effective dose of morphine along with bupivacaine which has minimum side effects for arthroscopic knee surgery, our study was designed. In this study our primary aim is to assess analgesic efficacy of two different doses of morphine with bupivacaine and secondary aim is to assess side effects of intraarticular morphine.

2. Materials and Methods

This randomized, prospective double blind study was done in Tertiary Care Hospital over a period of one year. After approval of Institutional Ethical Committee and written informed consent, 80 patients of either sex, aged 18-55 yrs belonging to ASA grade I & II undergoing elective diagnostic or therapeutic arthroscopic knee surgery under spinal anesthesia were enrolled in the study. Patients were not included in the study if they refused to participate, or had acute traumatic injury to the knee, history of allergy to study medications, history of addiction or preoperative consumption of opioid drugs, history of chronic pain, history of consumption of MAO inhibitor drugs. Patients with pregnancy, severe cardiovascular, respiratory, metabolic or neurological disease, bleeding and clotting disorder, infection at site of lumbar puncture were excluded from the study. Patients were randomly allocated to two groups by using a computer generated random numbers after taking written informed consent. Group1(control arm)- included 40 patient who received Morphine 5 mg with 0.5% Bupivacaine 19 ml with 0.5 ml normal saline (in order to make it up to 20 ml volume) intra-articularly. Group 2(study arm) - included 40 patients who received Morphine 10 mg with 0.5% Bupivacaine 19 ml intra-articularly. Study drugs were prepared in a coded syringe according to randomization under all aseptic precaution by a senior anesthesiologist who was not involved in either intraoperative or postoperative care of patient.

All patients were investigated and clinically examined before surgery. They were informed and explained about the assessment of pain on a 10 point visual analog scale (VAS), where 0 – no pain at all and 10 – worst pain imaginable. Preoperatively the patients were nil by mouth for 6 hours. All the patients were premedicated with tablet alprazolam 0.25 mg night prior to surgery. Routine premedication was given Tab Pantoprazole 40mg orally with sips of water in the morning of surgery. Patients were instructed preoperatively to express their pain on the 0-10 VAS. On day of surgery, a 20 G IV catheter was secured and patient was preloaded with Ringer lactate solution 15 ml/kg. After the patient was shifted inside operation theatre, hemodynamic monitoring of Pulse, Non-Invasive blood pressure (NIBP), Oxygen saturation (SPO2), ECG was started and monitoring continued throughout the surgical procedure.

Under absolute aseptic precaution Subarachnoid block was performed in sitting position at L3 and L4 inter-vertebral space in median approach using 27-G Quincke spinal needle with 3 cc of 0.5% Bupivacaine heavy. Towards the end of arthroscopic knee surgery drug combination was injected by the orthopaedic surgeon after skin suturing, from superolateral aspect intra-articularly and dressing applied. Either 5 mg of Morphine in 0.5% Bupivacaine 19 ml and 0.5 ml of normal saline or 10 mg of Morphine in 0.5% Bupivacaine 19 ml was injected Intra-articularly into the knee via 18G needle. This was taken as the start time of the study. Tourniquet was kept inflated for 10 minutes post drug injection. Drain kept if any was clamped for half an hour post drug injection with tourniquet still inflated in situ. The tourniquet will be deflated and patient was shifted to post anesthesia recovery unit for monitoring. We will record incision time, time of completion of skin closure, duration of surgery, time of IA injection and time of request of first rescue analgesia. Duration of analgesia will be time since the administration of IA injection till the first request of Rescue analgesia. Post-operative pain was assessed with 10-point VAS. Pulse rate, respiratory rate and blood pressure were also recorded along with the VAS. VAS was recorded at 1, 2, 4, 6, 12, 18 and 24 hour postoperatively by an anaesthesiologist who is unaware of allocated patient group and injected IA study drug. The sensory blockade will be recorded by pin prick method. The intensity of motor block was noted at 1hr, 2hr and 6hr postoperatively in non – operated leg by Bromage score. When a patient's VAS score is $\geq$ 4 or the patient requests for analgesics, rescue analgesics were given. First rescue analgesic given was Inj.Paracetamol (20mg/kg). If patient was still having pain for next half an hour, next rescue analgesic Inj.Diclofenac (1mg/kg) will be administered. Total rescue analgesic consumption in first 24 hour postoperatively was recorded in terms of number of doses. Side effects of opioid administration like sedation, dizziness, nausea, vomiting, constipation, physical dependence, tolerance, and respiratory depression, urinary retention were noted. Postoperative nausea and vomiting (PONV) will be treated with inj. Ondansetron 4 mg i.v. Incidence of pruritus was treated with Inj. Pheniramine

maleate 2ml i.v. Respiratory depression was defined as respiratory rate <8 / min and will be treated with injection Naloxone as per the need. A sample size of 33 patients undergoing elective arthroscopic knee surgery under spinal anesthesia in each group was sufficient to detect a difference of 0.5 units in VAS score at 24 h post-operative pain, between two independent Group 1 and Group 2, assuming a mean VAS score 2.6±0.6 units in Group 1 while, 2.1±0.8 units in Group 2 (values from literature) using a two-tailed t-test of the difference between means, a power of 80%, and a significance level of 5%. This sample size was increased to 40 per group (total of 80), to allow for a predicted drop-out over a follow-up period. Simple randomization (in two groups) was performed using computer-generated random numbers. Statistical analysis was carried out with the help of SPSS (version 25) for Windows package (SPSS Science, Chicago, IL, USA). The description of the data was done in form of mean ± Standard deviation/ median (minimum - maximum) as appropriate for quantitative data while in the form of % proportion for qualitative (categorical) data. For quantitative data, Unpaired Student's t-test / Mann-Whitney U was used to test statistical significance of difference between two independent groups. For comparison of categorical variables (i.e. to examine the associations between qualitative/quantitative variables), chi-square test was used. p-value of less than 0.05 was considered statistically significant.

3. Results

There was no significant difference between the two morphine groups with respect to age, sex distribution and weight of the patients as shown in (Table 1). Distribution of different arthroscopic procedures performed in both groups were similar. Diagnostic arthroscopy with debridement being performed in 11, 10 patients, anterior cruciate ligament reconstruction in 14, 15 patients and meniscectomy was performed in 15, 15 patients in Group 1 and Group 2, respectively. Duration of surgery was similar in both groups (Figure 1).

The time of the request of first postoperative rescue analgesia i.e. duration of analgesia was significantly longer ($p < 0.01$) in Group 2 (464.88 ± 25.00 min) compared to Group 1(442.75 ± 39.79 min) as shown in (Figure 2). All our patients required first dose of paracetamol, however we found significant reduction (p-value < 0.05) in requirement of 2nd dose of paracetamol in Group 2 (Figure 2). There was significant reduction in requirement of number of doses of rescue analgesia in 24hrs postoperative in Group 2 indicating better pain relief. None of our patients required second rescue analgesia of diclofenac as first rescue analgesia of paracetamol provided adequate pain relief.

VAS score at different time interval were noted post-operatively as shown in (Table 2). The VAS score was 0 in both groups at first and second post-operative hours. There was no significant difference in VAS score at 4^{th} hr post-operatively between both groups. However, the VAS score in Group 2 was significantly ($p < 0.01$) lower at 6^{th}, 12^{th}, 18^{th} and 24^{th} hour after surgery than Group 1, indicating better analgesia. In our study, we noticed two side effects namely PONV and pruritus (Figure 3). 2.5% PONV incidence was observed in both groups whereas incidence of pruritus was 5% in Group 2, none in Group 1. We found no statistically significant difference between the two morphine groups for the complications such as pruritus, post- operative nausea and vomiting (PONV). No other side effects were observed in both groups.

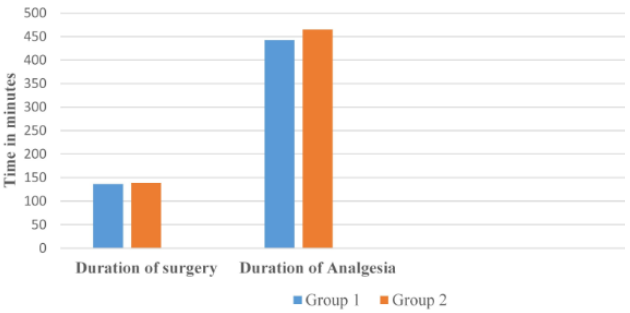

Fig. 1: Duration of surgery and Analgesia

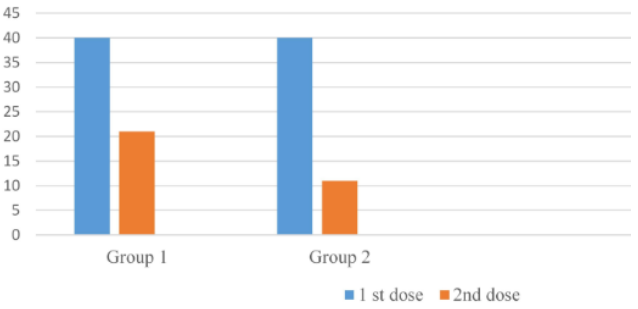

Fig. 2: Comparison of number of doses of rescue analgesia

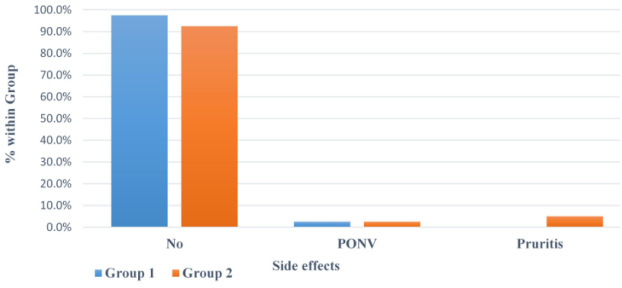

Fig. 3: Comparison of side effects between the two groups

Table 1: Comparison of demographic data

Mean ± SD Parameter	Group 1(n=40)	Group 2(n=40)	p-value
Age (years)	32.33 ± 10.60	32.15 ± 9.27	0.938
Weight (kg)	63.88 ± 6.43	63.10 ± 5.17	0.554
Gender (M:F)	28:12	22:18	0.248

Table 2: Comparison of VAS score at different time intervals after surgery.

Time in hr after surgery	Median VAS score(minimum-maximum) in Group A patients	Median VAS score(minimum-maximum) in Group B patients	p-value
1 hrs.	0	0	0.999
2 hrs.	0	0	0.999
4 hrs.	2(1-2)	2 (1-2)	0.824
6 hrs.	3(2-5)	2 (2-4)	0.004*
12 hrs.	5(3-7)	4 (2-7)	0.002*
18 hrs.	3(2-6)	3 (2-6)	0.013*
24 hrs	4(2-5)	3 (2-6)	0.001*

4. Discussion

Arthroscopic knee surgery is the most common, minimally invasive orthopaedic procedures performed as inpatient or day care surgery. Arthroscopic surgery helps to either diagnose, treat knee joint injuries like ACL tear and diseases like osteoarthritis that affect the joints. It is assumed that knee arthroscopy, being a minimally invasive surgery with small incision, will result in less pain. However, one of the most common complain seen after the procedure is the pain in operated knee which causes delay in ambulation and longer stay in hospital, thus defeating the whole purpose of day care surgery. So providing a pain free post- operative period has become primary concern for anaesthesiologist. Various studies involving regional blocks, local, intraarticular drugs, systemic drugs and pre-emptive analgesia[10] are done over years in view of finding effective and safe analgesia for knee arthroscopy. A multimodal approach involving intraarticular injection of opioids with or without local anesthetic drugs combined with systemic NSAIDs is becoming a popular technique for providing pain relief after knee arthroscopic procedures. Bupivacaine is an amino-amide type of local anesthetic drug commonly used to provide post-operative analgesia in knee arthroscopy. Chirwa SS et al. investigated the analgesic efficacy and safety of 20 ml of intraarticular 0.25% bupivacaine for pain relief in surgical knee arthroscopies. They noted an early onset of action of bupivacaine which was less than 5 mins and the duration of pain relief was extended upto 2 hr. They concluded that intra-articular bupivacaine is safe and effective method for achieving postoperative analgesia.[11] Weiker GG et al. studied the serum levels of 1% lidocaine with epinephrine (25 ml) and 0.25% bupivacaine (25 ml) following their intraarticular and subcutaneous injection (combined solution up to 40 ml) for providing local anaesthesia in knee arthroscopy. The total volume of local an aesthetic drugs used in their study was very high, but they found the serum levels of anaesthetic agents within safe limit. They also observed that the use of local an aesthetic technique resulted in good patient satisfaction and reduced costs.[12] The only reported exceptions of local anesthetic toxicity of IA Bupivacaine was observed due to IA fracture which resulted in absorption of drug into systemic circulation.[13] We have used 20ml of 0.5% IA Bupivacaine in our study considering the dose and volume to be safe and effective for post-operative analgesia in knee arthroscopy as shown in previous studies. Time of release of tourniquet after intraarticular injection of drugs is considered an important factor. The duration from intra- articular injection to tourniquet release if longer, results in the better binding of drugs to local tissues. We kept tourniquet inflated for 10 min and drain if kept, was also clamped for 20 min after administration of study drugs as suggested by earlier studies.[14,15]

Although it is widely accepted that opioids produce analgesia by its action on opioid receptors at the spinal and supraspinal levels, there is increasing speculation about action of opioids at peripheral sites. Various animal and experimental studies suggest that morphine exerts a direct effect on peripheral opioids receptors which were induced by inflammation in joints.[16–19] The longer duration of action of IA morphine may be explained firstly by its poor lipid solubility which impede its passage across the synovial membrane into the blood circulation and thus increasing the effective half-life of drug. Secondly by the production of active metabolites like morphine-6-glucoronide which may be the reason for the prolonged period of pain relief.[14] Analgesic effects of low dose morphine (1mg) is found to be dose-dependent, specific to opioid receptors and

antagonized by naloxone.[5]

Currently, many studies have showed that combination of intraarticular bupivacaine and. morphine give better pain relief in knee arthroscopy.[20,21] Keeping this in mind, we investigated two different doses of IA morphine combined with 0.5% bupivacaine for finding the optimal dose for effective post-operative analgesia. In our study, we found morphine 10 mg provides significantly prolonged (464.88 $\pm$ 25.00 min) and better post-operative analgesia than morphine 5 mg (442.75 $\pm$ 39.79 min) in combination with 0.5% bupivacaine. We noted patients in both groups had no pain (VAS score 0) in first and second hour after surgery. This can be due to the immediate extended analgesic effect of intraarticular bupivacaine. We did not found any significant difference between both groups in VAS score at 4^{th} hour postoperative. However, the VAS score in Group 2 was significantly ($p < 0.01$) lower at 6^{th}, 12^{th}, 18^{th} and 24^{th} hour after surgery than Group 1, indicating better analgesia. All our patients required first dose of paracetamol, however we found significant reduction (p-value < 0.05) in requirement of 2nd dose of paracetamol in Group 2. In Group 1, 21 patients required second dose of paracetamol compared to 11 patients in Group 2. The significant reduction in VAS score and number of rescue analgesia in 24 hrs in Group 2 indicates better analgesia than Group 1. We noted two complications pruritus and post-operative nausea and vomiting (PONV) in our study. There was no statistically significant difference in complications between Group 1 and Group 2. No other side effects like sedation, respiratory depression were observed in both groups. In our study, we have used higher doses of morphine (10mg and 5mg) with bupivacaine and found no significant side effects. So we can conclude that morphine 10 mg when compared to morphine 5 mg, can be safely used in knee arthroscopy with minimal side effects.

Yari et al.[20] studied three different doses of IA morphine (5, 10, 15mg respectively) with regards to postoperative analgesia. The authors found increase in level of analgesia as well as increased duration of analgesia in patients who are given IA morphine 15 mg combined with 0.5% Bupivacaine. They concluded that increasing the dose of intra-articular morphine resulted in better analgesic effect and showed a linear decrease in VAS score with less requirement of supplementary analgesics. In our study duration of analgesia was significantly longer ($p < 0.01$) in Group 2 compared to Group 1. We also found better analgesia in Group 2 in view of longer duration of analgesia and less requirement of rescue analgesia in 24 hr similar to their study. They found 15 mg morphine did not cause any drowsiness and there was no significant differences in terms of nausea and itching complications among all group. We did not use high dose (15 mg), as we had included both ASA 1 and ASA 2 patients in our study. With the morphine doses (5 mg and 10 mg) used in our study, we found one case of PONV in each group and two cases of pruritus in Group 2 which were not statistically significant.

Khoury et al.[21] compared IA morphine (1 mg), bupivacaine (20 ml, 0.25 %) or combination of the two for the evaluation of effect of morphine on pain following arthroscopic knee surgery. IA bupivacaine had better analgesia in first hour whereas IA morphine had better analgesic effect in later time period. Supplementary analgesic requirement in morphine group was higher in first hour. In our study we had taken both morphine and bupivacaine, so this initial first hour difference was not seen. None of our patient complained of pain during first two hours postoperatively. They concluded that morphine and bupivacaine combination is superior to either of drugs when injected alone.

In contrast to above studies, Raja et al.[22] compared analgesic efficacy of intra-articular morphine (3 mg), 0.25% bupivacaine and normal saline as control, combined with 100 microgram epinephrine in 47 patients undergoing knee arthroscopy under epidural anaesthesia. They found no evidence of action of morphine on peripheral opioid receptors. They have used epidural anaesthesia, which may have resulted in reduced postoperative pain. In another similar study, Heard et al.[23] found intra-articular morphine did not provided any prolonged analgesic effect compared to 0.25% bupivacaine. In this study, anaesthesia technique was not standardized which may explain conflicting result of the study. Arthroscopic knee surgery was done under either regional (spinal or epidural) or general anaesthesia. They found decreased VAS in patients receiving regional blocks compared to patients receiving general anaesthesia.

Garcia et al. compared the efficacy of IA Morphine 10 mg with placebo in 50 patients who underwent total knee arthroplasty.[8] They concluded that IA 10 mg Morphine results in longer period of analgesia with decreased consumption of rescue analgesia in first 24 hrs postoperative. They also observed decrease in VAS score at 2 and 6 hours. This study supports our study, as it confirms that longer duration of analgesia is achieved with higher dose of morphine.

We have done knee arthroscopy surgery under spinal anaesthesia in our study. Complication like urinary retention can be caused by either spinal anaesthesia or as systemic side effect of morphine drug. None of our patient had urinary retention. One of the limiting factor of our study is we did not follow our patients for observation of any long term toxic effects of study drugs . We recommend further studies for formulation of reliable and safe protocol for multimodal analgesia in knee arthroscopy.

5. Conclusion

We conclude that Intra-articular dose of 10 mg Morphine with 0.5% Bupivacaine is ideal drug for post-operative analgesia in knee arthroscopy when compared to 5mg

Morphine, with 20 ml of 0.5% Bupivacaine. It provides superior postoperative analgesia with longer duration and minimal side effects.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Solheim N, Rosseland LA, Stubhaug A. Intra-articular morphine 5 mg after knee arthroscopy does not produce significant pain relief when administered to patients with moderate to severe pain via an intra-articular catheter. *Reg Anesth Pain Med*. 2006;31(6):506–513.
2. Andres J, Bellver J, Barrera L, Febre E, Bolinches R. A comparative study of analgesia after knee surgery with intraarticular bupivacaine, intraarticular morphine, and lumbar plexus block. *Anesth Analgesia*. 1993;77(4):727–730.
3. Goranson BD, Lang S, Cassidy JD, Dust WN, Mckerrll J. A comparison of three regional anaesthesia techniques for outpatient knee arthroscopy. *Canadian J Anaesth*. 1997;44(4):371–376.
4. Zeidan A, Kassem R, Nahleh N, Maaliki H, El-Khatib M, Struys MM. Intraarticular Tramadol-Bupivacaine combination prolongs the duration of postoperative analgesia after outpatient arthroscopic knee surgery. *Anesth Analg*. 2008;107(1):292–299.
5. Stein C, Comisel K, Haimerl E, Yassouridis A, Lehrberger K, et al. Analgesic effect of intraarticular morphine after arthroscopic knee surgery. *New Engl J Med*. 1991;325(16):1123–1126.
6. Anz A, Smith MJ, Stoker A, Linville C, Markway H, et al. The effect of Bupivacaine and Morphine in a coculture model of diarthrodial joints. *Arthrosc*. 2009;25(3):225–231.
7. Joshi GP, Mccarroll SM, Brady OH, Hurson BJ, Walsh G. Intra-articular Morphine for pain relief after anterior cruciate ligament repair. *Br J Anesth*. 1993;70:87–88.
8. Garcia JB, O BNJ, Vasconcelos JW, Ferro LS, Silva RC. Analgesic efficacy of the intra-articular administration of high doses of morphine in patients undergoing total knee arthroplasty. *Rev Bras Anesthesiol*. 2010;60:1–12.
9. M, Bigoni RP, Vitale M, Marino G, Fraschini MR, N. Pre and postoperative intra-articular analgesia for arthroscopic surgery of the knee and arthroscopy-assisted anterior cruciate ligament reconstruction. A double-blind randomized, prospective study. *Knee Surg Sports Traumatol Arthrosc*. 1997;5:206–212.
10. Miskulin M, Maldini B. Outpatient Arthroscopic Knee Surgery Under Multimodal Analgesic Regimens. *Arthrosc*. 2006;22(9):978–983.
11. Chirwa SS, Macleod BA, Day B. Intraarticular bupivacaine (Marcaine) after arthroscopic meniscectomy: a randomized double-blind controlled study. *Arthrosc: J Arthrosc Related Surg*. 1989;5(1):33–35.
12. Weiker GG, Kuivila TE, Pippinger CE. Serum lidocaine and bupivacaine levels in local technique knee arthroscopy. *Am J Sports Med*. 1991;19(5):499–502.
13. Sullivan SG, Abbott PJ. Cardiovascular toxicity associated with IA Bupivacaine. *Anesth Analg*. 1994;79:591–593.
14. Joshi GP, Mccarroll SM, Cooney CM. Intra-articular morphine for pain relief after knee arthroscopy. *J Bone Joint Surg Br*. 1992;74:749–751.
15. Whitford A, Healy M, Joshi GP, Mccarroll SM, O'brien T. The effect of tourniquet release time on the analgesic efficacy of intraarticular morphine after arthroscopic knee surgery. *Anesth Analg*. 1997;84(4):791–793.
16. Joris JL, Dubner R, Hargreaves KM. Opioid Analgesia at Peripheral Sites: A Target for Opioids Released during Stress and Inflammation? *Anesth Analg*. 1987;66(12):1277–1281.
17. Ferreira SH, Nakamura M. II-Prostaglandin hyperalgesia: the peripheral analgesic activity of morphine, enkephalins and opioid antagonists. *Prostaglandins*. 1979;18(2):191–200.
18. Berg KA, Patwardhan AM, Sanchez TA, Silva YM, Hargreaves KM, Clarke WP. Rapid Modulation of -Opioid Receptor Signaling in Primary Sensory Neurons. *J Pharm Exp Ther*. 2007;321(3):839–847.
19. Stein C, Gramsch C, Hassan AH, Przewlocki R, Parsons CG, Peter K. Local opioid receptors mediating antinociception in inflammation: endogenous ligands. *Progress Clin Biological Res*. 1989;328:425–427.
20. Yari, c MS, Golfam P, Makhloogh Z. Analgesic efficacy of intra-articular Morphine after arthroscopic knee surgery in sport injury patients. *J Inj Violence Res*. 2013;5(2):84–88.
21. Khoury GF, Chen A, De G, Stein C, Morphine I. Bupivacaine, and Morphine/Bupivacaine for pain control after knee videoarthroscopy. *Anesthesiol*. 1992;77(2):263–266.
22. Raja SN, Dickstein RE, Johnson CA. Comparison of postoperative analgesic effects of intraarticular bupivacaine and morphine following arthroscopic knee surgery. *Anesthesiol*. 1992;77(6):1143–1147.
23. Heard SO, Edwards WT, Ferrari D, Hanna D, Wong PD, et al. Analgesic effect of intraarticular bupivacaine or morphine after arthroscopic knee surgery: a randomized, prospective, double-blind study. *Anesth Analgesia*. 1992;74(6):822–826.

Author biography

Geetha Acharya Senior Resident

Sumedha Mehta Assistant Professor

Cite this article: Acharya G, Mehta S. Comparison of postoperative analgesia after intraarticular injection of two different doses of morphine (5 mg) and Morphine (10 mg) with 0.5% bupivacaine in arthroscopic knee surgery : Randomized, double blinded prospective study. *Indian J Clin Anaesth* 2019;6(4):570-575.