

Comparison of analgesic effect of intraarticular buprenorphine, fentanyl and morphine following arthroscopic surgery of knee

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Abstract

Background and Aims: Pain after orthopaedic surgery depends on the site and extent of surgery and the preoperative use of analgesics by the patient. Arthroscopic procedures are routinely performed on outpatient basis and have spared patients large incisions and decreased morbidity compared with open incisions but has not eliminated pain. At present several techniques are available to treat pain following arthroscopic surgeries; these include the use of opioids (providing either peripherally or centrally mediated analgesia), local anaesthetics, non-steroidal anti-inflammatory drugs, corticosteroids, clonidine and cryotherapy. Here we sought to compare the analgesic effect of intra-articular administration of morphine, fentanyl, buprenorphine and placebo following arthroscopic surgery of knee. **Methods:** A prospective, randomised, placebo controlled, double blind comparative study conducted in 80 patients of either sex, who underwent arthroscopic surgery of knee, between the age group of 18 and 65 years and of ASA class I and II physical status were included in the study. pts were randomly assigned equally to one of the 4 groups of 20 each by a sealed envelope method. The groups were Group A: Patients receiving IA Buprenorphine 100mcg in 20 ml normal saline. Group B- Patients receiving IA Fentanyl 50mcg in 20 ml normal saline. Group C- Patients receiving IA Morphine 3mg in 20 ml normal saline. Group D- Patients receiving IA 20 ml normal saline as placebo. parameters monitored were degree of analgesia along with hemodynamic parameters and side effects. data were analysed using student's t-test for continuous variables and Chi-Square test was used to find out the association between categorical variables. **Results:** We found that 100mcg buprenorphine or 0.5% bupivacaine when injected intra-articularly produced good and comparable postoperative pain control and reduced supplementary analgesic requirement when compared to the groups. **Conclusion:** Intra-articular buprenorphine and fentanyl provided effective post-operative pain relief and reduced rescue analgesic requirement in the first 8 hours following arthroscopic knee procedures. It also revealed that buprenorphine and fentanyl are better intra-articular analgesics than morphine. While intra-articular morphine was found to provide good pain relief during early post-operative period, it lacked analgesic efficacy in the latter half of our observation period.

Keywords: Intraarticular, Analgesia, Opioids, Arthroscopy.

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Received Date: 05/08/2015 Revised Date: 30/08/2015 Accepted Date: 10/09/2015

Access this article online

Quick Response Code:



Website:

www.statperson.com

DOI: 11 September 2015

INTRODUCTION

Pain is a common human experience, a symptom frequently encountered in clinical practice that is usually associated with actual or impending tissue damage. "Failure to relieve pain is morally and ethically unacceptable." Adequate pain relief could be considered a basic human right. Pain is not a straightforward sensory "perception". It is an "experience" as the physiological sensation is inseparable from the associated emotional distress. Post operative pain management is to reduce an individual patient's pain to a tolerable level with minimal or no associated suffering or distress. Pain after orthopaedic surgery depends on the site and extent of surgery and the preoperative use of analgesics by the

patient. Arthroscopic procedures are routinely performed on outpatient basis and have spared patients large incisions and decreased morbidity compared with open incisions but has not eliminated pain. At present several techniques are available to treat pain following arthroscopic surgeries; these include the use of opioids (providing either peripherally or centrally mediated analgesia), local anaesthetics, non-steroidal anti-inflammatory drugs, corticosteroids, clonidine and cryotherapy. Common methods of postoperative pain management in hospitalized patients (parenteral or extradural opioids) appear to be unsuitable for outpatient surgery. The evidence of synovial opioid receptors supports the use of intra-articular (IA) opioids to achieve a peripheral opiate receptor-mediated analgesia. Morphine is the most frequently used opioid analgesic. Buprenorphine is a partial agonist with a higher receptor affinity than morphine, which accounts for intense and prolonged analgesia. Better postoperative analgesia was reported with intra-articular fentanyl when compared to morphine. The effects of intra-articular application of opioids on postoperative pain relief had been evaluated by various direct (visual, numerical or verbal scales) and indirect (consumption of supplementary analgesic and time elapsed before the first supplementary analgesic request made) measures. Here we sought to compare the analgesic effect of intra-articular administration of morphine, fentanyl, buprenorphine and placebo following arthroscopic surgery of knee.

MATERIAL AND METHODS

The study designed was a prospective, randomised, placebo controlled, double blind comparative study conducted at Amrita Institute of Medical Sciences and Research centre, Kochi. 80 patients of either sex, who underwent arthroscopic surgery of knee, between the age group of 18 and 65 years and of ASA class I and II physical status were included in the study. Patients of ASA III and IV physical status and patients on chronic medications were excluded from the study. After approval from the hospital ethics committee, 80 patients enrolled in this study were randomly assigned equally to one of the 4 groups of 20 each by a sealed envelope method. The groups were:

Group A: Patients receiving IA Buprenorphine 100mcg in 20 ml normal saline.

Group B: Patients receiving IA Fentanyl 50mcg in 20 ml normal saline.

Group C: Patients receiving IA Morphine 3mg in 20 ml normal saline.

Group D: Patients receiving IA 20 ml normal saline as placebo.

The randomized assignment was sealed in an envelope and handed over to a senior anaesthesia technician, who

would verify the group on the day of surgery and prepared the bolus solution of drug with 20ml 0.9% Normal saline under aseptic precautions. This was injected intra-articularly at the end of the arthroscopic surgery by the operating surgeon. This senior technician did not participate in any other phase of the study. The patient, the operating surgeon, the anaesthesiologist conducting the case and the nursing staff who assessed the pain and delivered rescue medication, if required, were blinded regarding the drug used.

Anaesthetic technique and performance

All patients were premeditated with histamine-2 blocker (Ranitidine 150 mg) and benzodiazepine (Alprazolam 0.5mg) the night before and on the day of surgery. Postoperative pain intensity was assessed by visual analogue scale which is a "0 to 10" cm Scale, with score 0 as "No Pain", up to 3 mild bearable pain, "3 to 5" as "Moderate Pain", greater than "5" as "Severe Pain" and "10" as "Worst Pain". All patients were explained about visual analogue scale before surgery and written informed consent was obtained. After shifting the patient to operation theatre, an 18G intravenous cannula was secured and connected to intravenous fluid. Pre-induction monitoring included pulse-oximeter, non-invasive blood pressure monitoring and continuous electrocardiography. Injection midazolam 1mg and injection glycopyrrolate 0.01mg/kg was administered intravenously. After pre-oxygenation for 3 minutes with 100% oxygen, anaesthesia was induced with injection fentanyl 2mcg/kg and injection propofol 2mg/kg intravenously. After loss of consciousness and eye lash reflex, appropriate size laryngeal mask airway (LMA) was placed. After confirming proper placement of LMA, patient's ventilation was assisted or left breathing spontaneously if found satisfactory with continuous capnography monitoring. Oxygen, nitrous-oxide combination was administered in 1:2 ratios with isoflurane 0.6% to 2% concentration throughout the procedure. No further analgesics or sedative medications were given for the duration of the procedure. At the end of the surgical procedure, before tourniquet was released the surgeon injected study drug intra-articularly and patient was extubated.

Pain assessment and data collection

Post operative pain intensity scores and hemodynamic data (heart rate and blood pressure) were recorded 15 min after extubation and noted as the score at 0 hour, further pain scores were recorded at 1, 2, 4 and 8 hours by the bedside nursing staff who was explained about visual analogue scale and rescue analgesia. Any visual analogue score greater than 3 were given injection tramadol 50mg intravenously as rescue analgesia. The nursing staff recorded the time of first rescue analgesia and total dose

of rescue analgesia during 8 hours. Side effects like nausea, vomiting, pruritis, urinary retention and respiratory depression were specifically looked for during the observation period.

Statistical methodology

The study sample size was determined to be at least 18 patients in each of the 4 groups studied, which would provide 80% power for detecting a significant difference in analgesic effect between the groups. The student t – test was used both to assess homogeneity and to compare the main results and also to find difference between the groups for continuous variables. Data were analyzed using SPSS 11.0 software. A descriptive statistical tool such as mean was used to represent the continuous data. Differences within the groups were analyzed using analysis of variance and Post Hoc test was used to test the difference between individual groups. Chi-Square test was used to find out the association between categorical variables. In all cases, the level of statistical significance (P value) was less than 0.05.

OBSERVATIONS AND RESULTS

During the period of August 2006 and November 2007, 80 patients in age group of 18-65 years with mean age of 35 years were studied. Distribution of patients in each of the 4 groups was similar with respect to demographics, diagnosis and operative procedures.

Age distribution

The mean age in the study population was 35 years. The age comparison was done by student t test, which demonstrated no significant difference in its distribution among 4 groups.

Table 1: Age distribution among 4 groups sex distribution

	GROUP (mean + /std deviation)			
	A(Buprenorphine)	B (Fentanyl)	C(Morphine)	(Placebo)
AGE (years)	36.4±11.9	33.3±10.5	36.8±12.0	34.0±10.4

Table 2: Sex distribution among 4 groups

SEX	GROUP (NO OF PATIENTS)			
	A(Buprenorphine)	B (Fentanyl)	C(Morphine)	D(Placebo)
F	3	3	5	3
M	17	17	15	17

There was no difference between groups in terms of sex ($p = 0.792$). 66 male and 14 female patients were enrolled in this study. The group comparison was done by student t test, which demonstrated no significant difference in its distribution among 4 groups with regard to distribution of sex and also there was no difference between groups in terms of ASA ($p = 0.951$). The group comparison was done by student t test, which demonstrated no significant difference in its distribution among 4 groups with regard to distribution of ASA physical status

Surgery

Table 3: Surgeries among 4 groups

SURGERY	GROUP (NO. OF PATIENTS)			
	A (Buprenorphine)	B (Fentanyl)	C (Morphine)	D (Placebo)
ACL Reconstruction	11	11	10	13
Meniscectomy	6	4	3	5
Partial Meniscectomy	0	0	2	0
Synovectomy	3	5	5	2

There is no difference between groups in terms of surgeries ($p = 0.846$). The group comparison was done by student t test, which demonstrated no significant difference in its distribution among 4 groups with respect to operative procedures.

COMPARISON OF ANALGESIA

Visual analogue scores assessed at 0, 1, 2, 4, and 8 hours were compared with chi-square test for statistical difference among the groups. **Visual Analogue Score with respect to groups at 0 hour;**

Table 4: Visual analogue score at 0 hour

VAS	group (no. of patients)			
	A(Buprenorphine)	B (Fentanyl)	C(Morphine)	D (Placebo)
0	20	20	20	0
3	0	0	0	2
4	0	0	0	9
5	0	0	0	6
6	0	0	0	3

Table 5: Comparison of analgesia at 0 hour

	Group (no. Of patients)			
	A (Buprenorphine)	B (Fentanyl)	C (Morphine)	D(Placebo)
VAS <3	20	20	20	0
VAS >3	0	0	0	20

Visual Analogue Score <3 - Adequate analgesia. Visual Analogue Score >3 - Inadequate analgesia. Mean visual analogue scores analysed during the 0 hour were lower (VAS=0) in A, B and C groups when compared to placebo group (D) (Table 5). There was statistically significant difference among 4 groups with respect to visual analogue score at 0 hour ($p = 0.000$) when analysed by chi-square test. Pain intensity scores were higher in placebo group (D) when compared with other 3 groups. But there was no statistical difference among A, B and C groups ($p = 0.944$). In placebo group all patients received rescue analgesia during 0 hour (VAS > 3) which indicated inadequate analgesia (Table 6). None of the patients received rescue analgesics in the other 3 groups (VAS >3). Visual Analogue Score with respect to groups at 1 hour;

Table 6: Visual analogue score At 1 hour

GROUP (NO. OF PATIENTS)				
VAS	A (Buprenorphine)	B (Fentanyl)	C (Morphine)	D (Placebo)
0	20	20	20	0
3	0	0	0	0
5	0	0	0	5
6	0	0	0	10
7	0	0	0	5

Table 7: Comparison of analgesia at 1 hour

GROUP (NO. OF PATIENTS)				
	A (Buprenorphine)	B (Fentanyl)	C (Morphine)	D (Placebo)
VAS <3	20	20	20	0
VAS >3	0	0	0	20

Visual analogue scores compared at 1 hour after the first assessment in the post operative period is depicted in the table 7 which had high scores in placebo group in comparison with A, B and C groups. There was significant difference ($p=0.000$) between placebo group and the drug groups. But there was no significant difference ($p=0.944$) among the 3 drug groups. All 20 patients had VAS>3 in placebo group which showed inadequate analgesia (Table 8). *Visual Analogue Score with respect to groups at 2 hours;*

Table 8: Visual analogue score at 2 hours

GROUP (NO. OF PATIENTS)				
VAS	A (Buprenorphine)	B (Fentanyl)	C (Morphine)	D (Placebo)
0	20	20	8	0
1	0	0	7	0
2	0	0	5	0
3	0	0	0	0
4	0	0	0	1
5	0	0	0	5
6	0	0	0	10
7	0	0	0	4

Table 9: Comparison of analgesia at 2 hours

GROUP (NO. OF PATIENTS)				
	A (Buprenorphine)	B (Fentanyl)	C (Morphine)	D (Placebo)
VAS <3	20	20	20	0
VAS >3	0	0	0	20

At 2nd hour VAS score (Table 9) showed significant difference between placebo group and A, B, and C groups ($p=0.000$). Pain intensity scores were significantly different ($p=0.002$) between group C and other 2 groups (A and B). There was no significant difference in terms of VAS score between A and B groups ($p=0.965$). Even though morphine had significant p values when compared to A and B groups, none of the patients received rescue

analgesia (Table 10). Visual Analogue Score with respect to groups at 4 hours;

Table 10: Visual analogue score at 4 hours

GROUP (NO. OF PATIENTS)				
VAS	A (Buprenorphine)	B (Fentanyl)	C (Morphine)	D (Placebo)
0	20	11	2	0
1	0	6	2	0
2	0	3	10	0
3	0	0	6	1
4	0	0	0	7
5	0	0	0	7
6	0	0	0	1
7	0	0	0	3
8	0	0	0	1

Table 11: Comparison of analgesia at 4 hours

GROUP (NO. OF PATIENTS)				
	A (Buprenorphine)	B (Fentanyl)	C (Morphine)	D (Placebo)
VAS <3	20	20	14	0
VAS >3	0	0	6	20

At 4 hours there was significant difference with respect to VAS score among all 4 groups (Table 11). Placebo group had high scores ($p=0.000$) compared to other 3 groups. A and B groups differed significantly from morphine ($p=0.04$), as 6 patients had inadequate analgesia with VAS>3. There was significant difference ($p=0.012$) between A and B groups in terms of VAS score, but none of the patients had inadequate analgesia (VAS>3) in either group (table 12) Visual Analogue Score with respect to groups at 8 hours;

Table 12: Visual analogue score at 8 hours

GROUP (NO. OF PATIENTS)				
VAS	A (Buprenorphine)	B (Fentanyl)	C (Morphine)	D (Placebo)
0	14	10	0	0
1	3	1	0	0
2	3	8	0	0
3	0	1	4	0
4	0	0	10	3
5	0	0	5	8
6	0	0	1	7
7	0	0	0	2

Table 13: Comparison of analgesia at 8 hours

GROUP (NO. OF PATIENTS)				
	A (Buprenorphine)	B (Fentanyl)	C (Morphine)	D (Placebo)
VAS <3	20	19	0	0
VAS >3	0	1	20	0

At 8 hours P values were significantly different among 4 groups. Placebo group was significantly different ($p=0.000$) from A, B and C groups, in terms of VAS score (Table 14). But the number of patients with inadequate analgesia (VAS>3) was same in morphine and placebo

group (Table 15). VAS score in morphine group showed significant difference when compared to A and B groups. Finally between fentanyl and buprenorphine groups VAS score was statistically significant with $p=0.02$ but only one patient received analgesic drug in the fentanyl group (Table 15) Heart Rate with respect to groups from 0 to 8 hour.

Table 14: Comparison of heart rate from 0 to 8 hour

HEART RATE (mean \pm std deviation)				
Time	A (Buprenorphine)	B (Fentanyl)	C (Morphine)	D (Placebo)
Hour-0	75.15 \pm 8.9	70.7 \pm 10.6	75.15 \pm 7.3	80.05 \pm 5.9
Hour-1	72.05 \pm 7.1	69.85 \pm 8.9	72.25 \pm 4.8	86.55 \pm 4.6
Hour-2	71.45 \pm 5.5	71.2 \pm 9.0	75.5 \pm 4.7	88.45 \pm 4.2
Hour-4	70.60 \pm 4.4	71.15 \pm 9.1	78.75 \pm 5.2	83.25 \pm 5.0
Hour-8	71.45 \pm 4.7	74.75 \pm 7.6	84.6 \pm 5.6	84.65 \pm 4.0

Heart rate was higher in the placebo group when compared to A, B and C groups (Table 16) throughout the observation period and was statistically significant ($p=0.01$). But there was no significant difference ($p=0.00$) between 3 drug groups.

Table 15: Mean arterial pressure with respect to groups from 0 to 8 hours

MAP (mean \pm std deviation)				
Time	A(Buprenorphine)	B(Fentanyl)	C(Morphine)	D (Placebo)
Hour-0	89.8 \pm 7.9	90.3 \pm 6.3	90.4 \pm 5.5	94.1 \pm 5.7
Hour-1	87.3 \pm 6.4	87.6 \pm 6.3	86.8 \pm 3.9	98.6 \pm 3.7
Hour-2	88.1 \pm 6.8	88.6 \pm 4.2	85.2 \pm 4.0	101.8 \pm 4.4
Hour-4	91.3 \pm 7.2	89.6 \pm 4.6	86.3 \pm 3.4	96.8 \pm 5.1
Hour-8	95.8 \pm 7.0	89.7 \pm 3.9	87.2 \pm 4.2	98.4 \pm 3.1

Mean arterial blood pressure was higher in the placebo group when compared to A, B and C groups (Table 17) throughout observation period and was statistically significant ($p=0.01$). But there was no significant difference between the other 3 drug groups ($p=0.00$).

Table 16: Time of first rescue analgesia

DURATION (hour)	NO. OF PATIENTS								
	0	1	2	3	4	5	6	7	8
Buprenorphine	0	0	0	0	0	0	0	0	0
Fentanyl	0	0	0	0	0	0	0	0	1
Morphine	0	0	0	0	6	7	5	2	0
Placebo	20	0	0	0	0	0	0	0	0

This table indicates the requirement of first rescue analgesia by patients during 0 to 8 hours of postoperative period observation. All 20 patients in placebo group required first rescue analgesia at 0 hour (15 minutes after extubation). None of the patients required first rescue

analgesia in buprenorphine group, while only one patient required first rescue analgesia at 8th hour in fentanyl group.

Table 17: Total dose of analgesic received in 8 hours

	No. of Patients	Total dose of Tramadol in mg.
Buprenorphine	0	0
Fentanyl	1	50
Morphine	20	1000
Placebo	20	2050

This table indicates the total dose of analgesic consumption in 8 hours observation. Placebo group had highest dose followed by morphine group while buprenorphine and fentanyl groups had none or least respectively. None of the patients in any group had any of these side effects, mentioned earlier during the 8-hour period of observation.

DISCUSSION

The knee is a joint in which arthroscopy has the greatest IA surgical application. There is rich innervation to articular capsule, tendons, ligaments, synovium and periosteum via a mixture of free nerve endings and receptors. These sensory nerves respond to mechanical stimuli such as stretching of the joint capsule as well as intra-articular surgical instrumental intervention. Many nerve fibers, for example, are non-responsive under normal conditions but react after inflammation, therefore, there is a potential for acute injury or inflammation to sensitize nerves such that they respond even when the original stimuli is removed. Hence, just like any other surgical procedure, the arthroscopic intervention of the knee joint can cause considerable postoperative pain that limits ambulation and combined with a stress induced hypercoagulable state, may contribute to an increased incidence of deep vein thrombosis. Postoperative analgesia following arthroscopic knee surgery can be provided either by systemic administration of narcotic and non narcotic analgesic drugs¹ or IA administration of local anaesthetic drugs,⁹ non-narcotic analgesic drugs (ketorolac)¹⁰ and narcotic analgesic drugs (morphine,¹¹ pethidine and fentanyl). Each route has its own merits and demerits. Intermittent systemic analgesic administration cannot keep the patient totally pain free for all times where as IA route requires specialized technique, possible only when patient undergoes surgical procedure. But IA route provides qualitatively better analgesia without major side effects, e.g. respiratory depression. Various studies compared the analgesic effect of different opioids with different doses. Varrassi G *et al*⁴ in their study compared 100mcg of IA buprenorphine, 50mg 0.5% IA bupivacaine with placebo. They found that 100mcg buprenorphine or 0.5% bupivacaine when

injected intra-articularly produced good and comparable postoperative pain control and reduced supplementary analgesic requirement. Rosseland *et al*⁷ evaluated the analgesic effect of morphine 1mg, 2mg and placebo (5ml 0.9% normal saline) when injected intra-articularly at the end of arthroscopic knee surgery. They found no significant differences in terms of analgesia between the groups. Kazemi *et al*² compared 3mg morphine, 5mcg of sufentanil and placebo and found that both morphine and sufentanil reduced post-arthroscopic knee procedure pain when injected intra-articularly and rescue analgesia requirement was less compared to placebo. Mandal P *et al*³ compared different doses of IA fentanyl (25 and 50mcg) with placebo group for postoperative analgesia and found that 50mcg fentanyl intra-articularly is the optimum dose for achieving 24 hours postoperative analgesia. In our study we sought to evaluate the analgesic effect and the need for rescue analgesia with 3mg morphine, 50mcg fentanyl and 100mcg buprenorphine and compared these with a placebo (20 ml 0.9% normal saline) when administered intra-articularly following arthroscopic knee surgery. Pain was assessed by Visual Analogue Scale, which corresponds with all other studies. Rescue analgesia was administered for any patient with moderate pain (VAS>3), which was similar in Varrassi G *et al* and Kazemi *et al* studies. In our study, out of 80 patients, 66 patients were male and 14 were female with mean age around 35 years. With respect to sex, ASA physical status and operative procedures all the 4 groups were comparable. We found that in immediate postoperative period i.e. at 0 and 1 hour, buprenorphine, fentanyl and morphine had good and equal analgesic effect as none of the patients required rescue analgesia. In contrast, all 20 patients in placebo group had moderate to severe pain and all required supplementary analgesics. These results were similar to inferences of Kazemi *et al*, Mandal P *et al*, Varrassi *et al*, and Varkel *et al* studies. Further comparing the analgesic efficacy at 2 hours postoperatively all 20 patients had no pain in buprenorphine and fentanyl group indicating equal analgesic effect. Even though morphine provided analgesia, 12 patients had mild pain but did not require rescue medication. This was significantly different from buprenorphine and fentanyl. This was similar to study by Rosseland *et al*, who concluded that postoperative analgesic effect of IA morphine was found only in subgroup of patients with higher pain intensity in the immediate post anaesthetic period. The possible reasons quoted were lack of inflammation that was prerequisite for peripheral opioid analgesia, lack of expression of opioid receptors and due to weak pain stimulus. Buprenorphine and fentanyl had no significant difference in terms of VAS scores and had good analgesia without

requiring rescue analgesics. At 4 hours the analgesic effect of morphine was wearing off with 6 patients having moderate pain and requiring analgesics supplementation but this was better than placebo group where, inspite of receiving rescue analgesics almost everybody had moderate pain. When morphine was compared to fentanyl, fentanyl had good analgesic effect with 9 patients having mild pain but without requiring analgesics indicating better analgesia than morphine. This was demonstrated by Varkel *et al*⁵ with similar doses of morphine and fentanyl as in our study and concluded that postoperative analgesia with IA fentanyl was better when compared with morphine during 8 hours of observation. Even though pain scores differed significantly between buprenorphine and fentanyl, none of the patients in either group received postoperative rescue analgesics. Nine patients in fentanyl group had mild pain (VAS<3) in comparison to none in the buprenorphine group, which indicates increased analgesic effect of buprenorphine. This could be explained with its partial agonist action, high receptor affinity and slow dissociation. It binds 4 times the number of receptors labeled by fentanyl. Boas R A *et al*⁸ demonstrated this in their study of significance of opioid receptor binding characteristics of fentanyl and buprenorphine. At 8 hours, morphine didn't differ much in analgesic action from that of placebo group as all 20 patients had inadequate pain relief and required supplementary analgesics. This was similar to the conclusion drawn by Heard *et al* who considered IA morphine no better than placebo, except for prolonging the time of first analgesic request and for its systemic effect. Fentanyl had similar analgesic efficacy as that of buprenorphine, with 9 patients having mild pain and only one requiring rescue analgesia. Fentanyl was a better analgesic than morphine when administered intra-articularly and differed significantly in terms of pain scores and rescue analgesic requirement in comparison to morphine. This was consistent with study of Mandal P *et al* who inferred 50mcg fentanyl provided longer duration of totally pain free state without any supplementary analgesic therapy and fentanyl was better analgesic than morphine at 8 hours duration. Buprenorphine had longer duration of analgesia with less pain scores and no rescue analgesics requirement by all 20 patients that was statistically significant when compared to fentanyl. This was consistent with the study by Varrassi *et al* who showed IA buprenorphine after knee arthroscopy was followed by long lasting pain relief. The efficacy of buprenorphine could be related to a local peripheral action as suggested by Stein C *et al*.⁶ We compared the hemodynamic data (heart rate and mean arterial pressure) during 0 to 8 hours postoperative period. The placebo group had higher heart rate and mean arterial

pressure than the 3 drug groups at all times during 8-hour observation period and this was statistically significant. This could be due to pain and anxiety causing sympathetic stimulation. But there was no significant difference with hemodynamic data among the 3 drug groups during same duration of observation. We also noted the time of request for first rescue analgesia, with placebo group requiring analgesics in all 20 patients during 0 hour, i.e. in the immediate postoperative period itself. In buprenorphine group, with better analgesic effect, none of the patients required rescue analgesia and it was similar in fentanyl group with only one patient requiring first rescue analgesia at 8th hour of observation. Six patients in morphine group required first rescue analgesia at 4th hour of observation. The total dose of analgesic consumption in 8 hours showed placebo group requiring highest dose (2050 mg of tramadol intravenously for 20 patients), followed by morphine group (1000mg of tramadol) while buprenorphine and fentanyl group hardly required any analgesic dose. None, in any of the three drug groups, had significant side effects during 8-hour observation period.

CONCLUSION

This study showed both intra-articular buprenorphine and fentanyl provided effective post-operative pain relief and reduced rescue analgesic requirement in the first 8 hours following arthroscopic knee procedures. It also revealed that buprenorphine and fentanyl are better intra-articular analgesics than morphine. While intra-articular morphine was found to provide good pain relief during early post-operative period, it lacked analgesic efficacy in the later half of our observation period.

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Source of Support: None Declared
Conflict of Interest: None Declared