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Research Article

Comparison of the Efficacy of Three Different Opioids as Adjuvants to Hyperbaric Bupivacaine for Subarachnoid Block in Lower Limb Orthopedic Surgeries - A Prospective Randomized and Double Blind Study

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ABSTRACT

Background: Regional anaesthesia provides effective intraoperative anaesthesia and postoperative analgesia for orthopaedic procedures. This prospective, randomized, double-blind study compared intrathecal buprenorphine, fentanyl, and nalbuphine as adjuvants to hyperbaric bupivacaine in lower-limb orthopaedic surgeries.

Materials and Methods: After IEC approval and written informed consent, 90 ASA I–II patients undergoing elective lower-limb orthopaedic surgery under combined spinal-epidural anaesthesia were randomized into three groups (n=30 each). All patients received 3 mL of 0.5% hyperbaric bupivacaine with either buprenorphine 150 µg, fentanyl 25 µg, or nalbuphine 1 mg intrathecally. Haemodynamic parameters were monitored throughout surgery and postoperatively. Sensory and motor block characteristics, duration of analgesia, VAS pain scores, sedation, patient satisfaction, and adverse effects were assessed. Appropriate statistical tests were applied.

Results: The three groups were comparable regarding demographic characteristics, sensory block characteristics, onset of motor block, duration of analgesia, haemodynamic parameters, and adverse effects. However, the duration of motor block was significantly longer in the fentanyl group compared with the buprenorphine and nalbuphine groups. Side effects were minimal and comparable among all groups.

Conclusion: Intrathecal fentanyl, nalbuphine, and buprenorphine, when added to hyperbaric bupivacaine, were safe and comparable regarding sensory block, analgesic duration, haemodynamic stability, and adverse effects. Fentanyl significantly prolonged motor block compared with buprenorphine and nalbuphine.

Keywords: Subarachnoid Block, Intrathecal Adjuvants, Opioids, Orthopaedic Surgeries.

INTRODUCTION

Hip and knee replacement are common operative procedures that relieve pain and improve mobility and quality of life in individuals with various rheumatologic conditions, especially osteoarthritis. Management options for osteoarthritic knee include medical and surgical, the latter in the form of arthrodesis, debridement, realignment osteotomy or prosthetic arthroplasty, depending on the patient's age, functional expectations, patient activity demands, the underlying disease and degree of cartilaginous loss.[1]

Joint replacement involves lot of tissue resection and tissue handling during the

removal of destroyed parts of the knee and replacing them with new metal or plastic elements either partly or fully which can lead to intense pain, some times more severe than that experienced by laparotomy patients[2] that can get worse in the immediate postoperative period [3,4] when the anaesthesia starts wearing off and has been considered especially difficult to manage.[5] Hence, an anaesthetic technique that provides good intra operative conditions and also extends the analgesia into post-operative period is needed so that less narcotic analgesics are required postoperatively.

A well conducted regional anaesthesia such as central neuraxial blockade will provide stable intra-operative conditions and rapid patient recovery whilst minimizing side effects such as sedation, post-operative nausea and vomiting (PONV) and hypotension, leading to improved functional recovery facilitated by more rapid and effective joint rehabilitation.[6]

Neuraxial anaesthesia has been associated with decreased morbidity, in particular, with a reduction in blood loss [7], operating time [8], incidence of thromboembolic disease [8, 9], surgical site infections [10] and a lower rate of admission to critical care services[11] and improved outcomes [12] for joint replacement surgeries compared to general anesthesia. Thus regional analgesia techniques allow for more intense early rehabilitation and accelerate functional recuperation and shorten the total (hospital and rehabilitation centre) duration of institutional stay.

Spinal anesthesia is quick, reliable, and simple to perform; the recovery profile and analgesia in the immediate post-operative period, make spinal anesthesia, in several ways, the optimal anesthetic technique. However, adequacy of spinal intrathecal anesthesia with bupivacaine for lower limb and lower abdominal surgeries is limited by fixed duration of action. It cannot be prolonged except with usage of spinal catheters which is associated with some times serious complications. [13] Several neuraxial adjuvants like opioids,[14] α2 agonists [15], ketamine[16] have been used to prolong the duration of the block and minimize the instability in hemodynamics (or by addition of an epidural catheter for providing postoperative analgesia).

Local anaesthetics and opioids given in combination intrathecally have shown synergistic and antinociceptive effects. [17] Low dose intrathecal opioids have been shown to provide prolonged analgesia after hip and to a lesser extent knee arthroplasty. [18]

Fentanyl is a μ opioid receptor agonist which is frequently used as an adjuvant to hyperbaric bupivacaine for spinal anesthesia. Being highly lipid soluble, it diffuses into the spinal cord and binds to dorsal horn receptors rapidly when administered intrathecally. This produces a rapid onset of analgesia with minimal cephalic spread. [19]

Nalbuphine, a derivative of 14-hydroxymorphine, is a strong analgesic with mixed kappa agonist μ antagonist properties. Though nalbuphine is equipotent analgesic to morphine but unlike morphine it exhibits a ceiling effect on respiratory depression. Nalbuphine has the potential to maintain or even enhance μ-opioid based analgesia while simultaneously mitigating the μ-opioid side effects. [20]

Buprenorphine is a centrally acting lipid soluble analogue of alkaloid thebaine. Analgesic property was observed at spinal and supra spinal levels. Buprenorphine is a mixed agonist — an antagonist narcotic with high affinity at both Mu (μ) and kappa (κ) opiate receptors. It is an effective analgesic, similar to morphine, in nearly all-clinical situations. [21]

Within our knowledge, we could not find any study which compared fentanyl, nalbuphine and buprenorphine as adjuvants to hyperbaric bupivacaine for subarachnoid block. Hence, we aimed to compare the efficacy of fentanyl, nalbuphine and buprenorphine as adjuvants to hyperbaric bupivacaine in patients undergoing elective lower limb orthopaedic surgeries.

MATERIAL AND METHODS

A prospective, randomized and double blind study was conducted in a university teaching hospital in south India, after obtaining approval from the Institutional Ethics Committee (AS/11/IEC/SVIMS/2017). The study was registered in Clinical Trial Registry India (CTRI/2020/02/023288). A written informed consent was obtained from all the study participants and they were given the right to opt out of the study at any stage without assigning any reason.

Patients aged between 18 to 65 years of either gender, belonging to American society of Anesthesiologists Physical Status (ASA PS) grades 1 and 2 and scheduled for elective lower limb orthopedic surgeries including joint replacement were included in this study.

Patients who were not willing to participate in the study, patients who did not give consent for spinal anesthesia; with a history of spinal surgeries, coagulation and bleeding disorders, hypersensitivity to study drugs , uncontrolled HTN, DM and CAD; neuropsychiatric disorders and communication problems and hence, cannot understand visual analog scale (VAS) measurements; increased serum creatinine and liver enzymes 2-3 times of normal, pregnant women and lactating mothers, height-<140 cm & BMI > 35 Kg/m^2 and patients with local site infections and any other contraindications to subarachnoid block were excluded from the study.

Before initiating the study, ninety patients were randomly allocated to one of the three groups of 30 patients each by computer generated random number table and sealed opaque envelope technique. The sealed envelope was prepared by an investigator not involved in the data collection and analysis. Both the patient and anesthesiologist performing the block were blinded to treatment allocation which was as follows:

1. Group F patients received 3ml of 0.5% hyperbaric bupivacaine + 25mcg of Fentanyl (preservative free).
2. Group N patients received 3ml of 0.5% hyperbaric bupivacaine + 1mg of nalbuphine (preservative free).
3. Group B patients received 3ml of 0.5% hyperbaric bupivacaine + 150mcg of buprenorphine (preservative free).

Volume of drug in all the groups was made to 3.5 ml by adding normal saline wherever necessary. Study drugs were prepared by a clinician who was not involved in the study.

All the ninety patients were thoroughly evaluated on the day before surgery and details were documented in the anaesthesia chart and were explained in detail about the spinal anesthesia, epidural catheter insertion and postoperative analgesia, usage of VAS and written informed consent was obtained.

All the patients were premedicated with Tab. alprazolam 0.25mg night before surgery and Tab ranitidine 150 mg orally the night before and on the morning of surgery and were kept fasting overnight as per the institutional protocol.

After shifting to operation theatre (OT), standard ASA monitoring including continuous electrocardiogram (ECG), non-invasive blood pressure (NIBP) and oxygen saturation (SpO2) by pulse oximetry was commenced and baseline values were recorded, A peripheral intra venous (IV) access was secured with 18- or 16-gauge cannula and intravenous infusion was started with lactated ringer solution.

In all patients, under strict aseptic precautions, in the lateral decubitus position, an 18G lumbar epidural catheter was inserted using loss of resistance to air technique in an appropriate space, and its position was confirmed by injecting a test dose of 2ml of 1.5% lignocaine with adrenaline (1:2, 00,000). Spinal subarachnoid block was then performed by using a 25G Quincke's spinal needle into L3-L4 space, different from that of epidural catheter insertion. After ensuring free flow of CSF, all patients were given 3ml of 0.5% hyperbaric bupivacaine intrathecally along with the study drug according to the group allocation and patients were placed in supine position immediately after injection. Confirmation of block was done using loss of sensation to cold swab and loss of muscle movement in lower limbs.

In addition to changes in the hemodynamic parameters such as heart rate (HR), systolic, diastolic and mean arterial pressures (SBP, DBP and MAP) the patients were also studied for sensory block characteristics in terms of onset of sensory block to L1 dermatome, maximum block height achieved, time taken to reach maximum height of block, duration of sensory block (time from onset of sensory block at L1 to two segment regression) and duration of analgesia (time from achievement of L1 dermatomal block to patient's first request of analgesia or VAS ≥ 4, whichever is earlier) and motor block characteristics in terms of time for onset of motor block and duration of motor block (from time of onset to modified Bromage 3 level) [17]. Postoperatively, pain was assessed using VAS scores at every 30 min for 4 hours and at every 2 hours until the patient's first request for supplemental analgesia or VAS ≥ 4, whichever was earlier.

The hemodynamic parameters and block characteristics were assessed continuously in the postoperative period till that time when rescue analgesia was administered for the first time. Rescue analgesia was given with Inj. tramadol 2mg /kg IV followed by inj. ondansetron 0.1 mg/kg, if not given already. Epidural infusion with 0.1% bupivacaine was activated simultaneously following a bolus dose.

Adverse effects like nausea and vomiting, respiratory depression, pruritus and excessive sedation if any, were noted. Overall patient satisfaction was assessed by VAS score after shifting the patient to recovery room.

Any episode of hypotension, defined as fall of SBP by more than 20% from baseline or an absolute value of 90 mmHg was treated with IV boluses of 3 mg of ephedrine repeated as necessary in addition to extra ivf boluses. Bradycardia defined as HR less than 60 bpm was treated with IV atropine 0.3 mg repeated as necessary to maintain HR.

After ruling out inadequate analgesia, hypertension and tachycardia were treated with boluses of esmolol and hypertension, if needed, with infusion of nitroglycerine as per institutional protocol. Nausea and vomiting were treated with IV ondansetron, and shivering and pruritus were also treated appropriately.

Statistical Analysis

All collected data was double checked to exclude any possible clerical errors and was saved in excel format. The data obtained was evaluated for normality using the Shapiro- Wilk test. Data was presented as mean and standard deviation, as median value (inter quartile range 25-75) or frequencies and percentages as appropriate. For comparison of normally distributed independent variables in 3groups one way Analysis of variance (ANOVA) and Bonferroni post hoc test were applied. For comparison of non-normal variables in 3groups Kruskal - Walli's test was applied. Categorical variables were compared in 3groups by Chi-square test. A p value <0.05 was considered statistically significant. All statistical analysis was done using SPSS, version 19 [IBM Inc. Chicago IL, USA, 2010].

RESULTS

For this prospective randomised double-blind study, 115 patients were screened initially for their eligibility. Out of 115 patients, 25 patients were excluded and 90 patients were included in the study All ninety patients have completed the study protocol and statistical analysis.

Patients in all three groups S, B, F and N were comparable in terms of demographic characteristics with respect to age, height, weight, body mass index, gender distribution and ASA PS grade (Table 1).

Table 1: Comparison of demographic data among the study groups

Quantitative data	Group B (n=30)	Group F (n=30)	Group N (n=30)	p value
Age(years)	55.5 ±4.9	54.6 ±4.2	56.1 ±4.2	0.400
Height (cms)	157.03 ±5.76	158.6 ±5.71	157.1 ±6.49	0.523
Weight(kg)	66.77 ±8.74	69.83 ±10.93	64.73±9.09	0.125
BMI(kg/m2)	27.05±3.2	27.9±14.8	26.45±3.2	0.349
Qualitative data				
Sex(Male/Female)(n)	15/15	11/19	13/17	0.581
ASA grade I/II (n)	9/21	9/21	15/15	0.175

Data presented as mean ± Standard Deviation (m ± (SD)). n = number of patients. Group B = Buprenorphine, Group F= Fentanyl, Group N= Nalbuphine.

With regards to the block characteristics, all three groups were comparable in terms of time of onset, maximum height of the block and time to reach that height, duration of sensory block, time to regression to below L1 level, duration of analgesia and time of onset of motor block. The duration of sensory block was slightly longer in fentanyl group than in buprenorphine and nalbuphine groups but this difference was not statistically significant (p = 0.246). The duration of motor block was significantly longer (p= **0.009**) (Table 2).

Table 2: Block Characteristics among the three groups

Block characteristics	Group B (n=30)	Group F(n=30)	Group N(n=30)	p value
Sensory Block				
Time to onset of block to L1(sec)	132.03 ±40.26	123.70 ± 40.33	127.23 ± 37.70	0.715
Time to reach maximum height(sec)	306.07 ±113.79	307.03±107.31	312.77 ±120.52	0.970

Maximum Height of the sensory block *	T4	0	0	1 (3.3%)	1 /90
	T6	12 (40%)	9 (30%)	11(36.6%)	32/ 90
	T8	15 (50%)	16 (53.3%)	10 (33.3%)	41 /90
	T10	3 (10%)	5 (16.7%)	8 (16.7%)	16 / 90
Duration of Sensory block (min)	135.83 ± 41.261		144.8 ± 43.68	126.80 ± 39.289	0.246
Time to block regression below L1 (min)	208.50 ± 49.10		207.90 ±37.54	211.47 ± 42.32	0.943
Duration of analgesia (min)	279± 56.16		273.70 ± 40.07	261.53 ± 45.79	0.288
Motor Block					
Time to onset of block(min)	6.27 ± 1.91		6.60 ± 2.31	6.17 ± 2.29	0.723
Duration of motor block (min)	212.2±48.9		253±51.3	231.8±50.6	**0.009**

Data presented as mean ± Standard Deviation (m ± (SD)). n = number of patients. Group B = Buprenorphine, Group F= Fentanyl; Group N= Nalbuphine. *Data expressed in frequencies and percentages

Post hoc analysis of duration of motor block showed that there was a statistically significant difference between Group B and Group F (212.26±48.92 min, 253.01±51.33 min respectively with a p value of **0.0024).** However, between Group B and Group N (212.26±48.92 min, 231.8±50.61 min respectively (p value of 0.13) and between Group F and Group N (253.0±51.33 min, 231.8±50.61 min respectively (p value of 0.11), no significant difference was found (Table 3).

Table 3: Comparison of Duration of motor block (min) within the three groups by post hoc analysis

Post hoc analysis of duration of motor block (min)	**Group B and Group N**	**Group F and Group N**	**Group B and Group F**
Sample size (n)	30	30	30
Mean ± SD	212.2±48.9 Vs. 231.8±50.6	253±51.3 Vs. 231.8±50.6	212.2±48.9 Vs. 253±51.3
p value	**0.13**	**0.11**	**0.002**

Data presented as mean ± Standard Deviation. n = number of patients. Group B = Buprenorphine, Group F= Fentanyl, Group N = Nalbuphine.

There was no statistically significant difference among the three groups with regards to the number of episodes of hypotension, hypertension, bradycardia and tachycardia (Table 4) and also the number of adverse events viz., nausea and vomiting, shivering and pruritus (Table 5).

Table 4: Comparison of hemodynamic events between study groups

No. of episodes of	**Group B n=30**	**Group F n=30**	**Group N n=30**	**p value**
Hypotension	4	3	5	0.591
Hypertension	8	12	9	0.324
Bradycardia	2	0	0	0.394
Tachycardia	0	2	3	0.227

Data presented as number of episodes. Group B = Buprenorphine, Group F= Fentanyl, Group N = Nalbuphine

Table 5: Comparison of adverse effects

Adverse effect	**Group-B (n=30)**	**Group-F (n=30)**	**Group-N (n=30)**	**p value**
Nausea and vomiting	4	1	3	0.410
Shivering	5	2	3	0.466
Pruritus	0	0	1	0.364

Comparatively more number of patients in nalbuphine group had higher VAS scores than in fentanyl or buprenorphine groups but this difference was not statistically significant. The highest VAS score observed in our study was 7 in Group B and Group N whereas it was 6 in Group F (Table 6).

Table 6: Comparison of VAS score of postoperative pain between study groups

VAS Score	Group B (n=30)	Group F (n=30)	Group N (n=30)	p value
4	10	10	5	0.468
5	11	12	11	
6	7	8	12	
7	2	0	2	

Group B = Buprenorphine, Group F= Fentanyl, Group N = Nalbuphine. Data represented as frequencies.

Mean sedation scores were comparable in all the three groups intraoperatively. Mean sedation scores in Group B were comparatively higher than Group F and Group N postoperatively but were not statistically significant at all the time interval (Table 7).

Table 7: Comparison of sedation scores among the three groups

Time in Minutes	Group-B (n=30)	Group-F (n=30)	Group N (n =30)	p value
Intraoperative sedation scores				
30 Min IO SS	2.0 ± 0.0	2.0 ± 0.0	2.0 ± 0.0	.a
60 Min IO SS	2.23 ± 0.626	2.13 ± 0.507	2.06 ± 0.365	0.449
90 Min IO SS	2.31 ± 0.760	2.23 ± 0.626	2.06 ± 0.365	0.290
120 Min IO SS	2.32 ± 0.748	2.12 ± 0.439	2.04 ± 0.208	0.169
150 Min IO SS	2.18 ± 0.603	2.0 ± 0.0	1.88 ± 0.333	0.314
180 Min IO SS	2.33 ± 0.816	2.0 ± 0.0	2.0 ± 0.00	0.600
Postoperative sedation scores				
30 Min PO SS	2.24 ± 0.739	1.96 ± 0.490	1.89 ± 0.409	0.053
60 Min PO SS	2.18 ± 0.622	1.96 ± 0.565	1.96 ± 0.587	0.286
90 Min PO SS	2.16 ± 0.481	1.95 ± 0.638	2.00 ± 0.510	0.381
120 Min PO SS	2.00 ± 0.00	1.95 ± 0.510	2.00 ± 0.365	0.882
150 Min PO SS	2.00 ± 0.00	1.84 ± 0.554	2.00 ± 0.00	0.425
180 Min PO SS	1.80 ± 0.44	1.80 ± 0.447	2.0 ± 0.00	0.208

a-No statistics are computed because 30min Intraoperative sedation score is constant. Data presented as mean ± Standard Deviation. n = number of patients. Group B = Buprenorphine, Group F= Fentanyl, Group N = Nalbuphine. IOSS – Intraoperative sedation score. POSS – Postoperative sedation score

Out of the 90 patients studied, 19 patients(21%) were completely satisfied (VAS score 4) and they wanted to recommend the same technique of anesthesia to others, 63 patients were satisfied with the technique of analgesia and they might recommend (VAS score 3) the same technique to others (70%), 7 patients were satisfied but did not want to recommend (VAS score 2) and only 1 patient was not satisfied and did not want to recommend (VAS score 1) the same technique of anesthesia to others (Table 8).

Table 8: VAS score of patient satisfaction among study groups

VAS score of patient satisfaction	Group B (n=30)	Group F (n=30)	Group N (n=30)	p value
Not satisfied	1	0	0	0.648
satisfied 2	2	2	3	
satisfied 3	20	21	22	
satisfied 4	7	7	5	

Score 1: Not satisfied: Patient is not satisfied and does not want to recommend the same technique of anesthesia to others.
Score 2: Satisfied: Patient is satisfied but does not want to recommend the same technique of anesthesia to others.
Score 3: Satisfied: Patient is satisfied and may recommend the same technique of anesthesia to others.
Score 4: Satisfied: Patient is completely satisfied and certainly wants to recommend the same technique of anesthesia to others.

DISCUSSION

In the present study we have compared the efficacy of buprenorphine, fentanyl and nalbuphine when added to hyperbaric bupivacaine for central neuraxial blockade in elective lower limb orthopedic surgeries.

Patients in all the three groups were comparable demographically. They also did not show any significant difference in hemodynamic parameters during the study period with regards to heart rate, systolic, diastolic and mean arterial pressures (HR, SBP, DBP and MAP respectively). This shows that the adjuvants (buprenorphine, fentanyl and nalbuphine) we have chosen to administer in their respective doses and route were safe to use in patients belonging to ASA grade I and II.

Since most studies involved comparison of two adjuvants, we did not have the opportunity to compare our results for sensory and motor block characteristics using three adjuvants. Hence, we tried to compare them in terms of study drugs used and the results of some sensory block characteristics achieved with that of other researchers with similar methodology (Table 9).

Table 9. Comparison of sensory block characteristics among different studies:

Variable	**Group name**	**Our study**	**Unlugenc et al** [22]	**Gupta K et al** [23]	**Neelam Singh et al** [24]	**Mahima Gupta et al** [25]	**KKS* et al** [26]	**Borse et al** [21]	**Jagtap et al** [27]	**Naaz et al** [28]
Time to onset of sensory block **(sec)**	F (25µg)	123 (L1)	180 (25µg, T10)	240 (25µg, T10)		-				
	N (1 mg)	127 (L1)	-	230 (2 mg, T10,)	600 (600 µg, T6)	-				
	B (150 µg)	132 (L1)	-	-		180 (60 µg, T8)	477 (75µg, T10)	70 (L2-3, 150 µg)		
Max. height of block & time to reach (sec)	F (25µg)	T6 307 sec							T6 424sec	
	N (1 mg)	T4 312 sec		T6 420 sec						
	B (150 µg)	T6 300 sec						T6 360 sec		
Time to regres-sion of sensory block (min)	F (25µg)	L1 207 min							L1 229 min	
	N (1 mg)	L1 312 sec		T12 127 min						S2 92 min (0.8 mg)
	B (150 µg)	L1 208 min				S2 225min (60 µg)				

In terms of maximum **height** of the block achieved among our three groups, there was no statistically significant difference. All patients in our study achieved a minimum of T10 level which was adequate for lower limb orthopedic surgeries in our study. However, these drugs used in respective doses may not provide sufficient anaesthesia for surgeries requiring blockade of T_4 level such as LSCS or some other abdominal surgeries which may require block up to T_6. A higher block height may be obtained with a lower dose of intrathecal drug as was the observation with Ravindran et al [29] who achieved a block height of T2 segment with only 60 µg of buprenorphine in elective LSCS patients. These differences in recording the maximum height of the sensory block may be attributed to the way of assessing sensory block. We used loss of cold sensation to assess the block whereas the other researchers in the above-mentioned studies have used loss of pin prick sensation to assess the block which takes longer time to disappear.

We attribute the differences in the mean time to onset of block, height of block and regression of block between our study and that of other studies to different doses of drug used and different segments for assessing height of block or regression of the block or different end points to assess the block (loss of cold sensation Vs pin prick sensation) even though similar doses were used.

The mean duration of sensory block in Buprenorphine group (135.83±41.261min) was much longer than Borse et al [21] (84±12 min) who have used same dose of Buprenorphine. The mean duration of sensory block in Fentanyl group (144.8±43.68 min) which was shorter than study by Gurunath BB et al [30] (167.41±30.17min) and Routray SS et al [31] (205.16±19.55 min). The mean duration of sensory block in Nalbuphine group (126.80±39.289 min) was much shorter when compared to study conducted by Tarangini et al [32] (230.8±6.3 min, 1mg) with same dosage of nalbuphine but in combination with isobaric levo-bupivacaine and Attri et al [33] (136.33 min) who have used 0.8mg of nalbuphine with 0.5% hyperbaric bupivacaine. The differences in duration of sensory block could be due to differences in time points used to define and assess the duration of the block and also differences in the type of local anesthetic agents used (hyperbaric bupivacaine vs isobaric levobupivacaine).

The mean duration of analgesia in Buprenorphine group (279.96±56.16 min**,** 150mcg) was much less when compared to study conducted by Kiran Nelamangala et al [34] (351.53±9.18 min, 100mcg) and comparable with Krishna Kumar et al [35] (294.00±17.93 min, 75mcg). The mean duration of analgesia in Nalbuphine group (261.53±45.79 min, 1mg) was much lower than studies by Naaz et al [28] (450±109.38 min,1.6mg), and Gupta K et al [23] (318.64±21.92 min, 2mg). Longer duration of analgesia might be due to higher dose of nalbuphine used in their studies than that used in our study. The mean duration of analgesia in Fentanyl group (273.70±40.07min) was similar to that in the studies conducted by Naaz et al [28] (300±88.53 min) and Gupta K et al [23] (278.74±29.67 min) who used same dose as in our study which was 25 µg.

The mean time to onset of motor block (Bromage 3) in Nalbuphine group (6.17±2.29 min, 1mg) was much longer than study by Tarangini Das et al [32] who used levobuvacaine (3.7±0.6 min,1mg) and shorter to the study conducted by Attri et al [33] (7.30 min,0.8mg). The mean time to onset of motor block in Fentanyl group (6.60±2.31min) was shorter than study by Gupta K et al [23] (8.63±2.43 min) and slightly longer than Naaz et al [28] (5.4±12.96 min). The mean time to onset of motor block in Buprenorphine group (6.27±1.91min) was longer than studies by Mahima Gupta et al [25] (3.30±0.97 min) and Krishna Kumar et al [26] (274±56.11 sec).

The mean duration of motor block in Fentanyl group (253±51.3 min) was longest in our study compared to studies by Naaz et al [28] (204.5±40.03 min) and Gupta K et al [23] (141.63±18.05 min) .The mean duration of motor block in Nalbuphine group (231.8±50.6 min) was longer compared to studies conducted by Tarangini Das et al [32] (204.8± 9.5 min, 1mg) and Attri et al [33] (188.5 min, 0.8mg).The mean duration of motor block in Buprenorphine group (212.2±48.9min) was comparable to studies by Borse Y M et al [21] (215.4±26.2 min, 150mcg) and Krishna Kumar et al [34] (222.66±24.34 min, 60 mcg) and Mahima Gupta et al [25] (205.17±63.0 min, 75mcg).

The variations in the time of onset of and duration of motor block between various study groups could be attributed to the differences in the study drugs and their doses along with

the type of local anaesthetic chosen in addition to the type of patients and different needs for postoperative early ambulation in these patient populations.

None of our patients required conversion to general anaesthesia or activation of epidural infusion during intraoperative period itself because of pain or movement of the limb implying that our anaesthetic technique (SAB with heavy bupivacaine 15mg along with three different opioid adjuvants in the doses used) was adequate for the procedures done.

With regards to number of episodes of hypotension, hypertension, bradycardia and tachycardia, there was no statistically significant difference among the three groups. When observed, these episodes were managed as appropriately though none of our patients experienced any serious hemodynamic disturbances indicating the safety of the study drugs we have chosen in their respective doses.

Mean VAS score for pain in fentanyl group in our study were comparable to study by Bindra TK et al [36] and in buprenorphine group in our study it was higher compared to that observed by Ravindran R et al [29] both involving pregnant women. In nalbuphine group in our study the mean VAS scores were higher compared to study conducted by Tarangini Das et al [32] and Attri et al [33] who used different doses of nalbuphine.

Mean sedation scores in our fentanyl group and nalbuphine group were more compared to sedation scores in studies conducted by Naaz et al [28] and Gupta K et al [23] with same dose of fentanyl but with different doses of nalpbuphine. Mean sedation scores in our buprenorphine group were comparable to study by Mahima Gupta et al.[25] All of our patients were calm and comfortable and easily reusable during the study period both intraoperatively and postoperatively. Similarly none of the studies mentioned any untoward sedation or agitation in their patients as well.

With regards to adverse effects**,** 3.3% of patients developed pruritus with nalbuphine and none with fentanyl and buprenorphine but statistically insignificant. Shivering was observed to be higher with buprenorphine (16.6%) compared to nalbuphine (10%) and fentanyl (6.6%) with no statistical significance. Buprenorphine group showed higher incidence of nausea and vomiting (13.3%) compared to nalbuphine (10%) and fentanyl (3.3%) which was also statistically not significant. All those patients who developed the above mentioned adverse effects were reassured and treated appropriately. None of our patients experienced any serious complications requiring major interventions.

VAS score of patient satisfaction was recorded among the study groups postoperatively after the end of study period. Only 1 patient from Group B out of 90 patients was not satisfied (score 1) and did not want to recommend the same technique of anesthesia to others. More than 65% of patients in all the three groups were satisfied the technique and they might recommend it to others (score 3) and 21% of patients out of 90 patients, in all the groups were completely satisfied and they definitely want to recommend the technique to others (score 4). This indicates that our study drugs provided satisfactory analgesia both intraoperatively and extending into postoperative period till the activation of epidural analgesia. The adequacy of anaesthesia and analgesia and the lower incidence of side effects with our study drugs showed that these drugs were safe haemodynamically and provided comfortable intraoperative and postoperative periods. This contributed to overall quality of anaesthetic experience and patient satisfaction of our anaesthetic technique which was indicated by higher VAS scores of patient satisfaction.

Limitations of this Study

1. T10 dermatomal level was achieved in all patients in our study and this was adequate for lower limb surgery but may not be sufficient for surgeries like infra umbilical surgeries and cesarean sections.
2. We did not compare the equi-analgesic doses of adjuvants used in our study which would have been a better indicator for comparison of analgesic efficacy, side effects and patient satisfaction.
3. We did not study the effect of adjuvants on minimizing the quantity of rescue analgesics (analgesic sparing effect).
4. We did not have a control group to compare the efficacy of each adjuvant individually against a control group and thus to find out which is better on its own.

Conclusion

From the findings of our study, we conclude that the adjuvants viz., fentanyl, nalbuphine,

and buprenorphine in the doses used in our study were safe and satisfactory and were comparable in terms of sensory block characteristics and onset of motor block, duration of analgesia, side effect profile and hemodynamic disturbances with minimal incidence of side effects. Fentanyl produced slightly but statistically significantly longer duration of motor block than buprenorphine and nalbuphine.

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