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COMPARATIVE STUDY OF INTRATHECAL BUPRENORPHINE VERSUS FENTANYL AS ADJUVANTS TO 0.75% ISOBARIC ROPIVACAINE FOR LOWER LIMB SURGERIES

Anaesthesiology

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ABSTRACT

Introduction: Various adjuvants have been clinically studied for prolongation of intraoperative and postoperative analgesia.

Methods: In this randomized,double blind study,120 ASA I/II patients of either sex, age 25-50years undergoing lower limb surgery were selected and randomly allocated into three groups(n=40). In addition to 3ml of 0.75% isobaric ropivacaine , patients of groups A, B and C received 0.9% normal saline (0.5ml), 60mcg Buprenorphine (1:2.5 dilution) and 25mcg fentanyl (0.5ml) respectively (Total volume 3.5ml). Onset time and duration of sensory and motor block, duration of analgesia, hemodynamics,VAS score, sedation score and adverse effects were assessed.

Results: The duration of analgesia was longest in Group B (8.30±0.85hrs), followed by Group C (6.03±0.54hrs, P <0.001) and Group A (4.12±0.60hrs, P<0.001).

Conclusion: Both intrathecal Fentanyl (25mcg) and buprenorphine (60mcg) produce significantly longer duration and better quality of postoperative analgesia than ropivacaine alone. On comparing, Buprenorphine appeared to be superior to fentanyl.

KEYWORDS

fentanyl, buprenorphine, intrathecal, postoperative analgesia

INTRODUCTION

Subarachnoid block is a safe and effective method of anaesthesia for lower limb surgeries but it produces a fixed and short duration of anaesthesia.[1] Local anaesthetics when used alone leads to early weaning off of anaesthesia which requires analgesic intervention in postoperative period. Numerous drugs have been used as adjuvants intrathecally with the aim of improving the quality and duration of spinal anaesthesia with better postoperative analgesia like epinephrine, neostigmine, midazolam, ketamine, fentanyl, buprenorphine[1] and many more but there is no ideal adjuvant till now. We compared the efficacy of intrathecal fentanyl and buprenorphine as adjuvants to isobaric ropivacaine in terms of duration of analgesia, onset and duration of sensory and motor block, sedation and adverse effects.

MATERIAL and METHODS

This randomized, double blind study was done at a tertiary care center after the approval of the Institutional Ethical Committee and obtaining written informed consent from all patients before participation. 120 patients of the ASA Grade I and II, aged 25-50 years, of either sex, scheduled for elective lower limb surgeries (duration 60-90mins) under subarachnoid block were included in the study.

All the patients were thoroughly examined preoperatively which included history, general physical examination, vital parameters, systemic examination and ASA grading. The patients with a contraindication to spinal anaesthesia (e.g. coagulation defects, infection at puncture site and preexisting neurological deficits in the lower extremities) and cardiovascular, respiratory, psychological and hepatic or renal disease were excluded from the study.

The visual analog scale (VAS) scoring system was explained to all the patients.

On the day of surgery, 120 patients were randomized into three groups of 40 patients using sealed envelope technique. The patients and the anaesthetist who were involved in randomization and drug preparation were masked about the information regarding further steps of the study (drug administration, data collection and analysis).

After confirming overnight fasting, iv 18 G cannula was inserted and all patients were preloaded with Ringer's lactate 10ml/kg over 10minutes. All the routine monitors were attached, and the preoperative baseline readings of noninvasive blood pressure, pulse rate (PR) and saturation were noted. Under all aseptic precautions, spinal anaesthesia was performed at the L_3-L_4 interspace with the patient in sitting position. A total of 3.5ml study drug was administered over 30 seconds through a 25G spinal needle. The intrathecal drug compositions depended on the group to which patients were randomized. Patients in Group A received 3ml of 0.75% isobaric ropivacaine with 0.5ml of normal saline, those in Group B received 3ml of 0.75% isobaric ropivacaine with 0.5ml (60mcg) of buprenorphine (1:2.5 dilution) and patients in Group C received 3ml of 0.75% isobaric ropivacaine with 0.5ml (25mcg) of fentanyl. All the patients were placed in supine position immediately after spinal injection. All the patients in three groups received identical volume (3.5ml) of study drug prepared in an identical syringe by an anaesthesiologist who was not involved in the anaesthetic management of the patients.

Sensory blockade was assessed by pinprick test bilaterally in the midclavicular line using a 25-gauge needle every 2 minutes till the highest level of block was achieved and required time was noted. The onset of sensory block was defined as the time from the intrathecal injection of the study drug to the time taken to achieve T_{10} level of sensory block. Recovery time for sensory blockade was defined as two-dermatome regression of anaesthesia from the highest level achieved. Motor blockade was assessed using a Modified Bromage Scale . The onset of motor block was defined as the time from intrathecal injection of the study drug to the time taken to achieve complete motor block (Bromage Score-3). Duration of motor block was the time elapsed from the maximum to the lowest Bromage score (3- 0)

Intraoperatively, all patients were given oxygen through a facemask at a flow rate of 4L/min. The values of mean arterial pressure (MAP), systolic (SBP) and diastolic (DBP) blood pressure, pulse rate (PR) and SpO_2 monitored till the end of the surgery. Hypotension was defined as a fall of MAP by more than 30% from baseline or a fall in SBP below 90mmHg and it was treated with incremental doses of mephentermine 6mg IV and IV fluids. Bradycardia, defined as heart rate below 55bpm, was treated with injection atropine 0.3mg-0.6mg IV.

Postoperative pain was assessed by the patient using the VAS(0-10). It was assessed every 30minutes. Patients were allowed to receive rescue analgesic (IV Diclofenac 75mg) on VAS score of 3. This time from intrathecal injection to first administration of rescue analgesic (duration of analgesia) was noted. This was the end point of the study.

Postoperative sedation level was measured by using "Four Point Sedation Scale". Side effects such as nausea, vomiting, hypotension, bradycardia, shivering and respiratory depression were observed for next 24 hours and managed.

STATISTICALANALYSIS

The sample size was calculated 35 subjects for each of the three groups at α error 0.05 and power 80% assuming minimal detectable difference in mean time to first rescue analgesic requirement in intrathecal buprenorphine, fentanyl and control group to be 1.5hours with SD of 2hours so for the study purpose 40 cases will be taken in each group (total 120 patients)

Statistical analysis was done using SPSS (Statistical Package for the Social Sciences) software version 20.0.0 (IBM Inc. Chicago, Illinois, USA). Kruskal –Wallis test was used to assess differences among the three groups with respect to nonparametric variables. If this revealed significant differences, Mann-Whitney U-test was used to analyze differences between the groups in pairs. Parametric testing was done using analysis of variance. Categorical data were analyzed using Chi-square test. Data are presented as mean± standard deviation or number of patients (percentage) as per category. P<0.05 was considered statistically significant.

RESULTS

All the groups were comparable with respect to age, weight, height, sex, ASA status, type of surgery and duration of surgery. There was no statistically significant differences in the demographic variables between the groups (P >0.05) (Table 1)

Table 1: DEMOGRAPHIC VARIABLES (Mean ±SD)

Variables	Group A (n=40)	Group B (n=40)	Group C (n=40)	p-Value
Age(years)	36.35±8.87	34.52±8.72	36.15±8.39	0.588
Weight(kg)	62.55±2.53	61.65±3.34	62.47±2.56	0.293
Height(cm)	166.1±4.30	164.07±3.58	165.77±4.59	0.071
Sex (M/F)	34/6	37/3	35/5	0.567
ASA I/II	35/5	33/7	36/4	0.603
Duration of surgery (mins)	75.12±9.19	74.89±9.44	76.37±8.40	0.728

Values presented as mean±SD. Statistical test used- ANOVA, Chi-square test Group A- Control; B-Buprenorphine; C-Fentanyl ASA-American Society of Anaesthesiologists; SD-Standard deviation The duration of analgesia (time to first request analgesia) was statistically significant amongst the groups (P <0.001). Group A had the shortest (4.12±0.60 hours) and Group B had the longest (8.30±0.85 hours) duration of analgesia amongst the groups (p<0.05). (Table 2 and Figure 1) The onset of both sensory and motor block was not statistically significant amongst the groups (P>0.05). The time to two segment regression was significantly longer with buprenorphine (207.80±12.55min, p<0.001) and fentanyl (194.20±17.36min, p<0.001) as compared to control (153.53±16.55min) and there was significant difference between the two (p>0.05). The duration of motor block was significantly longer in Group B (268.50±33.42min, p<0.001) as compared to Group A and Group C.

Intraoperatively and postoperatively (upto 360 minutes), there was no statistically significant difference amongst the groups between mean pulse rate, systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP).

Amongst the three groups, VAS scores were highest in Control group and lowest in Buprenorphine group (p<0.05) from 90minutes postoperatively, upto first request of rescue analgesic.(Figure2)

Postoperative sedation score was significantly (p<0.05) more in patients of Group B and Group C as compared to Group A.(Figure 3)
The incidences of intraoperative and early postoperative adverse effects such as nausea, vomiting, hypotension, bradycardia, shivering and respiratory depression were statistically insignificant (P>0.05) among all the three groups. (Table 3)

Table 2: Characteristics of motor and sensory block

Variable	Group A (n=40)	Group B (n=40)	Group C (n=40)	P-value (ANOVA)
Onset of sensory block (min)	8.55±1.63	8.3±1.84	8.50±2.01	0.812
Onset of motor block (min)	10.55±1.63	9.62±1.89	10.55±1.97	0.067
Time to two segment regression (min)	153.53±16.55	207.80±12.55	194.20±17.36	<0.001
Duration of motor block (min)	205.88±33.74	268.50±33.42	212.88±26.70	<0.001
Duration of analgesia (hours)	4.12±0.60	8.30±0.85	6.03±0.54	<0.001

Values are presented as mean±SD. Statistical test- ANOVA test. Group A- Control; B-Buprenorphine; C-Fentanyl. SD-standard deviation

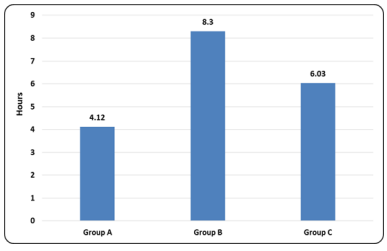

Figure 1: Comparison of duration of analgesia (time to first request analgesia)

Table 3: Incidence of intraoperative and early postoperative adverse effects

Adverse Event	Group A (N=40)		Group B (N=40)		Group C (N=40)		p-value
	Number	%	Number	%	Number	%	
Hypotension	3	7.5	4	10.0	2	5.0	0.697
Bradycardia	3	7.5	3	7.5	2	5.0	0.875
Nausea, Vomiting	1	2.5	1	2.5	1	2.5	1.000
Respiratory Depression	0	0	0	0	0	0	0
Shivering	1	2.5	1	2.5	1	2.5	1.000
Pruritis	0	0	0	0	0	0	0

Values are presented as number. Statistical test- Chi-square test Group A- Control; B- Buprenorphine; C- Fentanyl

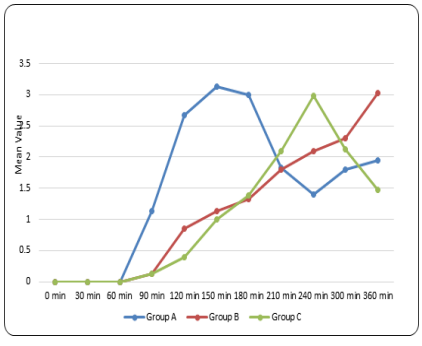

Figure 2 : Mean visual analogue scale score versus time. Values significantly different from 90min upto 360min by Kruskal-Wallis H test

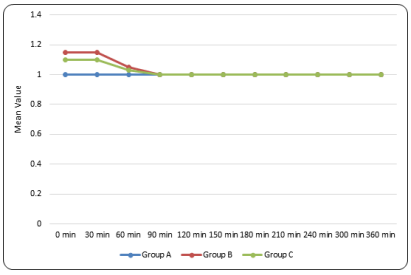

Figure 3: Mean Postoperative Sedation scores versus time. Values were significantly different upto 60min by Kruskal-Wallis H test

DISCUSSION

Postoperative pain is one of the most distressing complications for the patient. It amplifies the surgery induced stress response, hinders early ambulation and prolongs the time to discharge. Thus an effective anaesthetic approach should encompass pain management during the postoperative period, adequate sedation and analgesia. Spinal anaesthesia is the most common anaesthetic technique used for lower extremity surgery.(2) Numerous drugs have been used for spinal anaesthesia, among which Ropivacaine is a newer long acting amide local anaesthetic with improved safety profile over bupivacaine and hence is gaining favour.(3,4) Neuraxial administration of opioids along with local anaesthetics has gained popularity(5,6) as they improve the quality of intraoperative anaesthesia, permit lower doses of local anaesthetics(7,8) and reduces analgesic requirement in the postoperative period.(9,10) In our study, duration of analgesia was maximum (8.30hours) with intrathecal buprenorphine (60mcg) followed by intrathecal fentanyl (25mcg) and was least (4.12hours) with intrathecal 0.75% isobaric ropivacaine. Capogna et al(11) demonstrated prolonged analgesia with 30mcg buprenorphine (8hours) and 45mcg buprenorphine (12hours). However in our study analgesia duration with 60mcg dose was 8hours only which may be due to ceiling effect of buprenorphine. The analgesic effect is attributed to the fact that buprenorphine has a very high affinity for the opiate receptors present on the spinal cord and supraspinally.

Chung et al(12) showed that adding a small dose of fentanyl (10mcg) to 0.5% hyperbaric ropivacaine increased the duration of effective analgesia to a mean of 207minutes. Similarly, Biswas et al(13) also found that addition of 12.5mcg fentanyl to hyperbaric ropivacaine increased the duration to first time of rescue analgesia to a mean of 248minutes. Similar results were showed by Yegin et al(14) who used 25mcg of fentanyl. We also used 25mcg of fentanyl in our study which showed similar results to all above studies.

In our study, onset of sensory and motor block was not prolonged any of the three groups which matches well with studies conducted by Yegin et al(14), Khan FA et al(15), Gupta K et al(16) and Shaikh et al.(17) Duration of sensory anaesthesia and motor blockade were prolonged in buprenorphine group as compared to fentanyl group similar to study done by Khan FA et al(15) who used 30mcg of buprenorphine to 0.75% hyperbaric ropivacaine.

In our study, postoperative sedation scores were highest with buprenorphine group. Patients developed sedation as assessed by sedation scores but were easily arousable.

On comparing the three groups with regards to adverse effects like hypotension, bradycardia , nausea , vomiting, respiratory depression and shivering the difference was statistically insignificant. However, Khan FA et al(15) reported increased incidence of nausea ,vomiting and respiratory depression with 150mcg dose of buprenorphine. This difference could be due to the use of lower doses (60mcg) in our study.
One limitation of our study was that a therapeutic end point of VAS score 3 or request for analgesic was used. 24 hours total analgesic requirements were not recorded which would have better demonstrated the analgesic qualities of the studied drugs. However our study found buprenorphine and fentanyl both prolonged analgesia and decreased postoperative VAS scores.

CONCLUSION

Both buprenorphine (60mcg) and fentanyl (25mcg) were effective and safe as adjuvants to 0.75% isobaric ropivacaine when given intrathecally in patients undergoing lower limb surgeries. Buprenorphine appeared to be better in terms of prolongation of the duration of analgesia as compared to fentanyl, provided adequate sedation in the postoperative period without significant postoperative complications.

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Conflicts of interest
There were no conflicts of interest

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