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Original research article

Intrathecal buprenorphine-an adjuvant to 0.5% racemic bupivacaine for subarachnoid block in elective open gynaecological surgeries

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Abstract

Background & objectives: Subarachnoid block is commonly used for lower abdominal and lower limb surgeries. Racemic bupivacaine 0.5% is commonly used in spinal anaesthesia.Various additives are added for various reasons. Buprenorphine is a synthetic opioid analgesic with a mixed agonist-antagonist action and is a commonly used one such adjuvant. This study has been designed to evaluate the sensorimotor effects, onset and duration of analgesia, vital parameters and any adverse effects of addition of buprenorphine (60 μg) to 3 ml of 0.5% racemic bupivacaine intrathecally for elective open gynaecological surgeries.

Methods: In this randomized, double-blind prospective study, 60 patients (age 18- 60years) of ASA I and II were randomized into two groups: group BO and BB (n=30). Group BO received a 3ml of 0.5% racemic bupivacaine (15 mg) only and Group BB received 3ml of 0.5% racemic bupivacaine along with 60mcg buprenorphine.

Results: It was found that the onset of sensory block upto T10 and motor block is statistically significantly faster in group BB (109.33 sec and 153.5 sec) over group BO (133 sec and 167.67 sec). The mean time for two segment regression, the mean time to sensory regression to L1,the mean duration of analgesia and the mean duration of motor blockade is significantly prolonged in Group BB (106.67 min, 322 min, 343 min, x 330.5 min) over Group BO (132.67 min, 259.67 min, 290.67 min, 253.34 min) with $p<0.001$.

Conclusion:60μg of Buprenorphine used as an adjuvant in subarachnoid block was found to be a better adjuvant in prolonging the sensory and motor blockade intraoperatively and the duration of postoperative analgesia compared than 0.5% bupivacaine alone, without significant adverse effects making it a good option in prolonged surgeries and for good post-operative analgesia.

Keyword: spinal anaesthesia,racemic bupivacaine,buprenorphine, gynaecological surgery

Introduction

Pain is a complex, multidimensional perception.It is a dynamic process, involves actions at multiple sites starting from peripheral tissue injury provoking peripheral sensitization leading to central sensitization. Ultimately the inflammatory response leads to release of chemical mediators that act synergistically to convert high threshold nociceptors to low threshold nociceptors [1].

Prevention and treatment of postoperative pain plays an important role. It enables early ambulation, reduces morbidity, duration of hospital stay and improves the surgical outcome. The adequacy of postoperative pain control is one of the most important factors in determining safe discharge from Day care surgery [2].Systemic analgesia by nature is associated with numerous side effects like drowsiness, dizziness and disorientation. This may not allow the patient to ambulate early. Some drugs may cause nausea, vomiting and itching.

Spinal anaesthesia is the most commonly used technique for lower abdominal surgeries. It is easy to administer, has rapid onset of action, low risk of infection as from catheter in situ, less failure rates.

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Spinal is safe and economical [3-4].Patient is awake and conscious, so can describe and relate timely indicators of complications.
Spinal anaesthesia using traditional local anaesthetics only, without adjuvants have a shorter duration of action and so lead to an early analgesic requirement in the postoperative period.
Intrathecal narcotics potentiate the sensory blockade of local anaesthetics without affecting the sympathetic activity [5].They provide prolonged post-operative analgesia but are associated with increased risk of nausea, vomiting, itching and respiratory depression [6].
Buprenorphine, a μ receptor partial agonist with low intrinsic activity can be safely used in subarachnoid block. Buprenorphine is compatible with CSF. It is lipophilic and has high molecular weight. This may prevent its rostral spread and thus respiratory depression [7].
This study has been designed to compare the sensory and motor effects of Buprenorphine as adjuvant to 0.5% bupivacaine for spinal anaesthesia in elective open gynaecological surgeries.

Objectives and aim of the study
This study aims to investigate and compare the effects of intrathecal administrationBuprenorphine(60μg)to 3 ml of 0.5% racemic bupivacaine intrathecallyand 0.5%racemic bupivacaine alone for elective open gynaecological surgeries.

We aim to evaluate the following parameters in both the groups
- Time to onset of sensory and motor block.
- Duration of sensory and motor block.
- Duration of effective post-operative analgesia.
- Side effects.

Materials and Methods
This study was conducted at the Vijayanagar institute of medical sciences,BallariJanuary 2019 to January 2020.
This study was done after Ethical Committee approval and written informed consent from all patients included in the study.

Study design
This study was done in a prospective double blinded randomized manner.

Inclusion criteria
1. American Society of Anesthesiologists [ASA] grade 1 and 2 patients.
2. Adult patients aged between 18-60 years of both sex.
3. Patients undergoing elective lower abdominal surgeries.

Exclusion criteria
1. Patients belonging to ASA grade III, IV and V.
2. Patient refusal.
3. Liver and renal dysfunction.
4. Patients with cardiac dysrhythmias.
5. Patients using adrenergic receptor blockers,calcium channel blockers.
6. Weight >120 kg or height < 150 cm.
7. Patients with contraindications for spinal anaesthesia.
8. Allergy to drugs.

Source of data
This study was conductedinadultpatients aged between 18-60 years undergoing elective lower abdominal surgeries under spinal anaesthesia in VIMS,Ballari. 60 patients were divided into 2 groups by permuted block randomisation technique in the ratio 1:1.

Group BO: Received 3 ml 0.5% racemic bupivacaine only.
Group BB: Received 3 ml of 0.5% racemic bupivacaine and 60 micrograms of Buprenorphine.
In the O.T, appropriate equipment for airway management and emergency drugs were kept ready. The

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horizontal position of the operating table was checked and patient shifted to the table.18G i.v cannula was inserted and the patient was preloaded with 500ml of Lactated Ringer's solution. NIBP, SpO_2, ECG leads were connected to the patient. Preoperative baseline systolic and diastolic BP, PR, SpO_2 and RR were recorded. Under strict aseptic precautions, a midline lumbar puncture was performed using a 25G Quincke needle in sitting position. The patient was then immediately placed in supine position. The time for intrathecal injection was considered as 0 and the following parameters were observed-sensory blockade, motor blockade, and duration of analgesia.

The PR, systolic and diastolic BP, SpO_2 and RR were recorded every 2 min for 10minand then every 5 min throughout the intraoperative period. The above vital signs at the completion of surgery were noted.

Hypotension was defined as fall in systolic BP > 30% from baseline orMAP <60mmHg. This was managed with i.v Mephentermine 6mg in increments. Bradycardia was defined as HR < 60 /min and was managed with Inj.Atropine 0.01mg/kg i.v. Respiratory depression was defined as RR < 8/min and or SpO_2< 85%. This was planned to be managed with bag and mask ventilation or intubation and IPPV if necessary. Blood loss more than the allowable loss was replaced with blood.

Patient was shifted to recovery room after completion of surgery. The vital signs were recorded, every 15 minin the 1st hour after surgery and 30 min interval for next 2 hours and thereafter at hourly intervals for next 3hrs. Sensory and motor block were assessed every 15 min till recovery of pin prick sensation to L_1 and Bromage score of 1 respectively. Patients were shifted to post-operative ward after complete resolution of motor blockade.

Patients were monitored for 24 hours to detect the occurrence of side effects-respiratory depression, nausea, vomiting, dry mouth, urine retention and pruritis. Patients were also enquired about the occurrence of transient neurological symptoms which was described as pain/paraesthesia in the neck, buttocks, legs or pain radiating to lower extremities after initial recovery from SAB within 72 hrs.

Following subarachnoid block, sensory block was assessed by loss of sensation to pinprick using 23G sterile needle. The assessment was started immediately after injection and continued every 15 sec till loss of pinprick sensation at T_{10} level. Onset of sensory block was taken as time from intrathecal injection to loss of pinprick sensation at T_{10}.At 20mins interval after SAB, the dermatomal level of sensory block noted and this was considered as maximum level of sensory block.

Motor block was assessed using the Bromage score

Grade 1: Full flexion of knees and feet possible.
Grade 2: Just able to flex knees with free movement of feet.
Grade 3: Unable to flex knees but with free movement of feet.
Grade 4: Unable to move legs and feet.

Assessment of motor block was started immediately after the intrathecal injection. It was tested every 15 sec till Bromage Score of 4 was reached. Onset of motor block was taken as time taken to achieve Bromage score of 2 from subarachnoid block. The degree of motor block after 20min of injection was noted and this was considered the maximum degree of motor block. Thereafter, motor block regression was noted and duration of motor block was taken as time from initiation of SABto return of Bromage Scoreto 1.

At the end of surgery, the degree of pain was assessed using VAS scale till VAS score > 4 was reached. Whenever the patient complained of pain, the rescue analgesic, Inj. Diclofenac 75mgi.m was given. Duration of effective analgesia was defined as time interval between onset of SAB and the time to reach VAS ≥4.

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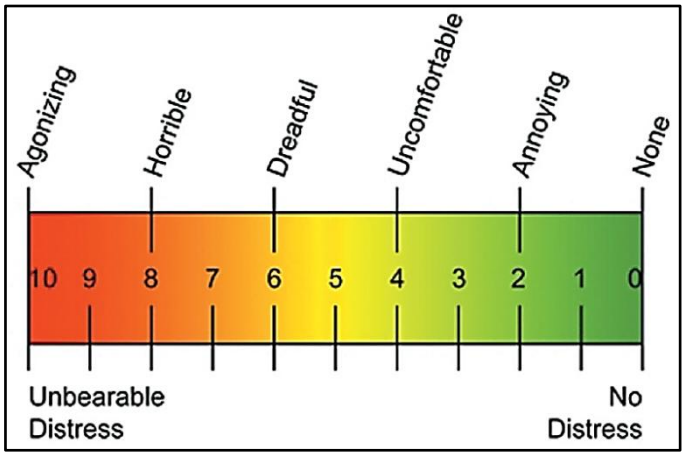

Fig 1: Visual Analogue Scale

Statistical analysis

All recorded data were entered using MS Excel software and analysed using SPSS 16 version software for determining the statistical significance.

Analysis of Variance was used to study the significance of mean of various study parameters between the three groups.

Chi-square test with Yates correction was used to study the significant association between sex distributions among the groups.

The p-value taken for significance is less than 0.05.

Ap-value < 0.001 was considered to be highly significant.

The median was used to compute the maximum sensory and motor block and the sedation scores.

Observations and Results

Patient characteristics

Age distribution

Table 1: Distribution of mean age by groups

	N	Mean Age	SD	Min.	Max.	'p' value
Group BB	30	33.87	10.197	18	56	0.2041*
Group BO	30	37.27	10.305	28	55	

The groups were comparable with respect to their age because there was no statistical significant difference among the groups ($p > 0.05$). The demographic profile of both the groups showed no significant differences statistically.

Onset of sensory block

There is a significant difference between groups with regard to onset of sensory block, with Group BB having a fast onset compared to Group BO ($p< 0.0001$). (Table 02)

Onset of motor block

There is no significant difference between groups in the onset of Motor block. (Table 02)

Time to two segment regression

There is significant difference between groups in two segments Regression, with Group BB requiring a much longer time compared to Group BO($p <0.0001$). (Table 02)

Time to sensory regression to l_1

There is significant difference between the groups in mean time to sensory regression to L_1 – with Group BB requiring a much longer time compared to Group BO ($p<0.0001$). (Table no 02)

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Mean duration of analgesia
There is a significant difference between the groups in the mean duration of analgesia with Group BB having a much longer duration compared to Group BO ($p < 0.0001$). (Table no 02)

Maximum level of sensory block
The median of the maximum level of sensory block reached in both the groups is $T_{6.}$ Therefore, there is no significant difference between the groups in this respect. (Table no 02)

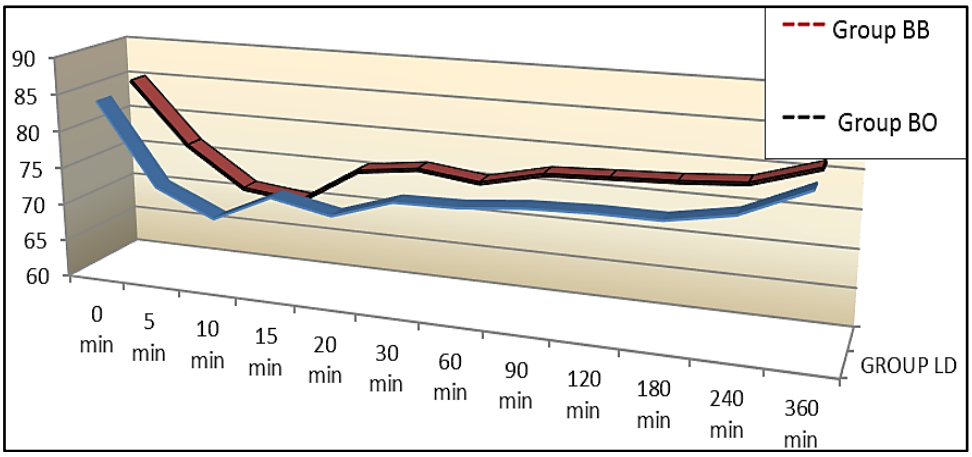
Mean duration of motor block
There is significant difference between groups in duration of motor block with group BB having longer duration compared to group BO ($p<0.0001$). (Table no 02)

Table 2: Comparison of sensory, motor analgesia parameters among the two groups

Parameter	Group BB (N=30)	Group BO (N=30)	P value
	Mean ± SD	Mean ± SD	
Sensory parameters			
Onset of sensory block (sec)	109.33 ± 12.98	133 ± 15.35	<0.001
Two segment regression (min)	132 ± 14.6	106.67 ± 15.77	<0.001
Time to sensory regression to L1	322 ± 40.39	259.67 ± 22.51	<0.001
Motor parameters			
Onsetof motor block (sec)	153 ± 59.83	167.67 ± 18.46	0.2202
Duration of motor block (min)	330.5 ± 39.85	253.34 ± 22.48	<0.001
Duration of analgesia			
Analgesia (min)	343 ± 43.02	290.67 ± 22.88	<0.001

Hemodynamic parameters
These included heart rate, systolic blood pressure, diastolic blood pressure and respiratory rate recorded at definite time intervals of 0 and every 5 minutes for first 30 minutes and there after every 10 minutes for the next 90 minutes.

Variation of heart rate among the groups
There is no significant difference between both the groups with respect to intra-operative and postoperative mean heart rates with $p>0.05$. (Graph 1)



Graph 1: Variation of heart rate among the groups

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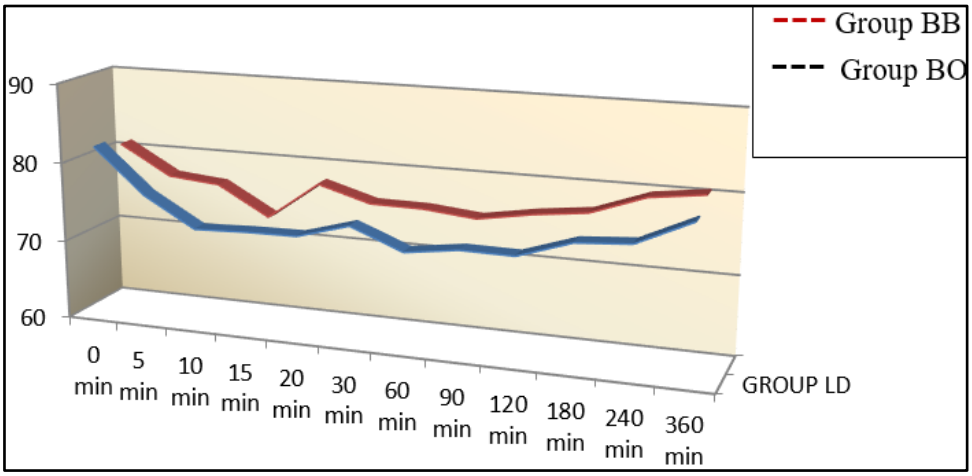

Graph 2: Variation of MAP by groups

Both the groups have similar mean SBP, DBP and MAP values throughout the intra-operative and postoperative periods with $p > 0.05$.(Graph 2)

Mean respiratory rate

There was no statistically significant difference in the mean respiratory rate between Group BB and Group BO at any point of time during the study.

Mean Oxygen saturation

There was no statistically significant difference in the mean oxygen saturation between the two groups at any point of time during the study.

Adverse effects

There was no statistically significant difference in the adverse effects among the two study groups. (Table 3). 6 patients in Group BB and 5 patients in Group BO had Bradycardia. 3 patients in group BB and 2 patients in group BO had hypotension. None of the patient s in Group BB had nausea, vomiting or Pruritis. In group BO 1 patient had Pruritis, 1 patient had nausea and two patients had vomiting.

Table 3: Comparison of adverse effects among the two groups

Side effects	Group BB		Group BO		P value
	Frequency	Percent	Frequency	Percent	
Bradycardia	6	20.0%	5	16.7%	0.494
Hypotension	3	10.0%	2	6.7%	
Nausea	0	0.0%	1	3.3%	
Pruritis	0	0.0%	1	3.3%	
Vomiting	0	0.0%	2	6.7%	
Nil	21	70.0%	19	63.3%	
Total	30	100.0%	30	100.0%	

Discussion

In our study, we compared the sensorimotor effectiveness of addition of buprenorphine (60 µg) to intrathecal racemic bupivacaine (0.5%) and racemic bupivacaine alone.

Onset of sensory block

The mean time to onset of sensory block is 109.34sec in Group BB and is 133 sec in group BO. Onset of sensory block upto T10 is statistically significantly faster in BB group over BO group with $p < 0.0001$.
It correlates with the study by F A Khan Gauhar[7]who found that the meantime of sensory block to reach T10 was 1.67$\pm$0.52min inbuprenorphine group and 2.04$\pm$0.6 min in group bupivacaine.

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Onset of motor block

The mean time to onset of Bromage 2 motor block is 153.5 sec in group BB and 167.67 sec in group BO. There was no statistically significant difference among the 2 groups (p = 0.2202).

It correlates with the study by B maharani *et al.*[14] who foundthatthe mean time to reach Bromage 3 scale was 3.56±1.13 with 10 µg Dexmedetomidine, 3.66±1.19 min with 60µg buprenorphine which was statistically insignificant (p 0.740).

Mean time to two segment regression and time to sensory regression to l_1

The mean time taken for two segment regression was 132.67 min in group BB compared to 106.67 min in group BO. The time for two segment regression is significantly prolonged in group BB compared to Group BO (p < 0.0001).

In our study, there is significant difference between the groups in terms of thetime to sensory regression to L_1 – with Group BB requiring a much longer time 322 min) compared to Group BO (259.7 min) which is highly significant withp<0.0001.

F A Khan Gauhar[7] also found that the regression time to S1 dermatome was 377.5±48.54 min in group buprenorphine and 304.6±73.67 min in group bupivacaine alone(p < 0.001).

Hala E A Eid MD *et al.*[12] also concluded that Buprenorphine significantly prolonged time to two segment regression, sensory regression to S_1.

Mean duration of analgesia (min)

There is significant difference between groups in total duration of analgesia with Group BB having a much longer duration compared to Group BO (p <0.0001). Group BB has a mean duration of analgesia of 343 min and Group BO has 290.6 min. Thus, the analgesic requirement in the first 24 hours postoperatively in Group BB was significantly lesser than that in Group BO.

FA Khan Gauhar[7]concluded that intrathecal buprenorphine significantly prolong the anaesthetic and analgesic effects of spinal hyperbaric bupivacaine.

Addition of 10 ug increased the duration of analgesia provided by spinal bupivacaine by about 375.83+48.59 min compared to 302.57+75.74 min with 60 µg buprenorphine (p <0.001).

Mean duration of motor block

The mean duration of motor block in Group BB and Group BO are 330.5 min, 253.34 min respectively (p<0.0001) which was statistically significant.

It correlates with the study by F A Khan Gauhar[7]who found thatmotor block regression to modified Bromage 0 were significantly prolonged in group Buprenorphine 342.11 ± 48.67than in group Bupivacaine alone 266.98 ± 73.47.

Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA*et al.*[11] observed that the regression to Bromage 0 was 302.9±36.7min in D10 (10µg dexmedetomidine) which was similar to our study.

Haemodynamic parameters

In our study, there is no significant difference between both the groups with respect to intraoperative and postoperative mean heart rates with p>0.05.Both the groups have similar mean SBP,DBP and MAP values throughout the intraoperative and postoperative periods with p > 0.05.

Side effects

In a study by FA Khan Gauhar[7] the incidence of nausea and vomiting was higher with intrathecal buprenorphine which correlates with the findings of our study.

5 patients in Buprenorphine group had transient bradycardia which responded to Intravenous atropine.

Conclusions

The following conclusions were drawn-60µg of Buprenorphine used as an adjuvant in subarachnoid block was found to be a better adjuvant in prolonging the sensory and motor blockade intraoperatively and the duration of postoperative analgesia compared than 0.5% bupivacaine alone, without significant adverse effects making it a good option in prolonged surgeries and for good post-operative analgesia.

The time to two segment regression was significantly prolonged with the addition of intrathecal buprenorphine to hyperbaric Bupivacaine.

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The time to motor regression was significantly prolonged with the addition of buprenorphine.
Addition of Buprenorphine along with hyperbaric Bupivacaine intrathecally does prolong duration of analgesia and reduce postoperative analgesic requirements.
There was no appreciable difference in the time to onset of either sensory or motor block.
Further studies to validate our findings recruiting larger patient population is considered essential.

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