

Comparative Study of Low and High Doses of Butorphanol as Adjuvant to Bupivacaine in Subarachnoid Block.

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ABSTRACT

Background: The goal of present study is to compare intraoperative and postoperative hemodynamic and sensory/ motor effects of low dose intrathecal butorphanol with bupivacaine versus high dose intrathecal butorphanol with bupivacaine in patients undergoing elective lower limb surgeries. **Methods:** This randomized, double blind comparative study was conducted in 60 patients belonging to ASA grade I or II, aged 20-60 years admitted for lower limb surgeries under spinal anesthesia. The patients were randomly divided into 2 groups. (A and B, n=30 for each group). Group A received combination of 0.5% hyperbaric bupivacaine (2.5 ml) with low dose butorphanol (25 microgram in 0.5 ml) intrathecally and group B received combination of 0.5% hyperbaric bupivacaine (2.5 ml) and high dose butorphanol (50 microgram in 0.5 ml) intrathecally. Preoperative and intraoperative vitals; side effects; intensity of motor blockade, time of onset of sensory and motor blockade; time taken for peak sensory and motor blockade; time for two segment sensory regression and time for rescue analgesia were compared in both group. **Results:** Time taken for peak sensory block was significantly lesser in group B and time for two-segment regression of sensory level and time to rescue analgesia were also significantly higher in group B, in which high dose intrathecal butorphanol-bupivacaine mixture was used. There was no difference in time taken to onset of sensory block, time taken to onset of motor block, time taken for peak motor block and in the intensity of motor blockade in using high dose intrathecal butorphanol-bupivacaine mixture as compared to low dose intrathecal butorphanol-bupivacaine mixture. **Conclusion:** We concluded that high dose intrathecal butorphanol (50 µg) with bupivacaine is well tolerated and potentiates the sensory block better than low dose intrathecal butorphanol (25 µg) with bupivacaine with out any major side effects. It did not increase postoperative motor block recovery time and has delayed the postoperative analgesic requirement.

Keywords: Butorphanol, Intrathecal, Opioid, Postoperative Analgesia, Rescue Analgesia.

INTRODUCTION

Subarachnoid block is very common preferred and reliable method of anesthesia in lower limb and abdominal surgeries.^[1] It is unparalleled in the way that a small mass of drug, virtually devoid of systemic pharmacologic effect, can produce surgical anesthesia but hemodynamic instability due to sympathetic blockade impedes the effective and safe use of spinal anesthesia.^[2] Many drugs have been used for spinal anesthesia for lower limb and abdominal surgeries, but intrathecal 0.5% hyperbaric bupivacaine is quite popular as it provides good sensory and motor block for longer duration without significant neurological side effect.^[3] Other agents like spinal opiates, α_2 agonists are also being used now a days to prolong the sensory motor blockade effect of anesthetic agent and to achieve long lasting

post operative analgesia for patients. Butorphanol is a synthetic opioid, which binds to both μ and κ opioid receptors. Therapeutic categories for butorphanol in humans are as an anesthesia or pre-anesthesia adjunct, narcotic analgesic for the relief of moderate to severe migraine, postoperative, or obstetric pain.^[4]

Butorphanol has been in use since 1978 in western countries and a number of studies have been performed establishing its efficacy and safety, but was not available in India till 2002. Since its launch in India, it has been commonly used by intravenous, intramuscular and epidural routes but its intrathecal use is less explored.^[5] The goal of present study is to compare intraoperative and postoperative hemodynamic and sensory/ motor effects of high dose intrathecal butorphanol with bupivacaine versus low dose intrathecal butorphanol with bupivacaine in patients undergoing elective lower limb surgeries.

MATERIALS AND METHODS

Present study was a randomized, double blind comparative study, which was conducted in

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Department of Anaesthesia, Rajkiya Medical College, Jalaun (Orai) for over duration of 2 years on 60 patients who have undergone for some lower limb surgeries in Department of Orthopaedics. Approval of the college ethics committee and written informed consent from all the patients were obtained for this study. Detailed history taking, complete general physical examination and systemic examination were done for each patient during the pre-anesthetic check-up by first observer. Only those patients were included in this study which were in ASA class I / II with age range between 20 to 60 years and who were admitted in Department of Orthopaedics and were scheduled for some lower limb surgery.

Exclusion criteria for our study were as follows

- Patient known allergic to local anesthetic agents
- Patient with severe cardiac disease or respiratory disease
- Spine deformities or skin infection at local sites
- Uncontrolled hypertensive patient or hypotensive patient
- Hematological disorder
- Patient with any acute infection
- Any kind of psychiatric illness
- Highly anemic patient
- Severe obese patient
- Age below 20 years and above 60 years
- Patients who refused to give consent for enrolling in study
- Patient known for opioid addiction or other drug abuse

Patients were randomly divided into two groups (group A and group B) with 30 patients in each group by observer 1. Group A received combination of 0.5% hyperbaric bupivacaine (2.5 ml) with low dose butorphanol (25 microgram in 0.5 ml) intrathecally and group B received combination of 0.5% hyperbaric bupivacaine (2.5 ml) and high dose butorphanol (50 microgram in 0.5 ml) intrathecally. Intrathecal drug administration to all the patients of both groups was done by observer 1, while preoperative and intraoperative heart rate, systolic blood pressure, diastolic blood pressure, respiratory rate and peripheral arterial oxygen saturation (SpO₂) was recorded by observer 2. These vitals were recorded at 5minutes intervals for the first 20 minutes from the time of injection of spinal solution and thereafter every 15 minutes during complete period of surgery by the observer 2. The highest level of sensory block was determined in the anterior axillary line bilaterally by pinprick test using a 20-G hypodermic needle every 2minutes till the level was stabilized for four consecutive tests. Time of onset of sensory block and the time of peak sensory block were noted in seconds by observer 2.

Time of onset of sensory blockade was defined as the time interval between the completion of intrathecal injection of local anaesthetic solution to the onset of loss of sensation to pinprick with 22G needle in anterior axillary line bilaterally. Time of peak sensory blockade was defined as the time taken to achieve the highest level of sensory blockade from the time of completion of intrathecal injection of local anaesthetic solution. [6] Duration of sensory blockade was assessed by two segments regression time in minutes. It is defined as the time interval from injection of local anaesthetic solution until the maximum level of sensory blockade has decreased by two segments. Degree of motor blockade was assessed by loss of antigravity movements of leg by using Bromage scale. Intraoperative and postoperative side effects such as bradycardia, hypotension, tachycardia, nausea, vomiting, headache, sedation, pruritus, shivering, urine retention and respiratory depression were also noted by observer 2. The time of first request of rescue analgesia was also noted in minutes by observer 2.

All the data were recorded in a pre-designed pro forma followed by its entry in Microsoft excel sheet. The quantitative variables were summarized by mean and standard deviation in each of the groups separately. To compare the mean value in the groups, unpaired t test was applied using Statistical Calculator 4.0. Categorical variables were summarized by frequency and Pearson chi square test was used to compare percentage across the groups. In this study all the statistical tests were two tailed and P value of <0.05 was considered statistically significant.

RESULTS

Table 1: Demography

	Group A (n=30)	Group B (n=30)	Comparison
Mean age in years	41.16 ± 5.03	39.3 ± 7.12	t=1.16 p=0.25
Mean height in cms.	166.1 ± 8.77	165.3 ± 6.15	t=0.41 p=0.68
Mean weight in kg	63.03 ± 6.31	61.23 ± 5.74	t=1.16 p=0.25
Mean BMI	22.84 ± 1.42	22.4 ± 1.66	t=1.10 p=0.27
Duration of surgery in minutes	143.6 ± 20.17	151.3 ± 18.89	t=1.53 p=0.13
Male/ female ratio	26/4	27/3	X ² =0.162 p=0.69
ASA grade I/II	25/5	26/4	X ² =0.131 p=0.71

Table 2: Intensity of motor blockade.

Bromage scale	Group A (n=30)	Group B (n=30)
1	0	0
2	0	0
3	6	7
4	24	23

X² =0.098 p= 0.75

Table 3: Anesthetic and analgesic effect.

Outcome	Group A (n=30) (Mean ± SD)	Group B (n=30) (Mean ± SD)	95% CI for the difference	P value
Highest level of sensory blockade	T7	T7	-	-
Onset of sensory block in seconds (start of tingling numbness)	22.76± 4.89	24.77± 4.12	-4.35 to 0.32	t=1.72 p= 0.09
Onset of motor block in seconds (unable to flex knee joint)	51.9 ± 7.39	52.47 ± 6.15	-4.08 to 2.94	t= 0.32 p= 0.75
Time of peak sensory block in seconds (time taken to reach at maximum sensory block upto level T7)	317.47 ± 19.79	297.27 ± 11.89	11.76 to 28.63	t=4.79 p<0.001
Time of peak motor block in seconds (when legs cannot be moved)	240.63 ± 44.46	219.40 ± 38.92	-0.36 to 42.82	t=1.97 p=0.054
Time for two segment sensory regression in minutes	96.9 ± 12.84	107.2 ± 13.96	-17.23 to -3.36	t=2.97 p=0.0043
Time to rescue analgesia in minutes	301.67 ± 36.25	600.4 ± 156.01	-357.26 to -240.19	t= 10.21 p<0.001

Table 4: Intraoperative/ postoperative side effects.

	Group A (n=30)	Group B (n=30)	X2 value and p value
Bradycardia	2	1	X2 =0.351 p= 0.55
Hypotension	1	2	X2 =0.351 p= 0.55
Nausea	2	3	X2 =0.218 p= 0.65
Vomiting	0	0	-
Headache	0	0	-
Sedation	0	0	-
Pruritus	0	0	-
Shivering	1	0	X2 =1.01 p= 0.31
Urine retention	0	0	-
Respiratory depression	0	0	-
Tachycardia	0	0	-

DISCUSSION

Demographic data of group A and group B is given in table-1. On comparison of age, weight, height and BMI of patients of group A and B, it was found that the difference was not significant. Gender ratio and ASA grade in group A and B were compared using chi-square test and the differences were again found insignificant. [Table 1]

Intensity of motor blockade was assessed using bromage scale. Frequency distribution of bromage score among group A and B did not showed any significant difference. [Table 2] It means that there was no difference in intensity of motor blockade in using high dose intrathecal butorphanol-bupivacaine mixture as compared to low dose intrathecal butorphanol-bupivacaine mixture.

Regarding time taken to onset of sensory / motor block and time taken for peak motor block in both the groups did not show any significant difference similar to the study of Panda et al (2018).^[5] Time taken for peak sensory block i.e. time taken to reach at maximum sensory block upto level T7 showed a significantly lower value in group B than group A. The time for two-segment regression of sensory level and time to rescue analgesia were shorter in Group A compared to group B. Analysis was done using unpaired 't' test, which showed statistically significant difference between the these groups. It means duration of sensory blockade and duration of postoperative analgesia was longer with high dose

intrathecal butorphanol-bupivacaine mixture as compared to low dose intrathecal butorphanol-bupivacaine mixture. [Table 3]

Panda et al (2018) reported higher time for two-segment regression of sensory level in patient group, which received high dose intrathecal butorphanol (50 µgm)-bupivacaine mixture as compared to low dose intrathecal butorphanol (25 µgm)-bupivacaine mixture.^[5] Though it has also been reported in various study that time for two-segment regression of sensory level increases significantly on addition of intrathecal butorphanol with bupivacaine.^[5,7]

Regarding intraoperative and postoperative haemodynamic parameters, most of the patients in both groups showed their blood pressure and pulse rate with in normal physiological range all the time. Bradycardia was shown in 6.66% patients in group A and 3.33% patient in group B, while hypotension was shown in 3.33% patients in group A and 6.66% patients in group B. Few patients from both group complained of nausea and only 1 patient from group A complained of shivering post operatively. No significant difference was found in incidence of intraoperative/ postoperative side effects between group A and group B. [Table 4]

In a similar study by Panda et al (2018) they reported higher incidence of bradycardia and hypotension in patient group, which received high dose intrathecal butorphanol (50 µgm) -bupivacaine mixture as compared to low dose intrathecal butorphanol (25 µgm) -bupivacaine mixture.^[5] They reported fall in systolic blood pressure from 3 minute to 60 minute in patient group which received high dose intrathecal butorphanol (50 µgm) -bupivacaine mixture, but this fall in systolic blood pressure was with in physiological range in their study.^[5] None of the patients in either group showed respiratory depression. Butorphanol is a kappa receptor agonist as well as a mu-receptor antagonist, resulting in analgesic and sedative properties without profound respiratory depression or euphoria. These properties make it a potentially useful drug for ambulatory surgical patients.^[8] There was no incidence of other side effects like urine retention, vomiting, headache, sedation and pruritus in any group. In some studies on animal models, butorphanol has been shown to

have antipruritic effect due to its effect on kappa receptors.^[9-11]

CONCLUSION

We concluded that high dose intrathecal butorphanol (50 µgm) with bupivacaine is well tolerated and potentiates the sensory block better than low dose intrathecal butorphanol (25 µgm) with bupivacaine with out any significant increase in postoperative motor block recovery time. Use of high dose intrathecal butorphanol with bupivacaine also reduced the postoperative analgesic requirement with out causing any major side effects to patients.

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