Research Article

Comparison of analgesic effects of equipotent doses of intrathecal morphine and buprenorphine during spinal anaesthesia with hyperbaric bupivacaine

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Abstract

Aims and objectives: A comparative study using equipotent doses of intrathecal morphine and buprenorphine during spinal anesthesia with 0.5% hyperbaric bupivacaine. **Methods:** A prospective randomized hospital basedcomparative study 200 patients belonging to ASA physical status I and II scheduled for various surgeries under spinal anaesthesia were grouped into two groups of 100 each. Group B consisting of 100 patients were given 3 ml of 0.5% hyperbaric bupivacaine along with 100 µg of buprenorphine and group M consisting of 100 patients were given 3 ml of 0.5% hyperbaric bupivacaine along with 100 µg of morphine intrathecally. Onset and duration of sensory and motor block, maximum height of sensory block, time to request for rescue analgesia, haemodynamic parameters and adverse effects were studied. **Results:** The mean time to request for rescue analgesia was longer in group B when compared to group M. The mean time of onset of sensory and motor block was marginally less in group B when compared to group M. The total duration of the sensory and motor block was more in group B when compared to group M. There was no significant difference among the study groups in attaining maximum height of sensory block, 2 segment regression, haemodynamic parameters, RR and sedation score. The incidence of side effects is less in group B when compared to group M. **Conclusion:** 100µg of buprenorphine used as an adjuvant to intrathecal 0.5% hyperbaric bupivacaine provides increase in duration of analgesia with much less side effects when compared to 100 µg of morphine.

Keywords: Buprenorphine, morphine, bupivacaine, intrathecal.

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INTRODUCTION

The spinal anaesthesia technique has been credited to J. Leonardcornig, a New York neurologist[1]. He accidentally pierced the dura mater while experimenting with cocaine on spinal nerves of a dog. Later he deliberately repeated the intradural injection, termed it spinal anaesthesia and suggested that it might be used in surgery. Lumbar puncture was standardized as a simple clinical procedure by Heinrich Iraneus Quincke in 1891andin 1898, August Bier[2] first used spinal anaesthesia as an anaesthetic technique for surgery. Bupivacaine was introduced by Eckenstam in 1957 and Dr Leo Telivuo published the first report on the clinical use of Bupivacaine in 1963. The disadvantage with spinal anaesthesia using bupivacaine alone has relatively short duration of action, which means that an early analgesic intervention is needed in the postoperative period. Pederson *et al*[3] demonstrated that, although the incidence of abdominal pain decreased with increasing doses of Bupivacaine (10-12.5mg Vs 7.5-10mg), almost one third of patients experienced pain. Opioid analgesics have long been recognized as among the most effective treatment for pain. The discovery of opioid receptors and subsequent development of the technique of epidural and intrathecal opioid administration is undoubtedly one of the most significant advances in pain management in the last three decades. The demonstration of opioid receptors in the substantiagelatinosa of spinal cord (Yakash and Rudy 1976) has created interest in the intrathecal administration of opiates in the management of Chronic Pain and Pain following surgery[5]. But the postoperative pain relief by means of intrathecal and epidural opioids are associated with problems like respiratory depression. This has paved the way for study of post operative pain relief with

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narcotic analgesics with local anaesthetic agents like lignocaine and bupivacaine with longer duration of action with minimal dose and minimal side effects. The opioids are unique in producing analgesia without affecting the sympathetic nervous system, motor weakness and loss of proprioception[6]. Though morphine is a prototype molecule, it has got some lacunae like causation of respiratory depression, relatively short duration of action and side effects like nausea, vomiting, pruritus and urinary retention[7]. Buprenorphine is a semi synthetic opioid with partial agonist and antagonist activity and a lipophilic compound. Hence the chances of causation of respiratory depression are unlikely and it has prolonged duration of action[7]. This study is designed to quantitatively examine the effects of adding intrathecal morphine and buprenorphine to hyperbaric bupivacaine on duration of onset, recovery of sensory block, motor block and postoperative analgesia.

MATERIALS AND METHODS

Study Design: A prospective randomised hospital based comparative study.

Source of Data

Patients under ASA physical status I and II undergoing elective surgery under spinal anaesthesia aged 18-50 yrs at Bowring and Lady Curzon Hospital, Victoria Hospital and Vani Vilas Hospital attached to BMC and RI, were taken into consideration for the study between Nov 2010 to Oct 2012. The study was conducted on 200 patients, 100 in Group B and 100 in Group M. Inclusion Criteria was, ASA physical status I and II, patients giving valid informed/explained consent and IN THE AGE GROUP OF 18-60 YEARS. EXCLUSION CRITERIA WAS patients who are allergic to amide local anaesthetic drug, Patient refusal, Patients with Chronic low backache, Patients who have any contra indication for spinal anaesthesia such as infection at the site of injection, bleeding or coagulation abnormalities, increased intracranial pressure, spinal deformities. Patients with cardiovascular, renal, liver diseases.

Pre anaesthetic Examination and Preparation

The study protocol was approved by Hospital ethics committee and ethical clearance was obtained from the institution for the study. Pre anaesthetic check up was done one day prior to surgery. Patients were evaluated for any systemic diseases and Laboratory investigations recorded. The procedure of spinal anaesthesia was explained to the patients and written consent was obtained. Patients posted for elective surgery were kept nil per orally for 10 hrs before the day of surgery. They were pre medicated with Tab Diazepam 10mg at the hour of sleep on the previous night of surgery. Patients were preloaded with IV infusion of one litre of Ringer lactate solution prior to the administration of spinal anaesthesia.

Method

Spinal anaesthesia was administered either in L_3-L_4 or L_4-L_5 space.

Total of two hundred patients were grouped into two groups.

Group B: 100 patients received 3cc of 0.5% hyperbaric bupivacaine with 100 µg of buprenorphine.

Group M: 100 patients received 3cc of 0.5% hyperbaric bupivacaine with 100 µg of morphine.

After administering the spinal anesthesia, HR, SBP,DBP, MAP, SPO_2 and RR were measured every 2min for first 10min, every 5min in the next 80 min and every 10min till the end of surgery. Hypotension and bradycardia was defined as 20% decrease from baseline values and was treated with IV boluses of ephedrine 6mg and 1mg of atropine IV respectively. Nausea and vomiting was treated with injOndansetron 4mg IV. Supplementary oxygen was given through a face mask. The level of sensory anaesthesia, defined as the loss of pin prick sensation with 23 G hypodermic needle at midclavicular level, was measured every min till it reached L_1, T_{10} and Maximum height of sensory block was also recorded. Two segment regression and regression to S_1 was recorded. The motor component was assessed for onset of motor block and duration of motor block. The motor block was assessed every min using modified Bromage scale (0 -3); (0 = no motor impairment, 3=complete motor block of lower limb and then every 10min until the return of normal motor function. The time to complete motor block and complete recovery were recorded. Time first complaint of pain and request for rescue analgesia was recorded. The patients observed for sedation and are recorded by six points by using

Ramsay sedation scale

Score	Response
1	Response
2	Anxious or Restless or both
3	C0-operative, oriented and tranquil
4	Responding to commands
5	Asleep, brisk response to light, glabellar. Ttap or auditory stimuli.
6	Asleep, sluggish response.
7	**Asleep, unarousable.**

The intensity of pain was assessed using 10 point **visual analogue scale**, as no pain, mild, moderate and severe pain.

Pain score	Degree of pain	Degree of analgesia
0	No pain	Profound analgesia
2 -4	Mild pain	Moderate analgesia
5 -7	Moderate pain	Mild analgesia
8-10	**Worst pain**	**No analgesia**

Supplemental analgesia was given when the patient had moderate pain with a pain score of 5-7.

Post operative Period

All the patients were observed in the post anaesthesia recovery room and then in ward. The parameters such as SPO_2, HR, SBP, DBP, MAP, and RR, sedation, pain and side effects (nausea, vomiting, pruritus, urinary retention and respiratory depression) were observed and recorded. They were recorded every 30 min till 3hrs, every hourly till 12 hrs and then every 4th hourly till 24 hrs.

Statistical analysis

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis). Mann Whitney U test has been used to find the significance between two groups for parameters on non-interval scale. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.* Moderately significant (P value: 0.01<P< 0.05),** Strongly significant (P value < 0.01).

RESULTS

Table 1: Demographic Data

Parameter	Group B	Group M	P Value
Age (yrs) (Mean ± SD)	34.45±8.36	32.49±9.44	P=0.121
Weight(kgs) (Mean ± SD)	54.27±7.46	55.26±7.32	P=0.344
Height (cm)	156.59±7.25	157.45±7.81	P=0.421
M:F (100)	**54:46**	**62:38**	**P=0.252**

Table 2: Comparison of sensory and motor variables in the two groups of patients studied

Variables	Group B	Group M	P value
Onset of sensory block at T10 (min)	4.05±0.74	4.71±0.80	<0.001*
Onset of sensory block at L1	2.62±0.52	2.95±0.70	<0.001**
2 segment regression	122.00±9.85	120.70±10.85	0.376
Total duration of sensory block (regression to S1)	203.80±10.62	196.80±10.81	<0.001**
Onset of motor block (min)modified bromage 3	4.51±0.58	4.92±0.69	<0.001**
Duration of motor block (min) modified bromage 0	182.50±8.69	178.42±8.35	0.001**
Time to request for resque analgesia (min)	**474.42±165.68**	**357.61±97.75**	**<0.001****

In both the groups, haemodynamic parameters like HR,SPO2, SBP, DBP, RR were studied and recorded with no significant p value.

Onset of sensory block at T10

Comparison of onset of sensory block at T_{10} in two, groups of patients studied showed that the mean time needed in Gp 'B' was 4.05 $\pm$0.74 min vs4.71 $\pm$0. 80 min in Gp 'M' with a 'P' value of < 0.001 which is statistically significant.

Onset of sensory block at L_1

The mean time of onset of sensory block at L_1 was 2.62 $\pm$ 0.525 in group B. It was 2.95 $\pm$ 0.70 min in group 'M' with a significant P value of < 0.001.

Two segment regression

There is no statistically significant difference in both the groups in mean time taken for 2 segment regression

Total duration of Sensory block (Regression to S_1)

The mean time taken in patients of Gp 'B' to regress to S_1 level was 203.80 $\pm$10.81 min vs 196.80$\pm$ 10.81min in group 'M'. This is statistically significant with a 'P' value of < 0.001.

Duration of motor Block (min) modified Bromage 0

The mean duration of motor block (min) was 182.50$\pm$ 8.69 (min) in group 'B' as against 178.42 $\pm$8.35(min) in group 'M'. This is statistically significant with a 'P' value of 0.001.

Time to request for rescue analgesia (min)

The mean time to request for rescue analgesia was 474.42 $\pm$ 165.68(min) in group 'B' as against 357.61 $\pm$97.75 (min) in group 'M'. This is statistically and clinically very significant in this study.

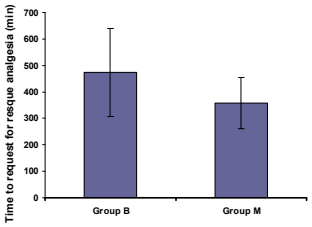

Figure 1:

Comparison of post operative pain score in two groups of patients studied showed, statistically significant 'P' value at different time points. There values are also very much significant clinically. The patients in Gp 'B' had longer pain free period post operatively when compared to group 'M' patients.

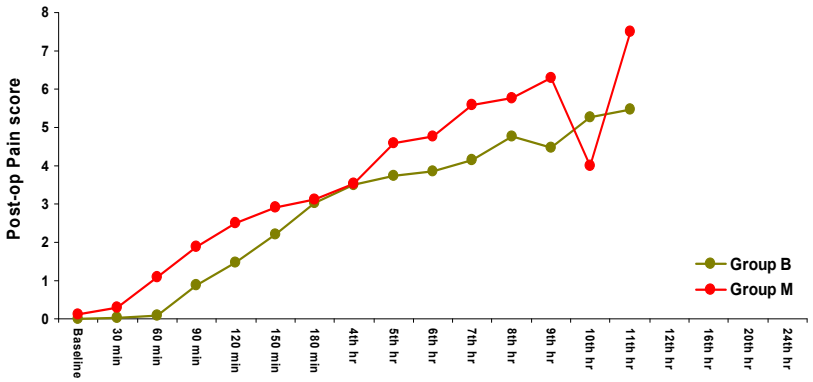

Figure 2:

Incidence of side effects like nausea, vomiting, pruritus are more in Group M (40.0%) when compared to Group B (23.0%) with P=0.010*

DISCUSSION

Sub arachanoid block is a commonly employed anaesthetic technique. The intrathecal procedure is easy to perform, less cumbersome and inexpensive. It also offers a high level of post anaesthesia satisfaction for patients. The combination of local anaesthetics with adjuvants enables us for use of lesser dose of local anaesthetics and increase the success of anaesthesia. The discovery of opioid receptors and pain modulating system in spinal cord, intrathecal opioids have been used as an adjunct to local anaesthetic bupivacaine vary widely. Thus neuraxial opioids provide excellent analgesia intra operatively and postoperatively[6]. Buprenorphine is a semi synthetic opioid with partial agonist and antagonist, causes less respiratory depression and has prolonged duration of action. The demographic data were comparable in both the groups of patients studied. Another unique feature of buprenorophine is its slow dissociation from µreceptors, which can lead to prolonged effects.

Sensory characterstics

Duration of onset of sensory block

In our study the mean time of sensory block at T_{10} was 4.05 $\pm$ 0.74min in Gp 'B' as against 4.71 $\pm$0.080min in group 'M' with a significant 'P value of < 0.001. In a study by shaik SI and Kiran M, they have found that the mean sensory onset time was 3.60 $\pm$ 1.002 (min), when they have used buprenorphine intrathecally at 1µg/kg. The distribution of maximum height of sensory block was similar in both the groups. The sensory block regressed to S_1 earlier in morphine group when compared to buprenorphine group (196.80 min, gp M Vs 203.80min gp B).

Motor Characteristics

The mean time of onset of motor block was earlier in buprenorphine group when compared to morphine group (4.51 min Vs 4.92 min) The mean duration of Motor block was longer in buprenorphine group in comparison with Morphine group, 182.50min Vs 178.42 min.

Analgesic characteristics

The total duration of analgesia was taken as the time interval between the injections of spinal drug to first dose of rescue analgesia. In our study the duration of analgesia was longer in buprenorphine group with 474.42 (min), where as it was 397.61(min) in morphine group. This was highly significant. This is because of high affinity of buprenorphine for both µ and ƙ receptors and it dissociates slowly from µ receptors. These findings are

consistent with the observation that, intrathecal buprenorphine produces prolonged analgesia, in some of the other studies conducted earlier. In a study by Shaik SI[10], KiranM, the mean duration of analgesia was 475.6±93.7 min with a range of 310 – 700 min by using 50µg of buprenorphine intrathecally. The total duration of analgesia in a study by Sunil Dixit[9] "post operative analgesia after caesarean section: an experience with intrathecal buprenorphine (60µg)" was 491.26 ± 153.97 min with minimal side effects. In a study by Capno G, etal[11], the duration of analgesia obtained with 45 µg of bupronorphineintrathecally in patients undergoing supra pubic prostatectomy ranged from 7-12hrs In a double blind study by Lipp M etal[12] found that 150 µg of intrthecal buprenorphine applied for post operative analgesia found that patients were pain free for 13 hrs.

Side Effects

The incidence of side effects are more with Morphine Group(40%) when compared with buprenorphine group (23%) with a significant 'P' value of 0.010.These findings are consistent with the study done by G Capogna, *et al*.

CONCLUSION

Our study reveals that intrathecal buprenorphine (100 µg) with 3 cc of 0.5% hyperbaric bupivacine provided prolonged post operative analgesia with much less side effects. Hence buprenorphine can be safely used for post operative analgesia.

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