Section: Anaesthesiology

Original Research Article

A PROSPECTIVE RANDOMISED DOUBLE BLIND COMPARATIVE STUDY OF INTRATHECAL HYPERBARIC BUPIVACAINE (0.5%) WITH DEXMEDETOMIDINE VERSUS INTRATHECAL HYPERBARIC BUPIVACAINE (0.5%) WITH MORPHINE FOR INFRAUMBILICAL SURGERIES FROM VARIOUS SPECIALITIES

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Abstract

Background: The aim is to assess, compare and evaluate the effect of Intrathecal Hyperbaric Bupivacaine (0.5%) and Dexmedetomidine (5 micrograms) versus Intrathecal Hyperbaric Bupivacaine (0.5%) and Morphine (250 mcg) for Infraumbilical surgeries. Primary objective is to compare and evaluate onset and duration of sensory and motor block. Secondary objectives are to compare Postoperative analgesia, sedation, hemodynamic parameters and any side effects. **Materials and Methods:** A Randomised, double blind, comparative study consisting of 50 patients fulfilling inclusion criteria were randomised into two groups of 25 each and included in the study according to inclusion, exclusion criteria. GROUP A: 3.4ml of 0.5% Hyperbaric Bupivacaine + 250 micrograms of Morphine. GROUP B: 3.4ml of 0.5% Hyperbaric Bupivacaine + 5 micrograms of Dexmedetomidine. Statistical methods: Chi-Square test, Fisher exact test. NPO confirmed. Informed consent obtained. Standard monitors connected. Spinal anaesthesia carried out in a lateral or sitting position while using aseptic precautions. Using 25G Quincke spinal needle in L3-L4 interspace, total volume of 3.4ml with study drug administered intrathecally. Outcome parameters: Modified Bromage scale, Numerical Rating Scale, Ramsay sedation scale. **Result:** Onset of sensory blockade and duration was faster and longer in group A compared to group B. Group A had prolonged duration of postoperative analgesia compared with group B. No significant differences in hemodynamics observed in both groups. Statistically significant higher sedation scores seen in group B with few statistically significant side effects like pruritus were noted in group A. **Conclusion:** Morphine is preferred over Dexmedetomidine as it provides faster sensory and motor blockade onset, prolonged post op analgesia with minimal side effects like pruritus.

INTRODUCTION

Various methods of regional or central neuraxial blocks can be used to achieve surgical anaesthesia over the lower extremities. Spinal anesthesia, a form of regional anesthesia is preferred over alternative anesthetic methods due to its ease of administration, effectiveness, and safety.[1]

For patients undergoing surgeries infraumbilically, spinal anaesthesia is the widely accepted technique unless contraindicated. Hyperbaric Bupivacaine 0.5% alone is known to have a brief duration of action but with additives prolongs the duration of action.[2]

Humans have faced difficulties in managing pain for thousands of years. The most popular anaesthetic for subarachnoid block is Bupivacaine, which is three to four times more potent than lignocaine and acts for a longer period of time.[3]

The amide group local anaesthetic, Bupivacaine, works by influencing voltage-gated sodium channels on the axonal membranes and inhibits the depolarization of nerve fibres thereby blocking the action potential's production and transmission along the nerve fiber.[4] Bupivacaine is highly protein bound. It has an effective half life of 2.5 to 6 hours. Cytochrome P-450 primarily metabolizes it in the liver and excreted via kidney with minimal amounts as unchanged drug.[5]

Over the years many drugs have been used to supplement spinal anaesthesia in order to hasten its

onset of action, decrease the time to surgical incision, extend the duration of action and to provide adequate postoperative analgesia.[2]

Morphine is considered a gold standard opioid in neuraxial blocks because of its effectiveness of postoperative analgesia and extended duration of action. The mu-receptor is the primary site of interaction for morphine. The posterior amygdala, hypothalamus, thalamus, caudate nucleus, putamen, and certain cortical regions all contain large densities of opioid mu-binding sites. It has a Half life of 2-4 hours. Morphine is primarily eliminated through the liver by glucuronidation. Morphine-3-glucuronide (M3G) and Morphine-6-glucuronide (M6G), the two main metabolites of Morphine, are eliminated via urine.[6-10]

Dexmedetomidine is a centrally acting α2 adrenoceptor agonist with a α2 to α1 ratio of 1620:1. It is highly protein bound with a volume of distribution of 1.31–2.46 L/kg (90–194 L).

Dexmedetomidine is metabolised by Direct N-glucuronidation by uridine 5′-diphospho-glucuronosyltransferase (UGT2B10, UGT1A4) and hydroxylation mediated by cytochrome P450 (CYP) enzymes (mainly CYP2A6). Eliminated through liver and majorly excreted renally with less than 1% drug unchanged. Its sedative, analgesic, and hemodynamic stabilizing properties make it a useful adjuvant to local anesthetics. It has been shown to prolong the duration of subarachnoid block following intrathecal administration.[11-13]

Activation of α_2 receptors at the level of the spinal cord leads to inhibition of norepinephrine release at the dorsal horn thereby decreasing the transmission of pain signals from peripheral nociceptors. Bradycardia and hypotension are side effects of Dexmedetomidine that typically arise due to pre and postsynaptic α2-receptor activation, which results in vasoconstriction, vasodilatation, and reflex Bradycardia. Low degrees of respiratory depression is observed with retention of the ventilatory response to CO2 at therapeutic plasma values up to 2.4 ng/mL.[14,15]

MATERIALS AND METHODS

This prospective, randomized, double-blind study was carried out with the Institutional Ethical Committee's consent at BGS Global Institute of Medical Sciences between July 2024 and December 2024.

50 volunteers of either gender, ages 18 to 60, posted from various specialties for elective infraumbilical surgeries, of ASA physical status I and II were selected after their informed written consents. The exclusion criteria consisted of Patient refusal, Patients having an anaphylaxis history to the study drugs used, individuals with a drug abuse history and psychiatric disease, and also BMI > 35 kg/m2. Computer-generated random number tables were used to divide the patients into two classes. There were 50 patients total, split into two groups of 25. Group A: 3.4 ml of 0.5% Hyperbaric Bupivacaine + 250 micrograms of Morphine. Group B : 3.4 ml of 0.5% Hyperbaric Bupivacaine + 5 micrograms of Dexmedetomidine.

The day before the procedure, patients received a comprehensive pre-anesthesia assessment and relevant haematological and radiological investigations were carried out. Study details were communicated to the patient including the type of surgery, anaesthesia, and risks associated. Nil per oral advised for 6 hours before surgery. Patients were premedicated with inj. Pantoprazole 40 mg and Informed written consent was obtained on the day of surgery. Separate consent was obtained for study enrollment and an 18G cannula was secured.

After shifting to OT, standard monitors were connected (pulse oximeter, noninvasive blood pressure, ECG), and vital parameters such as Heart rate, Blood pressure, and Oxygen saturation were noted. Under aseptic conditions, spinal anesthesia was administered in a lateral/sitting position after confirming L3-L4 interspace by palpation. Local anaesthetic (2% plain Lignocaine) was infiltrated. In L3-L4 interspace, using a 25G Quincke spinal needle, a midline approach was used to administer the subarachnoid block. After confirming continuous free flow of clear CSF, study drugs with a total volume of 3.4ml were administered intrathecally according to their group. Patients were placed in a supine position immediately as the injection was administered. The injection's completion was considered the anesthesia induction time zero. Oxygen was delivered at 5L/ min through a face mask.

The intraoperative evaluation was performed using a hypodermic needle and the pin prick test to assess the onset of sensory block. The onset of the motor block was assessed using the Modified Bromage score.

MODIFIED BROMAGE SCORE

SCORE	CRITERIA
1	Complete block (unable to move feet or knees)
2	Almost complete block (able to move feet only)
3	Partial block (just able to move knees)
4	Detectable weakness of hip flexion (between scores 3 and 5)
5	No detectable weakness of hip flexion while supine (full flexion of knees)
6	Able to perform partial knee bend

The amount of time needed for the motor block to reach Bromage score of 6 was recorded. Time for achieving maximum motor and sensory block was assessed every 5 minutes for 30 minutes and after that every 15 minutes up to 90 minutes. Heart rate, blood pressure, and saturation were measured at 5 min, 10min,15min, 20min, 30min, 45min, 60min and 90min.

Injection Ephedrine 6 mg IV was used to treat hypotension, which was defined as MAP <15–20% of the baseline value. Inj Atropine 0.6 mg

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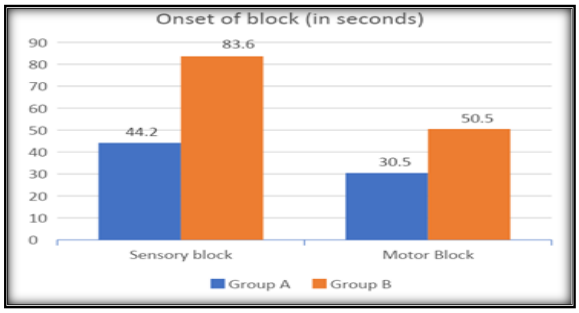
intravenously was used to treat bradycardia, which was described as a heart rate that was less than 15% to 20% of the baseline value.

The Numerical Rating Scale (0–10) was used to measure pain following surgery. Time for 2 segmental regression and time for regression to Modified Bromage 1 were assessed postoperatively. Sedation was assessed by the Ramsay sedation scale. Vitals were assessed and following adverse effects were noted: headache, giddiness, pruritus, nausea, vomiting, respiratory depression, and urine retention. As a rescue analgesic, 75 mg of injection Diclofenac was administered intramuscularly and time noted. Injection ondansetron 4 mg IV was used to treat nausea and vomiting. Injection Promethazine 25 mg IM injection was used to alleviate pruritus and was repeated after one hour if necessary. For patients whose respiratory rate was less than 8 breaths per minute, an IV bolus of 0.1– 0.2 mg of injection naloxone is given, to be repeated as necessary every 3–4 minutes.

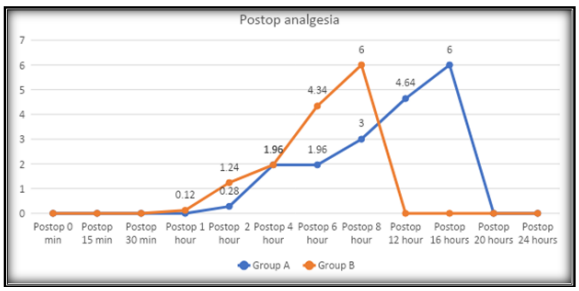
Statistical analysis was done based on the survey of previous literature for an outcome variable on mean changes in mean duration of Motor block the minimum difference of 20 and Standard deviation of 31.45 to attain significance at type I error (α error) of at least 5%, Type II error(β error) at 10% and keeping statistical power above 90%, the sample size of 50(25+25) is adequate for two group randomised pre-post clinical study after adjusting for lost-to-follow up, drop-out rats and withdrawals.

RESULTS

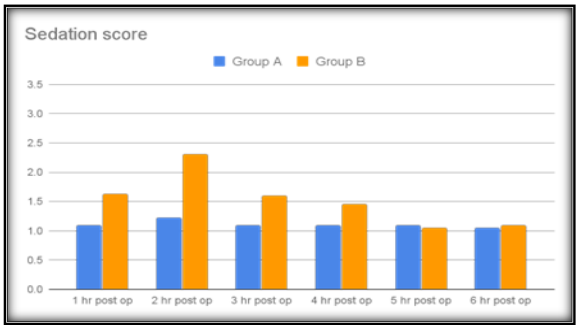
The mean age of participants in Group B was found to be slightly more than the mean age of participants in Group A. Gender distribution was similar in both the groups.



It became apparent that the onset of sensory block among participants in Group B was longer than the onset of block in Group A. Onset of motor block among participants in Group B was longer than the onset of block in Group A.



When it came to postoperative analgesia comparison between the two groups: Participants reported no discomfort from 0 to 30 minutes. Group B experienced increased pain than group A at 60 minutes. There was no statistically significant difference in the mean pain scores between the groups. Participants in group B reported increased pain scores at two hours than those in group A, which was statistically significant. Participants in Groups A and B showed comparable pain levels four hours after surgery. Participants in Group B reported more pain than those in Group A 6 hours after surgery, a difference that was statistically significant. Rescue analgesia was administered at 12.2 hours for participants in Group A when compared to 5.4 hours for participants in Group B. The mean difference was found to be statistically significant. The hemodynamics of groups A and B did not differ significantly.



Mean Sedation scores for the group B were significantly higher than those for group A at 1 hour and 3 hours post spinal which was statistically significant. At 4 hours group B had sedation scores that were higher than group A but not statistically significant. At 5 and 6 hours, sedation scores were similar between both the groups.

There were no cases of postoperative respiratory depression in either group.Participants in Group A were found to experience more pruritus episodes which was statistically significant and only one participant in Group B had vomiting.

Table 1: Comparison of Mean onset of sensory and motor block between Group A & Group B.

		Number	Mean	SD	t	P value
Sensory block	Group A	25	44.2	6.6	-22.4	P = 0.001**
	Group B	25	83.6	5.6		
Motor block	Group A	25	30.5	5.7	-4.52	P = 0.001**
	Group B	25	50.5	21.3		

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SD-standard deviation; **statistically significant using unpaired t-test

Table 2: Comparison of postoperative analgesia between Group A and group B at different time points

Post Op 0 min to Postop 30 min = No pain						
		Number	**Mean**	**SD**	**t**	**P value**
Postop 60 min	Group A	25	0	0	-1.8	P = 0.08
	Group B	25	0.12	0.33		NS
Post Op 2 hours	Group A	25	0.28	0.45	-6.9	P = 0.001**
	Group B	25	1.24	0.52		
Post Op 4 hours	Group A	25	1.96	0.2	0	P = 0.99
	Group B	25	1.96	0.45		NS
Post Op 6 hours	Group A	25	1.96	0.2	-7.8	P = 0.001**
	Group B	24	4.34	1.52		
Post Op 8 hours	Group A	25	3	0	-	-
	Group B	12	6	0		
Post Op 12 hours	Group A	25	4.64	1.5	-	-
	Group B	0	-	-		
Post Op 16 hours	Group A	11	6	0	-	-
	Group B	0	-	-		
Post Op 20 hours	Group A	-	-	-	-	-
	Group B	-	-	-	-	-
Post Op 24 hours	Group A	-	-	-	-	-
	Group B	-	-	-	-	-

SD-standard deviation; NS-not significant and **P < 0.01 using unpaired t-test
[statistical output was not computed between the groups from 8 hours till Postoperative 24 hours]

DISCUSSION

Bupivacaine heavy along with intrathecal Morphine or Dexmedetomidine are known to prolong the duration of analgesia. In our study, we reported that adding Morphine or Dexmedetomidine to Bupivacaine for sub arachnoid block prolonged the duration of the post op analgesia with Morphine being superior because of the cheaper cost, faster sensory and motor blockade onset and prolonged duration of post operative analgesia compared with Dexmedetomidine.

Kurhekar P et al observed that both Morphine 250 mcg or Dexmedetomidine 2.5mcg, when added to intrathecal 3ml hyperbaric Bupivacaine 0.5%, Dexmedetomidine group had a sensory block onset time of 56 ± 16 seconds compared to Morphine group at an average 58 ± 81 seconds. The Dexmedetomidine group had an average motor block onset time of 68 ± 35 seconds compared to the Morphine group at an average 96 ± 1 seconds. Bromage 6 was attained at 518 ± 126 mins with the Dexmedetomidine group compared with Morphine at 342 ± 85 mins.[16] However, our current study demonstrated that compared to Dexmedetomidine, Morphine had a faster sensory and motor blockade onset and prolonged duration of sensory and motor blockade. The mean sensory onset duration with Morphine as an additive was 44 sec compared to 83 sec with Dexmedetomidine. The mean motor onset duration with Morphine as an additive was 30 sec compared to 50 sec with Dexmedetomidine.

Both intrathecal Morphine and Dexmedetomidine are known to act on adrenergic receptors to produce hypotension. Patro SS et al in 2016 conducted a study to assess the efficacy of Dexmedetomidine 5 mcg as an adjuvant along with 0.5% Hyperbaric Bupivacaine 3 ml intrathecally for infraumbilical surgeries and found that there was hypotension following drug deposition which continued till 30 mins among both the groups.[17] In our study, intraoperative hypotension was noted with intrathecal Dexmedetomidine and Morphine groups around 18 mins and 13 mins respectively continuing for around 40 mins. Postoperative hemodynamic parameters were comparable between the either groups and no significant hemodynamic instability was noted.

E Kalso et al conducted a study in 1983 to compare the effects of intrathecal Morphine (0.4mg versus 0.2mg) as additive with 0.5% Bupivacaine heavy 4ml in orthopedic surgeries and observed that 4 of 10 patients who received 0.4mg Morphine intrathecally did not require any analgesic for 48 hours. In the group receiving 0.2mg Morphine intrathecally, there was a marked difference in the intensity of pain compared to group without intrathecal Morphine.[18] Within our study, with similar drug doses of intrathecal Morphine 0.2 mg + 3ml Bupivacaine heavy 0.5% showed prolonged duration of analgesia of around 12 hours.

Cole PJ et al in 2000 did a comparative study to assess the efficacy and respiratory effects of intrathecal Morphine 300 mcg with 0.5% Bupivacaine heavy 2-2.5ml when compared to patient controlled Morphine and IV Morphine. They found that the intrathecal Morphine group had better analgesia scores, minimal but statistically significant reduction in oxygen saturation from baseline 97 % to 95% compared with the placebo. No study groups showed severe hypoxemia. In our study, we did not find any patient having a saturation drop of less than 94% associated with intrathecal Morphine or Dexmedetomidine.[19]

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Pruritus commences 25–180 min after intrathecal Morphine, and peaks between 3 and 9 h post-injection. The peak concentration of CSF fluid at the cisterna magna corresponds with the peak in pruritus.[20] Aly M et al in 2018 conducted a study to assess the pruritus incidence, severity and its relation to serotonin levels with the use of intrathecal Morphine 0.2mg along with 3ml Bupivacaine heavy 0.5% and found that the incidence of pruritus was significant around 6 to 8 hours post spinal.[21] We found the incidence of pruritus was statistically significant with Morphine in the initial 3 hours of administering spinal anesthesia compared to Dexmedetomidine.

Intrathecally administered α2-agonists have a dose-dependent sedative effect. In july 2020, Sharma A et al conducted a study to assess the effects of intrathecal Dexmedetomidine versus intravenous Dexmedetomidine and found that study group intrathecal Dexmedetomidine 5mcg with 2.4 ml hyperbaric Bupivacaine 0.5% had a sedation score of 3 to 4 compared with only 2.4 ml hyperbaric Bupivacaine 0.5%. Intravenous Dexmedetomidine group had the highest number of patients with a sedation score of 3 to 4. None of the patients had respiratory depression and were easily arousable. We, in our study, found similar scores of sedation for the intrathecal Dexmedetomidine group without any complications.[22]

CONCLUSION

The study highlighted that Morphine has a faster onset of sensory and motor blockade. There was a significant prolongation in the duration of post op analgesia compared to Dexmedetomidine. The sedation scores with Dexmedetomidine were statistically significant. No significant differences in hemodynamics were noted. Pruritus was noted as an adverse effect with Morphine.

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