A Comparison of Intrathecal Dexmedetomidine and Fentanyl as Adjuvants to Hyperbaric Bupivacaine for Lower Limb Surgery: A Double Blind Controlled Study.

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ABSTRACT

Background: The aim of this study is to compare the effects of Dexmedetomidine and Fentanyl as intrathecal adjuvant to Bupivacaine on the onset and duration of sensory and motor block in orthopaedic lower limb surgeries. **Methods:** Ninety patients of ASA status I and II posted for lower limb surgery were randomly divided into three groups. Group D was administered Hyperbaric Bupivacaine 15 mg + Dexmedetomidine 5µg in 0.5 ml normal saline, group F was administered Hyperbaric Bupivacaine 15 mg + Fentanyl 25 µg in 0.5 ml normal saline and group C were administered Hyperbaric Bupivacaine 15 mg plus in 0.5 ml normal saline. Duration and quality of sensory and motor block were assessed. **Results:** Sensory and motor block in-group D patients were longer than group F and C patients. **Conclusion:** Intrathecal dexmedetomidine when added to bupivacaine heavy (0.5%) provide better and prolonged analgesia in comparison to fentanyl.

Keywords: Fentanyl, orthopaedic, Bupivacaine, intrathecal, Dexmedetomidine.

INTRODUCTION

Subarachnoid block is the most commonly used technique for orthopaedic lower limb and lower abdominal surgeries[1] Postoperative pain control is a major problem in these surgeries because of relatively short duration of action of local anaesthetics, so early analgesic intervention is needed in the postoperative period. A number of adjuvants, such as clonidine and midazolam, and opiods have been studied to prolong the effect of spinal aesthesia.[2,3]

Fentanyl, in recent years, has emerged as a useful intrathecal adjuvant for prolonging the effect of spinal anaesthesia. Although it is one of the most widely used intrathecal adjuvant in the present scenario, its intrathecal use has been shown to be associated with side effects like respiratory depression and pruritus.[4]

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Dexmedetomidine, a new highly selective α2-agonist, is under evaluation as a neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects. By virtue of its effect on spinal α-2 receptors, dexmedetomidine mediates its analgesic effects. Based on earlier human studies, it has been shown that a low dose of 5 µg, dexmedetomidine provides a prolonged anaesthesia and good quality post operative analgesia when used as an intrathecal adjuvant to bupivacaine with minimal effects on the hemodynamic status of the patient [5,6].

Hence, the present study is being undertaken to evaluate and compare the effects of dexmedetomidine and fentanyl as intrathecal adjuvants to bupivacaine.

MATERIALS AND METHODS

This study was carried out at SCB Medical College & Hospital, Cuttack after obtaining approval from the Hospital Ethical Committee and written informed consent from the patients from July 2014 to Feb. 2015.. Ninety ASA grade I or II patients of either sex, aged 18 to 60 years, weighing 50 to 90 kg and with a height of 150 cm to 180 cm, scheduled for lower limb surgery were included in the study. Exclusion criteria were Patients presenting with known contraindications to spinal anaesthesia, pregnant patients, Patients on therapy with adrenergic receptor antagonist, calcium channel blocker, and/or ACE inhibitor, with a history of heart block or dysarrythmia, hypersensitivity to any of the study drugs, who refused to consent to be part of the study.

The study population was randomized using a random number table generated from computer software. The random intervention assignment slip was placed in serially numbered opaque and sealed envelopes. These envelopes were opened following enrolment of the case.

90 total patients randomly divided into 3 groups (n = 30): Group D: Hyperbaric Bupivacaine 15 mg + Dexmedetomidine 5 µg in 0.5 ml normal saline administered intrathecally. Group F: Hyperbaric Bupivacaine 15 mg + Fentanyl 25 µg in 0.5 ml

normal saline administered intrathecally. Group B: Hyperbaric Bupivacaine 15 mg plus 0.5 ml normal saline administered intrathecally.

All the patients were kept for 6 hours fasting prior to surgery. Tablet Alprazolam (0.25 mg) was given as a premedication a night prior to surgery. Preloading was done with Ringer lactate solution (10 ml/kg body weight). Routine monitoring, including non-invasive blood pressure (NIBP), ECG, heart rate and pulse oximetry was done. All patients received supplemental oxygen via mask (3l/min).

Under proper aseptic conditions, spinal anaesthesia was given at the level of L3-L4 interspace in sitting position using a midline approach by a 25G Quincke spinal needle. The drug was injected slowly over 10-15 seconds with the bevel of the needle pointing upwards and all patients were made supine.

The intrathecal drug formula was prepared by a separate anaesthesiologist under strict aseptic conditions. The anaesthesiologist who administered anaesthesia was blinded to the group allocation. After administering anaesthesia, the vital signs of the patient were recorded. Vitals were recorded every 2 minutes up to the 10th minute and every 5 minutes thereafter up to 20 minutes. Beyond 20 minutes, the vitals were recorded every 20 minutes till the time of discharge from the PACU (Post Anaesthesia Care Unit).

The sensory dermatome level was assessed by loss of pinprick sensation of a 23 G hypodermic needle.

The motor dermatome level was assessed according to the Bromage[7] Scale:

- Bromage 0-Patient able to move the hip, knee and ankle.
- Bromage 1- Patient unable to move the hip, but able to move the knee and ankle.
- Bromage 2- Patient unable to move the hip and knee, but able to move the ankle.
- Bromage 3- Patient unable to move the hip, knee and ankle.

The sensory and motor status was assessed prior to the spinal injection, then every 2 minutes after the spinal injection for the first 10 minutes, every 5 minutes for the next 10 minutes and thereafter every 20 minutes until the time to regression of sensory level to dermatome S2 and motor scale to bromage 0.

Time to reach the sensory block up to the highest dermatome level and motor block of bromage 3 level was noted. On achieving T8 sensory blocked level, the surgical procedure was carried out. Then time to regression to dermatome S2 level and time to reach bromage 0 was noted in the postoperative care unit.

All durations were calculated taking the spinal injection time as time zero. If the sensory levels were not equal bilaterally, the higher dermatome level was used for statistical analysis. The patient was discharged after the sensory block regresses to S2 level and motor block to bromage 0.

Postoperatively, the pain scoring was done by using visual analog scale[8] (VAS) (0 = no pain, 10 = severe pain), with the vital recordings of the study until the patient was discharged. Paracetamol was given intravenous as rescue analgesia when VAS was greater than 4. Time of administering the first dose of rescue analgesia was noted.

Sedation was assessed by using a Modified Ramsay sedation score each time the vitals were noted.

Modified Ramsay sedation scale[9]:

1. Anxious, Agitated, Restless.
2. Cooperative, Oriented, Tranquil.
3. Responds to commands only.
4. Brisk response to light glabellar tap or loud noise.
5. Sluggish response to light glabellar tap or loud noise.
6. No Response.

For the purpose of the study hypotension was defined as a decrease in systolic blood pressure more than 30% of the baseline value or fall below 90 mmHg, which was treated by Ephedrine 6 mg i.v. and fluids. Bradycardia was defined as heart rate less than 60/min but the intervention with iv atropine 0.6 mg was done only when heart rate fell below 50/min.

Side effects, including nausea, vomiting, bradycardia, hypotension, pruritus, respiratory depression, urinary retention, shivering etc. were assessed both intra-operatively as well as post-operatively. All the patients were examined by the anaesthesiologist after 24 hours of the spinal block and were assessed for any postdural puncture headache or transient neurologic symptoms.

Highest dermatomal level of sensory blockade, time taken to reach the highest dermatomal level of sensory block, to reach up to bromage 3 motor block, for sensory regression to S2 level, for motor regression to bromage 0 were noted. Hemodynamic status of the patient, sedation score and side effects if any were noted.

All the statistical analysis was performed by using SPSS version 21. The various statistical tests that were used in this study were analysis of variance (ANOVA) test, Post hoc test (Bonferroni test) and nonparametric tests like Mann Whitney U test and Kruskal Wallis test.

For all statistical analysis $p < 0.05$ was considered statistically significant. The results and interpretations are explained below.

RESULTS

All the three groups were comparable as regard to age, sex, height and weight. There were no significant differences in heart rate, MAP, SPO2

between the three groups. Intergroup analysis showed a statistically significant difference in the highest level of sensory blockade amongst group D and F (p = 0.004), However, no significant difference was found between group B and F and group D. Two-segment regression, time was more in the dexmedetomidine group in comparison to fentanyl and control group.

Onset time to both sensory and motor block was faster on group D than group F and group B. Regression time of motor block to bromage 0 was slow and time to rescue analgesia was longer in the dexmedetomidine group in comparison to other groups. Sedation score was more in the dexmedetomidine group in comparison to other groups. VAS score was lower in the dexmedetimidine group than other groups. In our study the incidence of bradycardia, hypotension, nausea, vomiting, pruritus and urine retention was not statistically significant. There was no incidence of respiratory depression.

Table 1: Demographic profile.

Parameters	Group B	Group D	Group F	P value
Age (years)	39.16±10.12	43.6±10.5	41.63±9.85	0.245
Sex (m:f)	20:10	19:11	17:13	0.548
Weight (kg)	66.87±7.20	66±7.82	64.83±7.50	0.577
Height (cm)	166.47±6.40	164.43±5.92	163.6±5.62	0.168
ASA (I: II)	21:9	18:12	20:10	0.641
Duration of surgery (min)	48±17.84	47.67±15.24	46.47±11.99	0.734

Table 2: Characteristics of spinal block

Variable (min)	Group B	Group D	Group F	P value
Time of onset of sensory block	8.2±1.6	8.0±1.5	8.3±2.1	0.235
Time of onset of motor block	9.5±2.3	9.3±2.7	9.7±3.2	0.124
Time taken to reach highest level of sensory block	10.4±4.01	9.33±3.50	10.67±3.65	0.346
Duration of sensory block	198.67±32.35	396.67±24.12	205.67±26.12	0.0001
Duration of motor block	140.67±21.32	338±21.24	154±19.76	0.0001
Duration of Spinal anesthesia	224.4±36.2	402.6±32.7	234.6±29.6	0.0001
Time to first dose of rescue analgesia	153.67±27.88	299±33.92	166.83±20.66	0.0001

Table 3: Highest dermatome level of sensory block:

HIGHEST LEVEL OF SENSORY DERMATOME	GROUPS			TOTAL
	B	D	F	
T4	3	4	0	7
T5	9	14	6	29
T6	8	5	11	24
T7	2	4	6	12
T8	5	2	3	10
T9	3	1	3	7
T10	0	0	1	1

	Mann Whitney U test		Kruskal Wallis (p value)
B & D	B & F	D & F	0.017
0.149	0.191	0.004	

Table 4: Adverse effect of spinal block, (values are numbers)

Side effect	Group B	Group D	Group F	P value
Hypotension	4	3	3	0.895
Bradycardia	2	4	3	0.693
Resp. depression	0	0	0	1
Nausea, vomiting	3	1	2	0.589
Urinary retention	1	3	1	0.433
Pruritus	1	0	2	0.36
Dry mouth	3	2	2	0.858
Shivering	4	1	2	0.342
Sedation score	1.35±0.07	1.50±0.09	1.44±0.08	0.0001

Table 5: Postoperative visual analogue scale (VAS)

Time after surgery	Group B	Group D	Group F
1 hr	4 (2-5)	0 (0-3)	4 (2-4)
2 hr	4 (1-4)	1 (0-3)	3 (2-4)
3 hr	3 (1-4)	1 (0-2)	3 (1-3)
4 hr	3 (1-3)	2 (0-3)	2 (0-3)
5 hr	2 (1-3)	2 (0-2)	2 (0-3)

DISCUSSION

The results of our study show that the supplementation of intrathecal bupivacaine with 5 µg dexmedetomidine significantly prolonged both sensory and motor block compared with intrathecal 25 µg fentanyl and control group. Patients in the groups that received dexmedetomidine and fentanyl had reduced postoperative pain scores and a longer pain free period than those who received spinal bupivacaine alone. No hemodynamic instability or adverse effects were reported in any group. Time taken to achieve peak level of sensory and motor blockade was earlier in the dexmedetomidine group than other groups.

Al Ghanem et al[10] observed that the onset time of bromage 3 motor block was also not different between dexmedetomidine and fentanyl group. Regarding time taken to achieve peak motor blockade there was no statistically significant difference was seen amongst all the three groups. The time to regression of sensory block to S1 segment was significantly longer in group D than in group F ($p < 0.001$). The regression, time to reach bromage 0 in the dexmedetomidine group was significantly longer than that for fentanyl group ($p<0.001$). This was similar to our study in which dexmedetomidine group showed a statistically significant prolongation of both sensory and motor regression when compared to fentanyl and bupivacaine alone group.

Al-Mustafa M M, et al[11] studied the effect of adding different doses of dexmedetomidine (5µg or 10 µg) to bupivacaine (12.5 mg) for neuraxial anaesthesia. They observed a maximum sedation score of 2 without pre-medicating their patients with any type of benzodiazepines in both the groups. In our study, the mean blood pressure in the postoperative period, was found to be similar in all groups. Kanazi et al[12] noted that dexmedetomidine or clonidine when added to intrathecal bupivacaine did not cause a significant reduction in blood pressure but prolonged sensory and motor block characteristics.

El-Hennawy AM et al[13] found that addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. Alka Shah et al[14] studied Haemodynamic effects of intrathecal dexmedetomidine added to ropivacaine intraoperatively and found that it prolonged the postoperative analgesia. Gehan A. Tarbeeh et al[15] studied the effects of intrathecal bupivacaine–fentanyl versus bupivacaine–dexmedetomidine in diabetic surgical patients and concluded that dexmedetomidine produced better block characteristics. Jain et al[16] studied the perioperative effect of epidural dexmedetomidine with intrathecal bupivacaine on haemodynamic parameter and quality of analgesia and found that it is better than other adjuvants.

Bradycardia was seen in total, of 9 patients in our study and was more in the dexmedetomidine group (4 patients) compared to fentanyl and bupivacaine alone group, but it was transient and did not require any intervention. There was no statistically significant difference noted amongst the three groups.

Urinary retention was seen in 3 patients in the dexmedetomidine group compared to one patient each in the other two groups, but it was statistically not significant ($p>0.05$).

Nausea and vomiting were highest in a bupivacaine alone group followed by fentanyl group and least in dexmedetomidine group. It was also not statistically significant on analysis ($p>0.05$).

The administration of intrathecal opioids may provide benefits in augmenting intra operative anaesthesia but carries a risk of respiratory depression. Varassi et al[17] demonstrated that intrathecal administration of fentanyl 25 micrograms in non premeditated geriatric patients did not alter respiratory rate, ETCO2, minute ventilation, respiratory drive and ventilator response to CO2. On the contrary, 50 µg intrathecal fentanyl can cause an early respiratory depression in geriatric patients. In our study, none of the groups showed any effect on respiratory rate or any decrease in O2 saturation.

CONCLUSION

We conclude from our study that supplementation of bupivacaine spinal block with a low dose of 5µg intrathecal dexmedetomidine produces a significantly longer duration of sensory and motor block than 25 µg intrathecal fentanyl. It provides hemodynamically stable conditions, minimal side effects, and excellent quality of postoperative analgesia. Thus, 5 µg dexmedetomidine seems to be an attractive alternative to 25 µg fentanyl as an adjuvant to spinal bupivacaine in surgical procedures.

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