

SHOULD WE PREMIX FENTANYL AND BUPIVACAINE DURING SUBARACHNOID BLOCK FOR BELOW KNEE ORTHOPEDIC SURGERIES? - A RANDOMISED CLINICAL TRIAL

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Abstract

Background: Opioids used as adjuvants in subarachnoid block SAB improve the effectiveness of intraoperative analgesia and extend the length of postoperative pain relief. The addition of opioids reduces the dose of local anesthetic (LA) needed for optimal effect. Recently, there have been apprehensions regarding the effect of mixing two drugs (LA and adjuvant) as it can affect the baricity and spread of drugs. When these medications are combined in a syringe before injection, the density of both medications is altered, which affects how well they distribute in the cerebrospinal fluid; producing variable block characteristics and hemodynamic parameters.

Materials and Methods: There were three groups of 30 patients each, for a total of 90 individuals. In group 1, patients received premixed 2.8 mL (14 mg) bupivacaine heavy with 20 µg fentanyl (0.4 mL); in group 2, the patients received 2.8 mL (14 mg) bupivacaine heavy followed by 20 µg fentanyl (0.4mL) in separate syringes and group 3, the patients received 20 µg fentanyl followed by 2.8 mL bupivacaine heavy in separate syringes. Sensory and motor block characteristics in addition to hemodynamic parameters were observed. **Result:** According to our research, Group 2 experienced the onset of sensory block far more quickly (145.16±20.06sec vs. 127.00±25.75sec vs. 150.33±23.15sec in Groups 1, 2, and 3 correspondingly; P=0.008). In group 2, none of the patients achieved level T3 as compared to 4 and 3 patients in groups 1 and 3, correspondingly. In Group 2, the mean duration until T10 for sensory and motor blocks was substantially longer. Comparing Group 2 to Group 1 and 3, the mean duration of analgesia was much longer in Group 2. There was no statistically significant difference in the incidence of side effects across the groups. VAS scores and rescue analgesia were comparable in three groups. **Conclusion:** We concluded that patients who had hyperbaric bupivacaine and fentanyl in that order had superior outcomes in terms of the timing of the start of sensory and motor block, greater hemodynamic stability, and length of sensory and motor anesthesia. Additionally, it has been hypothesized that combining opioids like fentanyl with local anesthetics delays the onset of sensory and motor block, increases the amount of sensory block, and shortens the duration of analgesia.

INTRODUCTION

In recent years, the addition of intrathecal adjuvants has led to a reduction in the dose of bupivacaine and improved spinal anesthetic efficacy.^[1,2] Adding adjuvants in subarachnoid block (SAB) also

enhances and without causing any noticeable adverse effects, extends postoperative analgesia. Opioids used as adjuvants in SAB increase the effectiveness of intraoperative analgesia and extend the length of postoperative pain reduction.^[3,4,5,6]

Addition of opioids reduces the dose of local anesthetic (LA) needed for optimal effect.^[7,8,9]

Recently, there have been apprehensions regarding the effect of mixing two drugs (LA and adjuvant) as it can affect the baricity and spread of drugs. The density of both medications is altered when they are combined in a syringe before injection, which affects how well they distribute in the cerebrospinal fluid; producing variable block characteristics and hemodynamic parameters.^[7,10,11,12,13]

Dexmedetomidine, when administered in a separate syringe after intrathecal hyperbaric bupivacaine, has been shown to accelerate the onset of both motor as well as sensory block. Additionally, it increases the time that spinal anesthesia lasts, decreases clinically significant adverse effects, and lessens the need for postoperative analgesics.^[7]

We hypothesized that giving local anesthetics and adjuvants separately in distinct syringes would reduce the impact of changes in the densities and pH of both medications while maximizing their therapeutic benefits. In lower limb orthopedic procedures, there is a lack of information comparing the sequential and premixed dosing of fentanyl with local anesthetics.

According to the existing research, consecutive intrathecal injection of fentanyl and bupivacaine during lower abdominal procedures may reduce the likelihood of side effects, maintain hemodynamic effects, expedite the onset and slow the regression of motor and sensory block.^[7,10,11,12,13]

The purpose of this research was to assess the effects of sequential and premixed fentanyl as an adjuvant to intrathecal bupivacaine on block characteristics, hemodynamics, and postoperative analgesia in persons having below-knee orthopedic procedures under subarachnoid block.

MATERIALS AND METHODS

From June 2019 to December 2020, the study was carried out.

Randomization was done by the computer-generated table and group allocation sealed in an opaque envelope was opened by the concerned anesthetist, after shifting the patient to the operation theatre. Observer and interpreter were blinded to study groups. The anesthesiologist doing the procedure was not blinded in this study. To avoid subjectivity, one observer made all of the observations.

A thorough pre-anesthetic check-up, including coexisting heart disease, current medication, allergies, previous anesthetic, and surgical experience were noted. All the patients were informed during the preoperative visit in their vernacular language regarding the procedure and informed consent was taken. The VAS (visual analog scale) was explained to the patients during the preoperative visit and were instructed to demand rescue analgesia whenever required. Before surgery,

all patients were asked to fast for at least 8hr without solid food and 2hr for clear fluids.

Standard monitors were attached to the patient, baseline parameters were recorded and an intravenous line was secured with an 18G cannula. Co loading was done with 10mL/Kg of the lactated ringer. A 26-gauge Quincke spinal needle (0.45mm x 90mm) was used to deliver a subarachnoid puncture block in the L3-L4 interspace under all aseptic conditions.

Three groups of patients were formed: Group 1 (n=30) subjects received premixed 2.8mL (14mg) bupivacaine heavy with 20µg fentanyl (0.4 mL). Group 2 (n=30) subjects received 2.8mL (14mg) bupivacaine heavy followed by 20µg fentanyl (0.4mL) in separate syringes. In Group 3(n=30) the subjects were administered 20µg fentanyl followed by 2.8mL bupivacaine heavy in separate syringes. An insulin syringe was used to measure volume less than 1mL.

Monitoring and recording began at time 0 for blood pressure (systolic, diastolic, and mean arterial pressure), respiratory rate, heart rate, and SpO₂ (peripheral oxygen saturation) that was the time following completion of the injection, every 3 minutes for the first 30 minutes, then every five minutes for an hour, and then every ten minutes until the procedure is finished. Every 30 seconds up to the highest degree of sensory block, the mid-clavicular line was pinprick tested bilaterally for sensory block, and then every 10 minutes until regression to two segments below the maximum level.

When the medication was first injected into the subarachnoid space until full analgesia at the T10 level, the sensory block was considered to have started (umbilicus). After 20 minutes had passed after the injection was administered, the maximal degree of sensory block was measured. Regression of a block to two segments below its maximum block level was measured as a two-segment regression over time. The length of sensory anesthesia was determined as the time to regress to T10.

Duration of analgesia (spinal anesthesia) was measured from the time of intrathecal injection until the patient's first request for analgesia.

Modified Bromage Scale was used to measure motor block. Grade 0: No motor loss, grade 1: inability to lift an extended leg; ability to move feet and knee, grade 2: being unable to lift the extended leg and move the knee; can move feet, grade 3: Including a complete motor block

The time from the intrathecal injection to a modified Bromage score of 3 was utilized to determine when the motor block started, and the time it lasted from a modified Bromage score of 3 to 0 was utilized to determine how long it lasted. Sedation was graded by Ramsay's scoring every 10 minutes for the first 30 minutes and was observed in the intraoperative period hourly till the end of surgery. Using a VAS scale, the patient's postoperative pain at the surgical

site was assessed (0 = No pain, 10 = Worst pain). We assessed VAS scoring over 24 hours at different intervals i.e., at 1h, 2h, 4h, 6h, 8h, 12h, 15h, 18h, and 24h.

Time to 1st rescue analgesia was noted. Patients were given intravenous diclofenac sodium 1.5mg/kg if VAS score >4. If no response to the rescue analgesic within 30 minutes, the second rescue analgesia in the form of injection tramadol 1mg/kg was given slowly intravenously.

At the end of 24 hours, total rescue analgesic dosages were recorded in three groups.

Statistical Analysis

Where appropriate, data were given as percentages, frequency, standard deviation, and mean. Categorical variables were compared between two groups using the Chi-square test. When comparing quantitative factors between more than two groups, a one-way ANOVA was employed, followed by a Bonferroni/Post-hoc analysis. It was deemed significant at $P < 0.05$. The SPSS v21 statistical analysis software was used.

RESULTS

As shown in [Table 1], demographic characteristics (Age, gender, weight, height, BMI, and ASA grading) and baseline hemodynamic parameters (PR SBP, DBP, and MAP) were comparable among the three groups [Table 2].

In group 2, the sensory onset was significantly faster as compared to group 1 and group 3, whereas it was

similar in groups 1 and 3. Similar to group 1 and group 3, table 3 shows that the onset of motor blockage occurred much more quickly.

None of the patients in group 2 had a sensory level higher than T4 but in groups 1 four and group 2 three patients developed a sensory blockade level higher than T4.

The two-segment regression time was highest in group 2 which was significant as compared to both groups 1 & 3. Group 1 had the lowest two-segment regression time but it was not statistically significant when compared to group 3. [Table 3]

When compared to Groups 1 and 3, Group 2 had substantially longer mean times for sensory block to T10 level, analgesia, and motor blockade. All these parameters were comparable in Group 1 and Group 3. [Table 3]

The side effects profile was not statistically significant. We didn't observe any adverse effects like sedation, or respiratory depression with intrathecal use of fentanyl although hypotension was present in 8, 3, and 5 subjects in Groups 1, 2, and 3, correspondingly. Bradycardia was observed only in one patient in group 1.

Visual analog scoring was comparable in three groups till 4 hours postoperatively. After 5 hours the VAS didn't exceed 4 in any group till 10 hours postoperatively. The requirement of rescue analgesia between groups 1, 2, and 3 was comparable during the post-operative period of 24h.

Table 1: Demographic and baseline characteristics of the patients.

S No.		Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=30)	Statistics
1.	Age[yr] (mean±SD)	44.90±11.19	47.37±10.96	47.53±12.03	P=0.607
2.	Weight[kg] (mean±SD)	62.33±6.02	61.53±6.44	62.03±5.31	P=0.871
3.	Height (cm) (mean±SD)	162.60±7.48	161.63±7.37	160.30±7.47	P=0.489
4.	BMI (kg/m ²) * (mean±SD)	23.60±2.13	23.60±2.49	24.1±1.72	P=0.509
5.	ASA† Grade 1 Grade 2	29 1	28 2	26 4	$\chi^2=2.169$; P=0.338
6.	Duration of surgery(min) (mean±SD)	65± 10.45	63±9.32	66±10.25	

* BMI: Body mass index † ASA: American Society of Anaesthesiologists

Table 2: Baseline hemodynamic characteristics of the patients.

S. No	Variables	Group 1	Group 2	Group 3	Significance
1.	HR(mean±SD)*	93.57±14.99	93.33±13.55	98.50±12.26	P=0.259 9
2.	SBP(mean±SD)*	122.63±11.45	126.73±16.75	123.10±8.46	P=0.395
3.	DBP(mean±SD)*	72.87±12.06	78.93±7.51	75.93±8.89	P=0.057
4.	MAP(mean±SD)*	89.10±13.94	95.50±14.94	91.93±11.15	P=0.187

*data expressed as mean ±SD.HR: heart rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, MAP : mean blood pressure

Table 3: Comparison of different block characteristics in three groups

S.No.	Variable	Group 1(n=30)	Group 2(n=30)	Group 3(n=30)	Significance of difference
1.	Onset of sensory Block (seconds) (Mean±SD)	145.16±20.06	127.00±25.75	150.33±23.15	P=0.008 Gp1&2=0.003; Gp1&3=0.359 Gp 2&3=0.00
2.	Maximum sensory block level (number)	T3	4	0	P=0.003
T4		8	3	5	
T5		8	2	1	
T6		7	19	11	

		T7	3	5	10	
		T8	0	1	0	
3.	No of Segment (blocked above T12) (Mean±SD)		7.1±1.21	6.03±.88	6.33±1.37	P=0.03 Gp 1&2=0.00; Gp1&3=0.026 Gp 2&3=0.319
4.	Onset of motor block (sec) (Mean±SD)		214.33±27.02	176.00±31.90	219.50±22.10	P=0.021 Gp1&2=0.00; Gp1&3=0.421 Gp 2&3=0.003
5.	Two segment regression time min		95.83±17.86	122.50±18.51	103.66±15.13	P=0.01; Gp1&2=0.00 Gp1&3=0.072; Gp 2&3=0.00
6.	Duration of sensory block (minutes) till T10		129.33±20.54	143.83±18.69	130.16±14.35	P=0.01; Gp1&2=0.006; Gp1&3=0.856; Gp 2&3=0.002
7.	Duration of motor block(min)		195.50±41.65	230.33±40.21	200.66±33.13	P=0.01; Gp1&2=0.00 Gp1&3=0.597; Gp 2&3=0.003
8.	Duration of Analgesia (min)		251.66±26.59	293.66±42.63	256.50±42.28	P=0.01 Gp1&2=0.02; Gp1&3=0.59 Gp 2&3=0.001

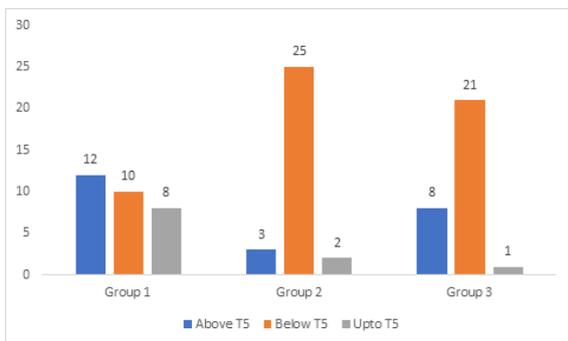


Figure 1: Bar diagram showing level of block above T5, below T5 and up to T5



Figure 2: Line diagram showing comparative analysis of Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and mean arterial pressure (MAP) among three groups

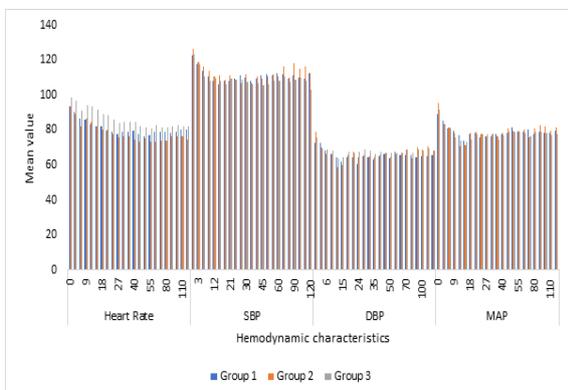


Figure 3: Bar plot showing comparative analysis of Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and mean arterial pressure (MAP) among three groups

Diastolic blood pressure (DBP) and mean arterial pressure (MAP) among three groups

DISCUSSION

The goal of the current research was to determine how sequential and premixed fentanyl, used in combination with bupivacaine, affected the block characteristics, hemodynamics, and postoperative analgesia in patients having below-the-knee orthopedic procedures under subarachnoid block.

Our study noticed that the onset time of sensory block was considerably faster in Group 2 in comparison to the other two groups. However, it is of minimal clinical consequence since a 20–30 second earlier onset is unlikely to be of any clinical value.

We compared our study with other studies using two syringe techniques for local anaesthetic and adjuvants. [Table 3]

Joshi et al,^[10] studied mixed vs. fentanyl (25µg) followed by bupivacaine heavy (10 mg) for spinal anesthesia in cesarean section. In addition, they found that the sequential group's onset was later than it was in the mixed group. But they have no sequential group in which bupivacaine heavy was followed by fentanyl. [Table 3]

Keera and colleagues studied premixed bupivacaine (10mg) and fentanyl (25µg) versus sequential fentanyl (25µg) and bupivacaine (10mg) for spinal anesthesia in patients undergoing cesarean section.^[11] It was noticed that onset was delayed in the premixed group (5.79± 3.03 min) as compared to the sequential group (5.07 ±2.4 min). These results are in contradiction to Joshi et al,^[10] and our findings. [Table 3]

In comparison to the other groups, group 2 attained a much lower maximum degree of sensory block. In group 2 (6.03±0.88), the total number of sensory segments blocked above T12 was substantially lower than in group 1 (7.1±1.21) and group 3 (6.33±1.37). Many studies clearly show that higher

levels of sensory blocks are linked with a higher occurrence of bradycardia and hypotension.^[14,15,16,17,18] Our study showed that Group 2 and Group 3 patients have many low levels of the sensory block as compared to Group 1.

Joshi et al,^[10] found that motor onset was significantly fast in the premixed group (4.2±0.66 min) in comparison to the sequential group (4.8±0.42 min). Though motor onset was delayed in the sequential (fentanyl followed by HB) group in our study too, it was non-significant. In the sequential group, the length of the motor block was much longer (223±17.04 min) as compared to the premixed group (188± 15.6 min) in their study. As we have used different doses of drugs and different groups of patients, a quantitative comparison of total duration cannot be made as compared to this study. [Table 3]

Sachan and colleagues studied three groups like our study,^[12] but with clonidine and in patients for cesarean sections. They concluded that the sequential method considerably increased the analgesia duration, delayed block regression, and decreased the time needed to achieve full sensory and motor block. Clonidine was given either before or after HB, but it made no difference. They also concluded that all three groups had similar maximum sensory block levels. In our study, we could not achieve similar results to that of Sachan et al.^[12] We discovered considerably greater levels in the premixed group compared to the sequential groups, but the greatest degree of sensory block in their investigation was the same in all three groups. However, study drugs and patient profiles were different in our study. [Table 3]

Among the sequential groups, we found significantly better block characteristics in group 2 in comparison to group 3. Sachan et al,^[12] found no difference in both the sequential groups. Different profiles of patients and different adjuvants in our study may have resulted in dissimilar outcomes. We know that the normal physiology of pregnancy has several impacts on spinal anesthesia.^[14,15,16] Changes in CSF (volume, pH, baricity, sensitivity to local anesthetics), anatomical changes in intrathecal and epidural space, raised intraabdominal pressure, and exaggerated lumbar lordosis can lead to a different block characteristic as compared to non-pregnant patients. The baricity of fentanyl may also be quite different from clonidine which must have led to a different result in our study as compared to Sachan et al.^[12]

In our study, we found that the group receiving initial administration of hyperbaric bupivacaine followed by fentanyl resulted in better block characteristics in the context of the onset of motor and sensory block delayed motor and sensory block regression, and significantly prolonged analgesia duration. As compared to the premixed group, we also noticed that the maximum sensory block level was much lower in both sequential groups.

There may be a delay of 15-30 seconds in giving supine position in group 2 after administration of hyperbaric bupivacaine (time consumed in the administration of fentanyl). This delay can lead to the settling down of drugs in the sacro-lumbar compartment. Though it may have contributed to faster sensory and motor onset in group 2, at the same time, it leads to a lesser height of the block and more hemodynamic stability. In the premixed group and sequential group (fentanyl followed by bupivacaine heavy), there is no delay in giving the supine position to the patient leading to a higher level of block.

Desai et al,^[13] have noted that combining an opioid with hyperbaric bupivacaine for intrathecal injection may increase the need for an opioid during the recovery phase. They proposed the densities at which both hyperbaric bupivacaine and opioids may have their greatest effects. Their combination changes the densities, which has an impact on the spread of the CSF and the analgesia duration.

As a consequence, sequential delivery maintains the physical characteristics of both medications and produces the best outcome. There was no statistically significant difference in the prevalence of side effects across the groups (P=0.236). In all three groups, according to Sachan et al,^[12] the prevalence of bradycardia, intraoperative hypotension, nausea/vomiting, dry mouth, respiratory depression, and the need for additional analgesics was similar.

CONCLUSION

We conclude that the two syringe techniques have better block characteristics, prolonged duration of action, and better hemodynamic stability. To achieve better block characteristics and hemodynamic stability in lower limb orthopedic procedures, it is advised that intrathecal hyperbaric bupivacaine be administered first, followed by fentanyl. However, further extensive randomized control trials with a wide range of samples are required to verify this hypothesis in the general population.

Limitation

We needed larger sample size for our research to be powered to reveal any hemodynamic parameter differences.

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