
ORIGINAL ARTICLE**Comparison of Premixed Hyperbaric Bupivacaine (0.5%) and Fentanyl via Single Syringe with Sequential Administration via Two Syringes in Spinal Anaesthesia for Lower Limb Orthopedic Surgeries***Amol P. Singam¹, Shrilekh G. Mankhair^{1*}**¹Department of Anaesthesiology, Jawaharlal Nehru Medical College,
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Abstract:

Background: Subarachnoid block is one of the most commonly used anaesthesia technique for lower limb surgeries. As adjuvants opioids are the most commonly used with Local Anesthetics (LA). Adjuvants are given premixed with LA loaded in a single syringe. This study was carried out to compare differences in level of sensory and motor block and incidence of hypotension whilst administering hyperbaric bupivacaine and fentanyl either in a single syringe or different syringes. The effect of administering opioid prior to LA and vice versa on abovementioned parameters were also assessed. **Material and Methods:** A study was performed in 100 ASA class I & II patients aged between 18-60 years, undergoing lower limb elective surgeries under spinal anaesthesia. Onset of sensory and motor block, duration of analgesia, hemodynamic stability parameters. **Results:** The frequency of hypotension was significantly lower in Group S compared to Group M ($P < 0.05$). Time till the onset of sensory block was non-significantly shorter with non-significantly higher mean level of maximal sensory block in Group S compared to Group M ($P > 0.05$). There was no significant difference in the time till occurrence of hypotension, duration of hypotension; mean dose of Mephentermine used for the treatment of hypotension and frequency of patients developed itching in-between the groups ($P > 0.05$). **Conclusion:** Separate syringe intrathecal injection of hyperbaric bupivacaine and Fentanyl provided a tangible improvement in the

quality of sensory block and significant reduction in episodes of hypotension as compared to injection of premixed medications. Administering hyperbaric bupivacaine first followed by fentanyl leads to an early onset and prolonged duration of sensory and motor blockade.

Keywords: Bupivacaine, Subarachnoid Block, Fentanyl, Mephentermine, Lower Limb Orthopedic Surgeries

Introduction:

Anaesthesia has evolved into an expertise subject over the period of time with many changes in the methods employed and drugs used to provide anaesthesia with less number of complications. With the coming of new class and safer local anaesthetics, regional anaesthesia has emerged as a choice of anaesthesia for lower limb orthopedic surgeries. Subarachnoid Block (SAB) is one of the most preferred regional anaesthesia techniques used for lower limb orthopedic procedures due to relatively less cost and lower incidence of major perioperative complications achieved by a limited and localized action of the drug. Local Anaesthetic (LA) used in SAB is based on the pharmacologic effect of the drug [1]. Hyperbaric bupivacaine is mostly used in subarachnoid block as it produces more predictable block with relatively less side

effects. Variety of adjuvants like opioids and non-opioid have been used along with bupivacaine to increase its duration of effect, also provide stable hemodynamics, and provide prolonged post-operative analgesia [2]. Due to their synergistic action with local anaesthetics Intrathecal opioids are most commonly used. Intrathecal use of fentanyl as adjuvant causes a decrease in visceral and somatic pain and improves the quality of block, decreases pain scores, and reduces postoperative analgesia demand. Alteration in density of hyperbaric solution due to mixing of opioids and hyperbaric bupivacaine affects spread of drug in intrathecal space [3]. The density of Cerebrospinal Fluid (CSF) is 1.00059 g/ml at temperature of 37°C [4]. Baricity of fentanyl is 0.99410 while that of hyperbaric bupivacaine is 1.02360. After addition of fentanyl in the same syringe as LA, baricity of the solution comes out to be 1.01850. Alterations in the baricity of a solution to the extent of 0.0006 can alter the spread of LA in CSF [2]. Hyperbaric solutions are more predictable, with greater spread in the direction of gravity and less inter-patient variability. Hence the rationale behind performing this study was to see differences in block characteristics mainly onset of block and duration of block along with determining effects on haemodynamics whilst administering hyperbaric bupivacaine and fentanyl in a single syringe or separate syringes. The effect of administering opioid prior to LA and vice versa on these parameters was also assessed. The study was aimed to compare duration of analgesia and hemodynamic effects after administration of premixed and sequential use of hyperbaric bupivacaine and fentanyl, to compare the onset analgesia achieved by premixed with sequential

hyperbaric bupivacaine and to compare the duration of analgesia in the two groups, to compare hemodynamic stability like heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure during spinal anaesthesia in the two groups.

Material and Methods:

The study was conducted in JLN Medical College, Sawangi, Meghe, Wardha. Institutional Ethics Committee Clearance was obtained for the study. Written informed consent was obtained from each of the study participants before enrolment.

Duration of study: 1 year

Place of study: Department of Anaesthesia JNMC and Acharya Vinoba Bhave Rural Hospital.

Study design: Prospective comparative study.

Inclusion criteria: Patients belonging to ASA 1 and 2, Patients of either gender between 18-65 years. Patients who will be undergoing elective lower limb orthopaedic surgeries.

Exclusion criteria: Patients with critical cardiovascular sickness, hypertension, diabetes, renal failure, hepatic dysfunction, on-going respiratory illness, neuro muscular disorders, bleeding disorders, skin disorders at local site, uncooperative patients.

The sample size was estimated as 100 by using The OpenEpi Collection of Epidemiologic Calculators Version 3.01, developed by The OpenEpi Project to have at least 90% power and an alpha of 0.05 to detect the expected difference between the two groups in accordance to previously published studies [1]. One including that compared to one syringe technique, two syringe technique of fentanyl and hyperbaric

bupivacaine provide significant improvement in the quality of sensory block without incidence of hypotension. All patients posted for lower limb surgeries were assessed pre-operatively and baseline heart rate and blood pressure were noted. After clinical evaluation, patients found fit for surgery were shifted to OT and multipara monitors like ECG, SPO₂, NIBP were connected to the patient. Eighteen G I.V. access was secured and infusion of Ringer's lactate was begun at the pace of 80 ml/hr, all baseline parameters were noted. Equipment for general anaesthesia were kept ready. Study drug was set up in a sterile bowl by taking 3 ml of hyperbaric bupivacaine (0.5%) and 25 mcg of fentanyl. One hundred patients of 18-65 years of age fulfilling all the inclusion and exclusion criteria and posted for surgery under spinal anaesthesia were randomly divided into two groups by a computer-generated randomization divided into two groups (i.e. 50 in each groups) as follows:

- Group M-receiving premixed 3 ml of hyperbaric bupivacaine (0.5%) and 25 mcg of fentanyl in single syringe
- Group S-receiving hyperbaric 3 ml bupivacaine (0.5%) and 25 mcg fentanyl in two separate syringes.

The drug codes sealed in envelopes with numbering from 1–100 were opened by the designated consultant of the work area just prior to administration of anaesthesia and drug was prepared using aseptic technique according to group allocated. Spinal anaesthesia was given with all due antiseptic precautions with Quincke spinal needle of 25 gauge in all the cases. Sensory block was assessed by a sterile pinprick every 2 min till 20 min and then after every 10 min till the

highest level was achieved. Onset was considered when the loss of sensation at T10 dermatome was achieved. The time to onset of motor blockade was considered as time to reach Modified Bromage score of 3 [2]. Time of sensory block regression was measured from maximal block height attained to regression till two dermal level. Time of regression of motor block was assessed from Modified Bromage score of 3 to score of 0. Vitals of the participating patients were noted down from time to time till the end of the surgery. Event was noted as hypotension when 20% decrease in systolic blood pressure seen from baseline or less than that and was treated with Mephentermine given intravenously. Bradycardia was noted when HR <60 beats per minute was observed and was treated with 0.6 mg of intravenous atropine sulfate. Events of complications such as nausea and vomiting were graded according to the respective scales [5]. The primary outcome of the study was the onset and duration of sensory and motor blocks in minutes while variation in Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), Heart Rate (HR) were secondary outcomes.

In sitting position with midline approach at vertebral level of L2-L3 or L3-L4 intervertebral space with 25 G spinal needle after free flow of clear CSF by using following drugs intrathecally and divided into two group: Group M received 25 ug fentanyl (0.5 ml) premixed with 0.5% bupivacaine heavy 15 mg (3 ml) in the same syringe. Group S received 25 ug fentanyl (0.5 ml) in one syringe and 0.5% bupivacaine heavy 15 mg (3 ml) without barbotage in a second syringe. All patients were kept in supine position immediately.

We observed the pulse, systolic blood pressure, diastolic blood pressure and SPO₂ at different time intervals at 2 min, 3 min, 4 min, 5 min, 10min, 20 min, 30 min, 45 min and 1 hr.

Modified Bromage scale

0- No motor block

1- Unable to raise an extended leg

2- Unable to flex the knee

3- Unable to flex the ankle

Time needed to attain maximum sensory and motor block level; time for regression of sensory and motor block was noted. Occurrence of intra operative complications like hypotension, bradycardia and their management were recorded for each patient. Hypotension (MAP <10% of baseline) treated with head low and given fluid challenges and (MAP <25% base line) treated with Inj. Mephentermine 0.3-0.5 mg/kg given and repeated when needed. Bradycardia was treated when heart rate dropped below 60/min with Inj. Atropine 0.6 mg IV. Rescue analgesia was treated with Inj. Diclofenac sodium 1.5 mg/kg IV or Inj. Tramadol 50 mg IV. The statistical analysis was done by unpaired t-test for quantitative data and chi-square test for qualitative data by medical

software. The 'p' value was considered statistically significant less than 0.05.

Results:

Groups M and S did not differ significantly with regard to the demographic data (Table 1). There was almost no difference of intraoperative pulse, SPO₂ between two groups. Hypotension was noted in 52% of patients in Group M compared to 12% patients in Group S. Mean time (in minutes) to onset of sensory and motor block was observed early in Group M (3.2; 4.1 respectively) than Group S (3.6; 4.8 respectively), which was statistically highly significant ($p < 0.001$). The mean time to maximum sensory and motor block observed between Group M and Group S was significantly different ($p < 0.05$ mean time required for 1st rescue analgesia was short in Group M (223) than in Group S (265), which was statistically highly significant ($p < 0.001$) (Table 2). The patients in Group M had incidence of hypotension (52.1%), nausea (24.1%) and vomiting (13.7%). The patients in Group S had incidence of hypotension, (12.1%) nausea (14.23%) and vomiting (10.3%) (Table 3).

Table 1: Patient Characteristics in Both the Groups

Parameter	Group M	Group S	p
Age (years)	50.65 ± 8.41	54.98 ± 10.62	0.132
Gender (male / female)	16/14	18/12	0.100
Height (cm)	164.21 ± 7.82	163.13 ± 7.02	0.132
Weight (kg)	59.24 ± 9.28	57.45 ± 8.76	0.126
Duration of surgery	82.13 ± 8.2	76.24 ± 9.4	0.102

Values were expressed in Mean ± SD, Group M – premixed drugs, Group S – Separate syringes

Table 2: Block Characteristics of the Two Groups

Time (min)	Group M	Group S	p
Onset of sensory block	3.24 ± 0.62	3.6 ± 0.39	P < 0.001
Onset of motor block	4.18 ± 0.64	4.80 ± 0.40	P < 0.001
Maximum sensory block	8.56 ± 3.24	8.63 ± 3.89	P < 0.05
Maximum motor block	5.22 ± 1.95	5.22 ± 1.96	P < 0.05
Regression of sensory block	217 ± 16.02	251 ± 17.02	P < 0.001
Regression of motor block	186 ± 15.4	221 ± 17.02	P < 0.001
1 st rescue analgesia	223 ± 29.6	265 ± 39.25	P < 0.001

Values were expressed in Mean ± SD

Table 3: Adverse effects

Adverse events	Group M	Group S
Hypotension	52.1%	12.1%
Nausea	24.1%	14.23%
Vomiting	13.7%	10.3%

Discussion:

The purpose of this study was to compare extent of subarachnoid block and Hemodynamic changes thereof, after administering drugs via same syringe by premixing and via two separate syringes. The drugs used for subarachnoid blockade were hyperbaric bupivacaine and hypobaric fentanyl. In this study, there was significant fall in mean blood pressure in Group M than in Group S at 4 min, after administration of drug ($p < 0.05$). Significantly more patients developed hypotension in Group M (27) than in Group S (7) ($P < 0.05$). Keera *et al.* concluded in their study that early hypotension occurred in Group M as compared to Group S and

also found that frequency of hypotension in group S was lower as compared to Group M [6]. Bansal *et al.* found that there was significant difference among study and control groups in view of systolic and diastolic blood pressure 10 min after induction of anesthesia [7]. Desai *et al.* studied that there was no difference between study and control groups in the incidence of hypotension, need for vasopressor or side-effects [8].

In present study, mean time to onset of sensory and motor block was observed early in Group M (3.2; 4.1 respectively) than Group S (3.6; 4.8 respectively), which was statistically highly significant

($p < 0.001$) Sharma *et al.* observed that onset of sensory block and motor block was quicker in premixed syringe group compared to sequential group which is in contrast to our study [9]. Bansal *et al.* observed that onset of sensory and motor blockade was quicker in sequential group as compared to premixed group [7]. Schen *et al.* reported that onset of sensory and motor block was quicker in sequential group as compared to premixed syringe group.

Time to achieve maximum sensory block level was observed to be higher in Group S (8.63) than Group M (8.56), which was statistically significant. ($P < 0.05$). [10] Keera *et al.* found that mean level of maximal sensory block was non-significantly higher in Group S as compared to Group M ($P > 0.05$).

Mean time to regression of sensory and motor block was observed early in Group M (217; 186 respectively) than Group S (251; 221 respectively), which was statistically highly significant ($p < 0.001$) [6]. Keera *et al.* observed that onset of sensory and motor block was quicker in sequential administration group as compared to premixed syringe group [6]. Bansal *et al.* came to conclusion that the mean time to regression of sensory and motor block was significantly quicker in control group (116.5; 124.0 respectively) than study group (173.5; 168.0.9 respectively) ($p < 0.001$) [7]. Schen *et al.* also came to similar conclusion [9-10]. Desai *et al.* reported that there was no significant difference in block regression in either group [8]. In another study by Malhotra *et al.*, it was concluded that sequential groups showed more time for regression of block [2]. Similar findings were as also observed by Bansal *et al.* [7] and Gaddam *et al.* [11].

Patients in Group S had postoperative analgesia for longer duration than patients of Group M ($p < 0.05$). Mean time of giving first rescue analgesia was needed significantly early in Group M (223 min) than Group S (265 min), ($P < 0.001$). Sharma *et al.* reported that the time of rescue analgesia was 148.6 min in premixed group and 242.4 min in sequentially drug administered groups [9]. Bansal *et al.* observed that time taken for rescue analgesia was 189 min in study group and 102 min in control group [7]. Keera *et al.* concluded that time to give 1st rescue was prolonged in sequential drug group as compared to premixed group [6]. First rescue analgesia time was noted to be less in Group M than Group S. This was also found in studies done by Desai *et al.* [8]. In a study by Malhotra *et al.* it was concluded that time to first requirement of analgesic in postoperative period was earliest when LA and fentanyl are premixed [2]. The reason for difference in analgesic effect might be due to mixture of fentanyl and bupivacaine diluting fentanyl's potency and receptor occupancy leading to reduced effect. Whereas fentanyl, when administered separately it bonds well with opioids receptors at spinal cord and leads to denser and longer block [10].

Conclusion:

This study finds that two-syringe technique of fentanyl and hyperbaric bupivacaine makes significant improvement in the quality of sensory blockade with relatively less occurrence of hypotension in patients as compared to one syringe technique.

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