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Original Research Article

Block Characteristics and Post-operative Analgesia Using Dexmedetomidine, Fentanyl or Nalbuphine as Adjuvants to 0.5% Levobupivacaine in Patients Undergoing Lower Limb Orthopedic Surgery

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Abstract: ***Background:*** Spinal anaesthesia is a preferred mode of anaesthesia for lower limb orthopedic surgery but limited duration of action remains a concern. Different adjuvants have been used intrathecally to prolong the duration of SAB .A quest for searching newer and safer adjuvant to local anaesthetic agents is always there as these orthopaedic procedures are associated with moderate to severe pain postoperatively. ***Aim:*** We compare the efficacy of intrathecal dexmedetomidine, fentanyl and nalbuphine for block characteristics and post operative analgesia in orthopedic surgeries. ***Material & Methods:*** 130 American Society of Anaesthesiologist 1and II patients undergoing lower limb orthopedic surgery requiring SAB were allocated randomly to four groups of 30 each to receive intrathecal dexmedetomidine 0.5mcg Group 1, fentanyl 25mcg Group 2, nalbuphine 0.4mg Group 3 and normal saline Group 4, added to 0.5% Isobaric levobupivacaine 12.5mg to make total volume 3 ml in each group. We assesed block characteristics, postoperative pain scores, time to use of first analgesic, 24 hour analgesic consumption, and additional analgesic consumption. ***Results:*** Onset of Motor blockade was fastest (8.67mins) in dexmedetomidine group (9.13mins) in fentanyl group, (10.07mins) in nalbuphine group and (12.18mins) in control group. Significant prolongation of time for need of first rescue analgesic was seen with the use of dexmedetomidine (485.35mins).Total 24 hours tramadol consumption was 196.42mg in dexmedetomidine group, 200mg in fentanyl group, 253.84mg in nalbuphine group and 222.72mg in control group. ***Conclusion:*** Dexmedetomidine as an adjuvant to 0.5% levobupivacaine seems to be a better alternative to fentanyl and nalbuphine.

Keywords: Intrathecal, dexmedetomidine, fentanyl, nalbuphine, local anaesthetic.

INTRODUCTION

Spinal anaesthesia is most valuable mode of anesthesia for lower limb orthopaedic surgeries because of its simplicity, ease of administration and absence of side-effects of general anesthesia. It provides effective sensory and motor blockade [1]. Different drugs used for spinal anaesthesia are lidocaine, bupivacaine, tetracaine, mepivacaine, ropivacaine, levobupivacaine, chloroprocaine [2]. Levobupivacaine, the pure S(-) enantiomer of racemic bupivacaine, is a new long – acting local anaesthetic that has recently been introduced in the clinical practice and seems to be alternative to bupivacaine because of its significantly decreased cardiovascular and central nervous system toxicity [3]. Moreover the regression of motar block is significantly more rapid after levobupivacaine than bupivacaine, which may be advantageous for early ambulation after surgery [4]. There is very little experience as yet with the use of levobupivacaine.

Various additives were added over time to the local anaesthetics to increase the duration of analgesia**.** Dexmedetomidine has been used to local anaesthesia in the intrathecal route and has significant effect on the onset and duration of spinal anesthesia [5]. Nalbuphine, a mixed agonist- antagonist opioid produce analgesia without the undesirable side effects of a mu-agonist [6]. Intrathecal opioids, like Fentanyl added to local anesthetics enhance analgesia without intensifying motor and sympathetic block, and make it possible to achieve successful anesthesia inspite of the use of a low

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dose local anesthetics.(7) 0.5%Levobupivaciane has not been extensively investigated in orthopedic surgeries and the published clinical studies are small despite its higher safety profile. Our research has high relevance as there is mounting awareness yet limited studies about safety profile and efficacy of newer local anaesthetic with adjuvants as dexmedetomidine, nalbuphine and fentanyl on block characteristic and post operative analgesia.

METHOD

After institutional ethics approval and written consent from the patients we conducted this prospective randomized, double blind study. A total of 130 American Society of Anesthesiologists (ASA) I and II patients, either sex, 20-60 years of age scheduled for elective orthopedic fixation of fracture of long bones of lower limbs under spinal anesthesia were included. Exclusion criteria's included patient's refusal for spinal anesthesia, ASA III and IV patients, age > 60 years, Body weight > 120 kg or height < 150 cm, known allergy to study drug and known contraindications to spinal anesthesia. Patients fulfilling inclusion criteria were randomized by computer generated randomization into four groups to receive. All patients were thoroughly assessed and examined in the preanesthetic clinic. Patients fit for inclusion, the patients were premeditated with the tablet diazepam 10mg night before surgery.

On the day of surgery, intravenous access was established and all patients were preloaded with 500 ml Ringer Lactate. Routine monitors such as Non Invasive Blood Pressure (NIBP), Pulse oximetery (SpO2), Electrocardiogram (ECG). Spinal anaesthesia was administered in L3-L4 intravertebral space, in sitting position, using 25G Quinkie's needle and after free flow of Cerebrospinal fluid (CSF) 12.50mg of injection 0.5% isobaric Levobupivacaine mixed with the study drugs as follows was given.

GROUP-1: Isobaric levobupivacaine (0.5%) 12.5mg (2.5ml) + dexmedetomidine 0.5mcg (0.5ml) to make a total volume of 3ml.

GROUP-2: Isobaric levobupivacaine (0.5%) 12.5mg (2.5ml) + fentanyl 25mcg (0.5ml) to make total volume of 3ml.

GROUP-3: Isobaric levobupivacaine (0.5%) 12.5mg (2.5ml) + nalbuphine 0.4mg (0.5ml) to make total volume of 3ml.

GROUP-4: Isobaric levobupivacaine (0.5%) 12.5mg (2.5ml) + normal saline (0.5ml) to make total volume of 3 ml.

Onset of spinal block was assessed. The level of sensory block was checked by pin-prick method. Motor blockade was evaluated by Modified Bromage scale (54).

The patient was handed over for surgery after achieving the sensory block of T10 or above and Bromage score of 3.Time taken to achieve these conditions was recorded in all the groups. NIBP, HR will be recorded before the induction of spinal anaesthesia, every 2 min for first 15 minutes of spinal administration and thereafter every 10 minutes upto 105 mins then every 15 mins till the end of surgery.

All these parameters were recorded by an independent investigator blinded to the group allotment of patients. At the end of surgery, the level of sensory and motor blockade was checked by pin-prick method and the Bromage criteria. The patients was shifted to post anaesthesia care unit (PACU). The pain was assessed on a 10 centimeter scale by Visual Analogue Scale where 0 = no pain and 10 = worst Possible pain and rescue analgesia was administered when VAS>4 in the form of inj. tramadol 100mg iv on demand for next 24 hours. In the PACU, VAS score, sensory level and motor blockade checked at 0 hours, 2 hours, 4 hours, 12 hours, 24 hours postoperatively. The patients were assessed for the time of demanding the first dose of analgesia in PACU. Rescue analgesic in form of inj. tramadol 100 mg i.v. was administered in all the patient demanding pain relief. Sample size calculation was based on previous study (8). The sample size was calculated 25 subjects in each group, using power analysis (α =0.05, β=0.8) to detect 50% difference in tramadol consumption at 24 hours post surgery. To prevent possible data loss, we took 30 subjects per group.

STATISTICAL ANALYSIS

The data generated in the study is presented as Mean ± standard deviation (SD), median and range, frequency, ratio and percentage. The data was analysed for statistical analysis using Microsoft Office Excel 2010 and SPSS IBM version 22. Normally distributed continuous variables were compared using analysis of variance ANOVA (analysis of variance).If the F value was significant and variance was homogeneous, Bonferroni multiple comparision test was used to assess the differences between the individual groups .The Kruskal Wallis test was used for variables that were not distributed normally and further comparisions done using Mann Whitney U test Categorical variables were analysed using the chi square test.

RESULT

Spinal anaesthesia was successfully performed in all the patients. A total of twelve patients were excluded from the study. Two patients each in group1, group3 and 8 patients needed general anaesthesia because of inadequate block height after successful intrathecal injection (Figure1).The Demographic Profile of patients in different groups is shown in (Table 1). Statistical insignificance was present among the group in relation to age, weight and ASA grade of the patients (p>0.05).The Block characteristics are shown in (Table 2)The mean time of onset of motor block were

8.67±4.33 mins in group1, 9.13±2.64 mins in group 2, 10.07±2.37 mins in group 3 and 12.18mins in group 4 respectively.

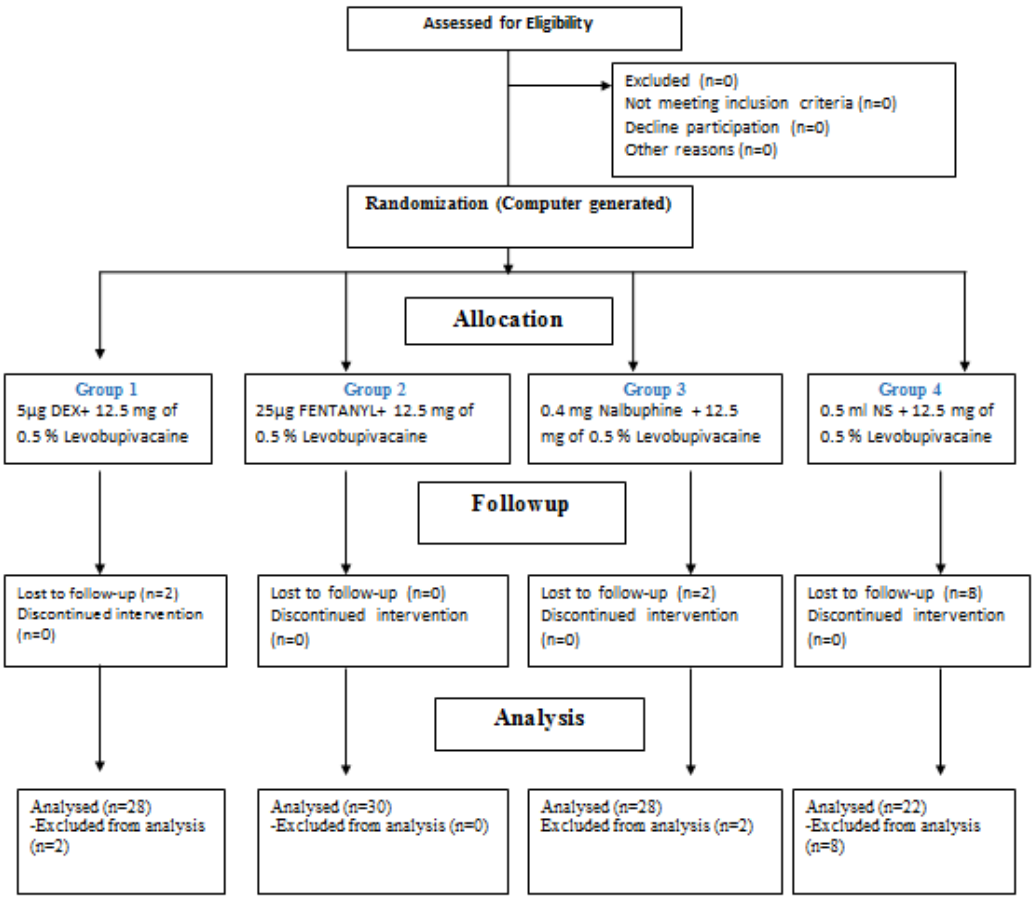

Fig-1: Consort Flow Diagram

Table-1: Demographic & Clinical Profile of Patients

	Group 1 (n=28)	**Group 2 (n=30)**	**Group 3 (n=28)**	**Group 4 (n=22)**
ASA I/II	25/3	22/8	25/3	22/0
Age in years (Mean±S.D.)	37.50±13.42	36.3±12.49	36.14±13.19	33.63±13.82
Sex M/F	20:8	21:9	24:4	20:2
Weight in Kgs (Mean±S.D.)	67.53±13.77	65.6±13.74	69.64±13.47	67.09±9.41
Block height median (range)	T8(6-10)	T6(6-10)	T8(4-10)	T8(6-10)

Table-2: Block Characteristics

	Group 1 (n=28)	**Group 2 (n=30)**	**Group 3 (n=28)**	**Group 4 (n=22)**	**P value**
Block height median (range)	T8(6-10)	T6(6-10)	T8(4-10)	T8(6-10)	
Onset of sensory block(min) mean±SD	5.96±4.94	5.03±3.22	4.76±2.20	5.00±1.92	0.560
Onset of motor block (min) mean±SD	8.67±4.33	9.13±2.64	10.07±2.37	12.18±2.15	0.001
Time to achieve BH t12/L1 mean±SD	311.64±85.51	224.06±44.83	209.46±41.14	235.90±49.58	0.001
Time for BS 0/1(MIN) mean±SD	401.42±121.51	267.4±54.71	252.5±49.09	286.45±54.16	0.001

One way ANOVA

The mean time of regression of motor block 0/1 was 401.42±121.51 min in group 1, 267.4±54.71 min in group 2, 252.5±49.09 min in group 3 and 286.45±54.16 min in group 4 respectively. The mean time for requirement of first analgesic in minutes were 485.35±142.84min, 312.58±85.74 min, 294.11±62.00 min, 343.45±101.01 min in Group 1 , 2, 3, and 4 respectively(Table 3).

Table-3: Comparison of Time of Requirement of Resque Analgesic in Different Groups

	Group 1 (n=28)	Group 2 (n=30)	Group 3 (n=28)	Group 4 (n=22)	P value
Time of requirement of 1st analgesic (min) mean±S.D.	485.35±142.84	312.58±85.74	294.11±62.00	343.45±101.01	0.001

VAS Score was assessed postoperatively in different groups (Table 4) at different intervals. Total dose of rescue analgesic Tramadol administration in each Group was 196.42±57.60 mg in Group 1, 200±53.45 mg in Group 2, 253.84±58.17 mg in Group 3, 222.72±75.16mg in Group 4 (Table 5).

Table-4: Vas Score at Different Time Interval in Different Groups

	Group 1 (n=28)	Group 2 (n=30)	Group 3 (n=28)	Group 4 (n=22)
Vas 0 hr	0	0	0	0
Vas 2 hr	0	0	0	0
Vas 4 hr	0	2	3	3
Vas 12 hr	2	3	3	3

Table-5: Comparison of Total Dose of Analgesic Required in First 24 Hours

	Group 1 (n=28)	Group 2 (n=30)	Group 3 (n=28)	Group 4 (n=22)	P value
Total dose of analgesic required in first 24 hrs (mgs of Tramadol) mean±S.D.	196.42±57.60	200±53.45	253.84±58.17	222.72±75.16	0.001

Intraoperative complications in different groups is shown in (Table 6).

Table-6: Incidence of Intraoperative Complications

	Group 1 (n=28)	Group 2 (n=30)	Group 3 (n=28)	Group 4 (n=22)
Bradycardia	0	0	0	0
Hypotension	8	2	0	0
Nausea	2	0	0	0
Vomiting	0	0	3	0
Respiratory depression	0	0	0	0
Pruritis	0	3	0	0
Shivering	3	4	0	0

DISCUSSION

We observed prolonged duration of postoperative analgesia and lower VAS scores at all interval with the addition of dexmedetomidine to levobupivacaine than other groups. Mechanism of action of α-2 adrenoreceptor agonist on duration of local anaesthetic is multifactorial. Intrathecal administration of α-2 adrenergic causes local vasoconstriction which leads to decrease absorption of local anaesthetic and increase duration of action [9].

Traditionally the dose of 0.5%Levobupivacaine used for spinal anaesthesia is 15mg providing sensory and motor blockade for approximately 6.5hrs. An up and down sequential design study recommends a minimum effective dose (MLAD) of Levobupivacaine 11.7mg [10].In our study, the intrathecal dose of dexmedetomidine, fentanyl and nalbuphine selected was based on previous human studies [11, 12, 13]. The total duration of motor blockade with intrathecal dexmedetomidine was significantly longer than other Groups .Our findings correlates with the previous studies by Basuni *et al* and Vania *et al* [14, 15].

Similarly, Calasans-Maia *et al* also reported that the duration of motor blockade induced by Levobupivacaine could be prolonged by intrathecal or intraperitoneal administration of dexmedetomidine in Guinea pigs [16]. Al Mustafa *et al* postulated early onset of sensory block with the use of 5µg and 10µg dexmedetomidine with hyperbaric bupivacaine as compared to control group [17]. Although the onset time observed in their study were relatively longer than those observed by us which can be attributed to their use of only 3µg intrathecal dexmedetomidine.

Lee *et al* [18] published the first study on the intrathecal use of 0.5% Levobupivacaine with fentanyl. They found no significant difference in haemodynamic changes and quality of sensory and motor block. Cuvas *et al* reported the characteristics of the spinal block

produced by 0.5% of Levobupivacaine without fentanyl versus 0.5% of Levobupivacaine with fentanyl. They observed no significant difference between time to reach sensory block at T10 (6.50±2.62 min vs 6.32±3.50 min) [19]. Our findings are in line with these studies. However, Akan *et al* studied the effect of intrathecal fentanyl with 0.5% Levobupivacaine in patients undergoing TURP. They reported that the combination provides faster onset of sensorial block compared to control group [20]. We also observed that the time to reach sensory block was clinically shorter with nalbuphine than the other groups but the difference was statistically insignificant. Although, we could not find any study in the existing literature on the use of intrathecal nalbuphine with 0.5% Levobupivacaine. Further studies are needed to address on this combination.

Hypotension and bradycardia are well documented in literature with the use of α2 adrenergic agonist's intrathecally. The presumed underlying mechanism is that, the use of dexmeditomidine reduces the biological stress responses and reduces the heart rate and blood pressure to moderate level by lowering catecholamine secretion. Hypotension was observed in more in patients receiving intrathecal dexmedetomidine. Esmaglue *et al* Similarly Gupta *et al* [21, 22] also reported similar observations.

We found that the quality of anaesthesia was inferior with 0.5% Levobupivacaine without additives and provided satisfactory anaesthesia in only 73.5% patients only as compared to 93.5% patients where dexmedetomidine and nalbuphine were used as an intrathecal adjuvant. De Sentiago *et al* also reported probability of spinal failure (0.5%) with low dose Levobupivacaine [23]. This may be attributed to the isobaric nature of levobupivacaine. The another explanation for inadequate anaesthesia could be due to assumption that intrathecal levobupivacaine in C.S.F acts indifferently to gravitational forces both immediately after the injection and later on.

Further studies are recommended to find the optimal dose and whether a higher sight of needle insertion or faster rate injection with measures correlated to gravity can provide better anaesthesia for surgeries.

The limitation of study are smaller sample size, relatively younger age of our study population and unequal distribution of patients in the group. Secondly baricity of the combination local anaesthetic and adjuvant also effects the spread in the intrathecal space (24), this factor was not considered by us in our study. Intravenous Tramadol 100mg on demand was used as rescue analgesic by us, use of patient control analgesia pumps (PCA) would have given us better idea for total rescue analgesics used.

Weighing the capability of dexmedetomodine as intrathecal adjuvant to intensify anaesthesia, and improve postoperative pain control, dexmedetomidine seems to be a safer and better alternative than fentanyl and nalbuphine in patients undergoing lower limb orthopedic surgery.

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Conflict of Interest: Nothing to declare.

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