Comparison of Effectiveness of Ropivacaine (0.5 %) with Fentanyl, and Bupivacaine (0.5 %) with Fentanyl, in Spinal Anaesthesia in Lower Limb and Lower Abdominal Surgeries

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ABSTRACT

BACKGROUND

We wanted to compare the efficacy of motor and sensory blockade in lower limb and lower abdomen surgeries achieved by ropivacaine-fentanyl and bupivacaine-fentanyl combinations administered intrathecally.

METHODS

A prospective, randomized [block randomization], interventional, comparative study was conducted on 116 American Society of Anesthesiologists physical status I – II patients. They were randomly divided into two groups of 58 patients each, to receive either 3 mL of 15 mg of 0.5 % ropivacaine with 25 mcg fentanyl [group RF] or 3 mL of 15 mg of 0.5 % bupivacaine with 25 mcg fentanyl [group BF] intrathecally. Pinprick test and Bromage scale was used to assess sensory and motor blockade, respectively.

RESULTS

Time taken for motor regression in group RF is lesser than that taken in group BF.

CONCLUSIONS

Ropivacaine along with fentanyl is more advantageous in spinal anaesthesia for infraumbilical surgeries due to brief duration of motor blockade.

KEYWORDS

Bupivacaine, Fentanyl, Ropivacaine, Spinal Anaesthesia

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BACKGROUND

Motor block from subarachnoid anaesthesia beyond the duration of surgery is undesirable, particularly in ambulatory setting. Spinal bupivacaine is the most commonly used anaesthetic in spinal anaesthesia during infraumbilical surgeries but since it induces dense motor blockade of prolonged duration it delays early post-operative mobilization and impedes early discharge and hence, cannot be used in day care surgeries.[1] The benefit with ropivacaine is that it provides sufficient sensory block along with prompt motor recovery.[2]

Our primary objective is to compare the effectiveness of motor blockade between the two study groups, taking Bromage scale as reference. Our secondary objective is to compare the effectiveness of sensory blockade, post-operative analgesia using VAS scale as reference and variability of haemodynamic parameters between the two study groups.

There are various studies available to compare ropivacaine with bupivacaine but literature regarding comparison using equal volume of ropivacaine and bupivacaine and their effects on perioperative haemodynamic is limited. Studies using fentanyl as adjuvant is further limited.

Hence, a study was conducted to evaluate the spinal anaesthesia characteristics of ropivacaine with fentanyl versus bupivacaine with fentanyl for infraumbilical surgeries.

Ropivacaine which is essentially a pure S-enantiomer, is the monohydrate of the hydrochloride salt of 1-propyl-2, 6-pipecoloxylidide. Its uptake from the epidural space is complete and biphasic with the mean half-life of the initial phase being approximately 14 minutes, followed by a slower phase of approximately 4.2 hours. 86 % of the drug is excreted in urine after a single intravenous dose administration, making kidney the main organ for elimination of the drug. It has a mean ± SD terminal half-life of 1.8 ± 0.7 h and 4.2 ± 1.0 h after intravenous and epidural administration, respectively.

Bupivacaine is 1–butyl-2', 6'-pipecoloxylidide. In adults, the terminal half-life of bupivacaine is 2.7 hours while in neonates and some young infants, terminal elimination half-lives could be as prolonged as 8 to 12 hours. Liver via conjugation with glucuronic acid, is the primary metabolizing organ for bupivacaine hydrochloride. Only 6 % of bupivacaine is excreted as is in the urine. Ropivacaine has climbed the steps of popularity owing to its improved safety profile and reduced central nervous system and cardio toxic potential.

It was approved in the European Union in February 2004 for intrathecal administration. The inclusion of adjuvants like opioids with local anaesthetics has shown to enhance the characteristics of spinal anaesthesia while prolonging the postoperative analgesia. They escalate the sensory block without prolonging the sympathetic block while achieving adequate quality of spinal anaesthesia at a much lower dosage of local anaesthetic.

METHODS

This is a prospective, randomized [type of randomization is block randomization] and interventional type of study. This clinical study was conducted in a single centre from 1st Nov 2017 to 31st March 2019. Approval from the institutional review board and scientific committee was taken. Written and informed consent was taken from all the patients. The study population consisted of 116 patients aged 18 - 60 years, American Society of Anesthesiologists (ASA) physical status I – II, body mass index between 18 to 30 kg / m^2 and posted for elective infraumbilical surgeries.

Two groups of patients were created, with 58 patients in each group, using a computer-generated random number table. Group RF = patients received ropivacaine with fentanyl (n = 58). Group BF = patients received bupivacaine-fentanyl (n = 58). Exclusion criteria were patients with contraindication to sub arachnoid block, allergy to amide local anaesthetic and pregnant female. The patients received tablet Alprazolam 0.25 mg tablet Ranitidine 75 mg one night prior to the day of surgery. After the administration of intrathecal drug, patients were placed supine immediately. The parameters that were monitored throughout the procedure were heart rate, blood pressure, oxygen saturation and respiratory rate. Hypotension was considered when the systolic blood pressure reduced more than 25 % from the initial value and a decline of more than 25 % from the initial heart rate was considered bradycardia. Intravenous Ephedrine 5 mg stat, intravenous bolus of crystalloids was used to treat hypotension and bradycardia was treated with intravenous Atropine 0.6 mg stat. The drugs were repeated in case of persistence of hypotension and bradycardia. The level of blockade, both sensory and motor was assessed at 2, 4, 6, 8, 10 and 15 mins and subsequently at 15 min interval till complete recovery of motor block occurred. The level of sensory block was assessed using blunted pin prick test while motor block was assessed with the standard Bromage scale.

The maximum sensory level block, time to achieve it and its recession to L1 dermatome was noted. For motor blockade, time to achieve maximum motor blockade and duration was assessed. Duration of analgesia was defined from the time of institution of a successful intrathecal block to the Visual Analogue Score (VAS pain score) more than 4. Analgesia was administered post operatively when VAS score was more than 4 or when patient requested for analgesia with diclofenac sodium 1 mg / kg bodyweight intramuscularly. Post-operative mobilization was achieved after reaching Bromage 0 (6 to 8 hours).

Study Design

Single blinded comparative, explanatory trial with block randomization.

Statistical Analysis

Calculation of sample size was based on; to assess the efficacy in terms of time for motor regression in two groups. The sample size was 58 per group. From an effect of 0.52

and a power of 80 % and alpha of 0.05 where the standard deviation of two groups was 47.06 and 49.9 respectively. Social science system version SPSS 17.0 was the statistical package used for conducting statistical testing. Here, categorical variables were expressed as frequencies with the percentages whereas continuous variables were presented with the mean ± SD when our continuous variable is normally distributed otherwise, we use median. The normality of continuous variable was checked by one sample Kolmogrov-Smirnov (KS) test. Association between two categorical variables was assessed using chi-square test / Fisher's exact test. (Fisher's test statistic was used when the cell frequency in contingency table was less than 5). The independent t–test / Mann Whitney U test was used for testing the mean of continuous variable between two groups according to the distribution of continuous variable. The significant difference was considered in case of p-value less than significance level (0.05).

RESULTS

The study was conducted in patients scheduled for infraumbilical surgery under spinal anaesthesia in Department of Anaesthesiology, PGIMER & Dr. RML Hospital. After approval from the Institutional Ethics Committee, 116 patients were allocated into two groups, randomly, RF group (ropivacaine and fentanyl group) and BF group (bupivacaine and fentanyl group), of 58 patients each, using a computer-generated random number table. Both the groups were comparable in terms of demographic data like age, gender, height, and weight.

Sl. No.	Parameters	Group RF	Group BF
1.	Age (in years)	34.43 ± 10.61	33.69 ± 10.19
2.	Weight (in Kg)	66.66 ± 12.32	65.22 ± 12.54
3.	Height (in Cm)	164.40 ± 8.91	162.14 ± 8.98
4.	Gender (Male / Female)	40 / 18	37 / 21

Table 1. Demographic Data (Group n = 58)

The peak sensory level achieved was comparable at T6 dermatome. There was no statistically significant difference in the time required to achieve peak sensory level (Group RF – 6.91 ± 1.16 min, Group BF – 6.5 ± 1.67 min) with p value being 0.132. There was no statistically significant difference in the time required to reach highest motor blockade, Bromage Grade III, (TPM) (Group RF - 7.491 ± 1.1 min, Group BF - 7.164 ± 1.66 min) with p value being 0.213. No statistically significant difference was noted in the time required for sensory regression to L1 Dermatome (TS) (Group RF - 233.1 ± 19.15 min, Group BF - 226.41 ± 17.38 min) with p value being 0.051.

There was statistically significant difference in the time required for motor regression to Bromage Grade I, (TMR) in two groups (Group RF - 248.14 ± 18.03 min, Group BF - 262.05 ± 21.89 min) with p value being < 0.001. There was statistically significant difference in the duration of analgesia i.e. the time for first analgesic demand, in two groups (Group RF 239.02 ± 18.35 min, Group BF 252.1 ± 19.73 - min) with p value being < 0.001.

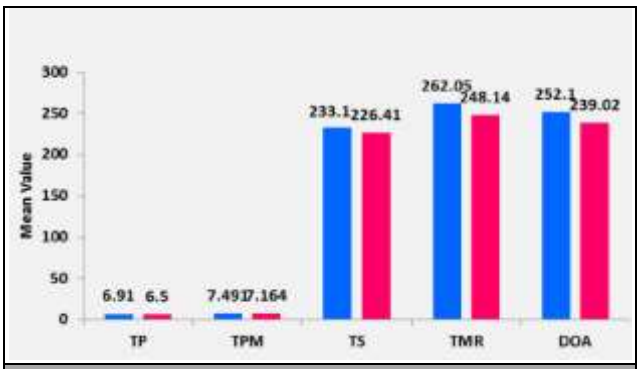

Figure 1. Comparison of Various Time Intervals in the Two Groups

- TP Time to reach Peak Sensory level.
- TPM Time to reach Peak Motor Blockade.
- TS Time for Sensory Regression.
- TMR Time for Motor Regression.
- DOA Duration of Analgesia.

Moderate fall in blood pressure following spinal anaesthesia is a common occurrence due to arterial and venous vasodilatation as a result of blockade of sympathetic nervous system. Hypotension needing to be treated with ephedrine occurred in 3 (5.2 %) patients in Group RF as compared to 8 (13.8 %) patients in Group BF, however, this difference was statistically insignificant with p value being 0.204. Bradycardia requiring treatment with atropine occurred in 2 (3.4 %) patients in Group RF as compared to 4 (6.9 %) patients in Group BF, however, this difference was statistically insignificant with p value being 0.679. Pruritis was seen in 6 (10.3 %) patients in both the groups, with p value being 1.00. Nausea and vomiting were seen in only 1 (1.7 %) patient in each of the groups, with p value being 1.00.

Sl. No.	Side Effects	Group BF	Group RF	P Value
1.	Hypotension	13.8 %	5.2 %	.204
2.	Bradycardia	6.9 %	3.4 %	.679
3.	Pruritis	10.3 %	10.3 %	1.00
4.	Nausea, Vomiting	1.7 %	1.7 %	1.00

Table 2. Side Effects

DISCUSSION

In surgeries of lower abdomen, lower extremities, perineum and infraumbilical areas, neuraxial anaesthesia has always been considered safe and effective choice for anaesthesia, which avoids airway manipulation and other complications of general anaesthesia.

Long-acting local anaesthetics reversibly inhibit the excitation of nerve endings and block the conduction of nerve impulses in peripheral nerves, hence, causing a prolonged sensory or motor blockade providing adequate anaesthetic condition required in different types of surgeries.[3] Moreover, it provides postoperative pain relief. This advantage of immediate postoperative pain relief by prolonged action of long acting local anaesthetics comes with disadvantage of prolonged sensory and motor blockade too which is unnecessary in the postoperative period. Long

recovery time for regression of motor blockade will delay the discharge of the patient. Moreover, it can cause urinary retention which in turn prolongs the unnecessary hospital stay. Bupivacaine, a long-acting amide local anaesthetic, is safe to use if administered correctly but when compared to its fellow local anaesthetics, it shows severe cardio toxicity as adverse drug reaction. Adverse drug reaction happens when used in high concentration, high absorption from injection site, slow degradation or when administered intravascularly by accident.

Ropivacaine is also a long-acting amino amide local anaesthetic that is same class as bupivacaine and both the drugs shows structural similarity. Main difference between them is that ropivacaine is a pure S (-) enantiomer, unlike bupivacaine, which is a raceme. Ropivacaine is less lipophilic when compared to bupivacaine, which explains its inability to penetrate large myelinated motor fibres therefore, causing less motor blockade. Motor sensory differentiation of greater degree is a desirable feature of this drug. With this local anaesthetic nerve fibres involved in pain transmission that is Aδ and C fibres are blocked to a larger extent than Aβ fibres, which control the motor functions.[4]

Our study elicited that both ropivacaine and bupivacaine along with fentanyl as a supplemental drug, for subarachnoid block, provided adequate anaesthetic environment for the infraumbilical surgeries. The demographic data and most sub-arachnoid block features such as highest sensory level achieved, time required to achieve highest sensory level, time to reach peak motor block and time for sensory regression, were comparable in the two study groups. There was early motor recovery with ropivacaine fentanyl, which was statistically significant although bupivacaine fentanyl provided longer duration of analgesia in post-operative period. In the study we had used equal milligram dose (15 mg) of the two local anaesthetics, as used by Luck et al.[5] The intra-operative quality of anaesthesia was improved with opioid adjuvant (fentanyl), which resulted in enhancement of duration of sensory analgesia without escalating the motor blockade or extending recovery.[6,7] Marret et a.l[8] Mantouvalou et al.[9] and Ogun et al.[10] found a similar cephalad extent of sensory block after isobaric bupivacaine or ropivacaine spinal anaesthesia. But Malinovsky et al[11] in their study encountered a lesser cephalad extent of block and also a block of shorter duration, as they had not used intrathecal opioid as adjunct. Malinovsky et al., found a lower cephalad extent (median dermatome level T9) of anaesthesia along with less dense anaesthetic blockade in the ropivacaine group, resulting in need of additional analgesia to perform surgery. This difference can be explained by use of fentanyl as adjuvant in our study which improves the quality of the block as well as the increased drug volume could have led to a higher cephalad extent of the local anaesthetic solution.[12]

Our results are consistent with those of Jagtap et al[4], and Lee et a.,l[13] as we observed that levels of highest dermatome blocked (T6) was comparable, the time taken to reach the peak sensory and motor level was comparable and the duration of the sensory block up to L1 dermatome was comparable too. The motor block with Group RF (248.14 ± 18.03 min) had significantly shorter duration when compared with bupivacaine but persisted well beyond the duration of surgery. This shorter duration of motor blockade allows early ambulation of the patient, permits self-voiding and movement of limbs which gives assurance to patient, shorter hospital stay and eventually reduced economic burden. If any neurological side effects come up which are rare though, it can be identified promptly. The average duration of analgesia is notably more in Group BF as compared to Group RF (252.1 ± 19.73 vs. 239.02 ± 18.35). There was no requirement of intra-operative supplementary analgesics.

When compared in terms of haemodynamics very few patients in the Group RF presented with side effects like hypotension and bradycardia. Group RF showed more stability. 5.2 % patients in the group RF presented with hypotension compared to 13.8 % patients in the group BF. This finding is little contradictory to McNamee's study in which he observed hypotension when he compared ropivacaine (17.5 mg) and bupivacaine (17.5 mg) in 12 % and 26 % patients respectively.[14]

Bradycardia was observed in 6.9 % of the patients belonging to bupivacaine fentanyl group as compared to 3.4 % patients of ropivacaine-fentanyl group. However, this difference in the haemodynamic stability between the two groups in statistically insignificant with p value being more than 0.05. Pruritus is a well-established adverse effect of intrathecal opioids. Six patients (10.3 %) in both the groups complained of pruritus. Patra et al. and Khanna and Singh also had used fentanyl as additive intrathecally in their study.[15,16] They reported pruritus in 46 % and 20 % respectively. The incidence of postoperative nausea, vomiting in the two groups was almost same.

CONCLUSIONS

Intrathecal ropivacaine-fentanyl in comparison to intrathecal bupivacaine-fentanyl produces a shorter time span of motor blockade and a shorter time span of analgesia. Sensory blockade and haemodynamic stability are comparable in the two groups. Shorter duration of motor blockade is advantageous for early ambulation, voiding and physiotherapy. Hence, we recommend increased usage of ropivacaine and fentanyl over bupivacaine and fentanyl in infraumbilical surgeries requiring subarachnoid block.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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