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A Comparison of Intrathecal administration of hyperbaric Ropivacaine 0.75% with Fentanyl (25ug) and Butorphanol (100ug) as adjuvants in Patients Undergoing Elective lower limb Surgeries

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Abstract: This study aims to compare the effectiveness of intrathecal hyperbaric ropivacaine 0.75% with fentanyl (25 µg) and butorphanol (100 µg) as adjuvants in patients undergoing elective lower limb surgeries. The comparison focuses on the maximum dermatome level achieved, the duration of sensory and motor blocks, the quality of anesthesia, and the incidence of side effects. Eighty patients were randomly allocated into two equal groups: Group RF (ropivacaine + fentanyl) and Group RB (ropivacaine + butorphanol). The results indicated that while both combinations provided effective anesthesia, the ropivacaine-butorphanol group offered superior analgesia duration with fewer adverse effects, whereas the ropivacaine-fentanyl group showed slightly better motor block quality.

Keywords: Intrathecal administration, Hyperbaricropivacaine, Fentanyl, Butorphanol,

INTRODUCTION:

The subarachnoid block is a popular anesthesia procedure practiced worldwide. It is a standard of care for lower abdominal, lower limb and perineal surgeries.

Lidocaine has been the most widely used local anesthetic for subarachnoid block because of its faster onset and shorter duration of the block. It is also less popular because of its association with transient neurologic symptoms and caudaequina condition. [1]

Newer local anesthetics for instance Ropivacaine was synthesized simultaneously with Bupivacaine by E Kenstam almost 50 years ago and was first launched in1996. It is the first pure S enantiomeric local anesthetic to be clinically introduced. Several clinical studies confirm that Ropivacaine has a lower and different toxicity profile compared to Bupivacaine.[2]Ropivacaine with high pka and low lipid solubility is considered to block sensory nerves to a greater degree than motor nerves and has similar local anesthetic properties and chemical structures compared to Bupivacaine. Because of sensorimotor dissociation Ropivacaine should be a favorable drug for day care surgeries and could be associated with early post-operative mobilization.[3]

Various adjutants like opioids, α agonists, neostigmine, midazolam and others have been shown to improve the analgesic duration post-spinal anesthesia. However, opioids because of their motor-sparing property are more popular than others for the same thereby improving the quality and success of anesthesia.

Hence we aimed to compare Intrathecal administration of hyperbaric Ropivacaine 0.75% with Fentanyl (25ug) and Butorphanol (100ug) as adjuvants in Patients Undergoing Elective lower limb Surgeries.

Objectives

- Comparison of maximum dermatome achieved
- Comparison of total duration of sensory and motor block in each group

MATERIAL AND METHODS;

This study was conducted over 80 patients undergoing elective surgeries at the Department of Anaesthesiology, Integral Institute of Medical Sciences and Research, Lucknow between September 2022 and March 2024 after obtaining approval from the institutional ethics committee.

Inclusion criteria

- Patient of either sex belonging to ASA status I & II
- Patients aged between 20 - 50 years Patients undergoing elective lower limb surgical procedures underspinal anesthesia

Exclusion Criteria:

- Patient refusal
- Patient having a prior history of allergy with any of the drugs used in the study.
- ASA grade >2
- Patients with body mass index >30 kg/m2
- Patients shorter than 150 cm
- Planned cases longer than 3hrs

Methods:

The research population is randomly allocated into two equal groups using the shuffled closed envelope approach.

- Group Ropivacaine + Fentanyl (RF): 3 ml of 0.75% hyperbaric ropivacaine solution with 25 micrograms of fentanyl (0.5ml)
- Group Ropivacaine + Butorphanol (RB): 3ml of 0.75% hyperbaric ropivacaine solution with 100ug of butorphanol(0.1ml) and 0.4ml distilled water.

Every patient underwent a preoperative evaluation, abstaining from solid food for 6 hours and clear fluids for 2 hours before surgery. An 18G cannula was used to establish an intravenous (IV) line, filled with 15 mL/kg of Ringer lactate. Monitoring was conducted with a multiparameter monitor featuring pulse oximetry, electrocardiography (ECG) and noninvasive blood pressure measurement. Patients were positioned upright with the table horizontal. A lumbar puncture was performed using a 25G Quincke's spinal needle at the L2-L3 or L3-L4 level, following aseptic measures. A 3.5 mL solution of 0.75% hyperbaric ropivacaine with either 100 µg of butorphanol or 25 µg of fentanyl was administered into the subarachnoid space after confirming unobstructed cerebrospinal fluid flow within 15 to 20 seconds. Patients were placed in a supine position immediately after receiving the spinal anesthetic.

The following parameters are to be noted

- Onset and duration of sensory blockade
- Maximum level of sensory blockade attained and the time taken for the same
- Onset and duration of motor blockade
- Quality of motor block
- Total duration of analgesia
- Time of rescue analgesia if needed

Statistical Analysis:

The statistical analysis was performed with SPSS version 23.0. The data were presented in the form of mean (standard deviation) and percentage (%). The chi-square test was used to compare the categorical variables, while the independent t-test was used to assess discrete variables between groups. A p-value of 0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS;

The study included a total of 80 patients. Out of these, 40 patients were assigned to receive a combination of Ropivacaine and Fentanyl (RF): 3 ml of 0.75% hyperbaric ropivacaine with fentanyl 25ug(0.5ml) (group RF). The other 40 patients were assigned to receive a combination of Ropivacaine and Butorphanol (RB): 3ml of 0.75% hyperbaric ropivacaine with butorphanol 100ug(0.1ml) and distilled water 0.4ml(group RB) (Table 1).

Table 1: Distribution of patients in groups

		n	%
Group RF	Ropivacaine + Fentanyl (RF) : 3 ml of 0.75% hyperbaric ropivacaine with fentanyl 25ug(0.5ml)	40	50.0
Group RB	Ropivacaine+Butorphanol (RB): 3ml of 0.75% hyperbaric ropivacaine with butorphanol 100ug(0.1ml) and distilled water 0.4ml	40	50.0

Table 2: Association of mean age (years) between group RF and group RB

	Group RF (n=40)		**Group RB (n=40)**		**t**	**p-Value**
	Mean	±SD	Mean	±SD		
Age (years)	37.03	9.15	35.58	10.72	0.65	0.517

Table 2 show the correlation between the average age (in years) of the RF group and the RB group. The mean age was 37.03±9.15 years in the RF group and 35.58±10.72 years in the RB group. There was no significant difference in the average age (in years) between the RF group and the RB group.

The correlation between the average weight (kg), height (m), and BMI (kg/m2) of the RF group and the RB group. The mean weight (kg), height (m), and BMI (kg/m2) were 69.88±9.20, 1.61±0.08 and 26.80±2.31 in the RF group and 68.23±10.43, 1.61±0.09 and 26.08±2.61 in the RB group, respectively. There was no significant difference in average weight (kg), height (m), and BMI (kg/m2) between the RF group and the RB group.

Table 3: **Association of mean duration of surgery (min) between group RF and group RB**

	Group RF (n=40)		**Group RB (n=40)**		**t**	**p-Value**
	Mean	±SD	Mean	±SD		
Duration of surgery (min)	98.63	14.28	100.88	12.24	-0.76	0.452

Table 3 show the correlation between the mean duration of surgery (min) of the RF group and the RB group. The mean duration of surgery (min) was 98.63±14.28 in the RF group and 100.88±12.24 in the RB group. There was no significant difference in the average mean duration of surgery (min) between the RF group and the RB group.

The correlation between the mean onset of sensory blockade in the RF group and the RB group. The mean onset of sensory blockade was 4.35±0.89 in the RF group and 4.70±0.94 in the RB group. There was no significant difference between the mean onset of sensory blockade in the RF group and the RB group. and correlation between the mean motor block bromage score in the RF group and the RB group. The mean motor block bromage score was 2.90±0.30 in the RF group and 2.70±0.46 in the RB group. The mean motor block bromage score was significantly higher in the RF group than in the RB group.

Table 4: **Association of mean time of onset of motor block between group RF and group RB**

	Group RF (n=40)		**Group RB (n=40)**		**t**	**p-Value**
	Mean	±SD	Mean	±SD		
Time of onset of motor block	5.83	0.68	6.08	1.16	-1.18	0.243

Table 4 show the correlation between the mean time of onset of motor block in the RF group and the RB group. The mean time of onset of motor block was 5.83±0.68 in the RF group and 6.08±1.16 in the RB group. There was no significant difference between the mean time of onset of motor block in the RF group and the RB group. Correlation between the mean total duration of sensory block (min) till L5 in the RF group and the RB group. The mean total duration of sensory block (min) till L5 was 153.00±7.23 in the RF group and 154.25±8.44 in the RB group. There was no significant difference between the mean total duration of sensory block (min) till L5 in the RF group and the RB group.

Table 5: **Association of mean total duration of motor block between group RF and group RB**

	Group RF (n=40)		**Group RB (n=40)**		**t**	**p-Value**
	Mean	±SD	Mean	±SD		
Total duration of motor block	125.75	8.74	119.5	11.31	2.765	0.0071

Table 5 show the correlation between the mean total duration of motor block in the RF group and the RB group. The mean total duration of the motor block was 125.75±8.74 in the RF group and 119.5±11.31 in the RB group. There was a significantly longer mean total duration of motor block in the RF group than in the RB group.

Figure 1: Bar chart shows the frequencies of maximum height of sensory block in group RF and group RB

Table 6: **Association of mean duration of analgesia (min) between group RF and group RB**

	Group RF (n=40)		**Group RB (n=40)**		**t**	**p-Value**
	Mean	±SD	Mean	±SD		
Duration of analgesia (min)	273.75	13.34	302.00	14.88	-8.94	<0.001

Table 6 show the correlation between the mean duration of analgesia (min) in the RF group and the RB group. The mean duration of analgesia (min) was 153.00±7.23 in the RF group and 154.25±8.44 in the RB group. The mean duration of analgesia (min) was significantly longer in the RB group as compared to the RF group.

Table**7: Association of frequencies of different side effects between group RF and group RB**

	Group RF (n=40)		**Group RB (n=40)**		**Chi Sq.**	**p-Value**
	N	%	N	%		
Bradycardia	7	17.50	7	17.50	-	1.00
Hypotension	10	25.00	11	27.50	0.06	0.799
Nausea	5	12.50	4	10.00	0.13	0.724
vomiting	1	2.50	0	0.00	1.01	0.314
Pruritus	0	0.00	0	0.00	-	-
Sedation	0	0.00	0	0.00	-	-

In the RF group, bradycardia occurred in a total of 7 subjects (17.50%), hypotension in 10 subjects (25.00%), nausea in 5 subjects (12.50%), and vomiting in 1 subject (2.50%), out of a sample size of 40 subjects. In the RB group, bradycardia was observed in 7 subjects (17.50%), hypotension in 11 subjects (27.5%), and nausea in 4 subjects (10.0%). No cases of vomiting were observed in the RB group. Both groups also showed similar results for adverse effects (Table 13).

DISCUSSION:

The pursuit of safer anesthetic therapy, accomplished by decreasing the dosage of local anesthetics by the use of adjuvants, seems to be a continuous effort with no conclusive outcome. The findings of the current investigation demonstrate that the combined use of butorphanol and fentanyl, along with the more recent local anestheticropivacaine, yielded enhanced anesthetic and analgesic advantages compared to the sole administration of ropivacaine during lower limb procedures while inducing fewer adverse effects.

Ropivacaine, a more recent aminoamide local anesthetic, with a chemical structure that closely resembles bupivacaine, however with a potency that is roughly 30-40% lower. Evidence has demonstrated that it is safe, with a shorter period of effectiveness compared to bupivacaine and a reduced occurrence of temporary neurological effects [4]. Ropivacaine is an enantiomerically pure molecule that closely resembles bupivacaine chemically. This indicates that it carries a reduced likelihood of inducing cardiovascular and central nervous system damage in comparison to bupivacaine. [5] We initiated our inquiry because of the advantageous characteristics of ropivacaine.

Fentanyl is a synthetic opioid that functions as a potent agonist on μ-receptors. When utilized as a supplementary treatment in spinal anesthesia, this medication is suggested for off-label usage because of its quick onset of effects, brief duration of effects, and reduced occurrence of respiratory depression [6].

Butorphanol is categorized as a μ-opioid receptor antagonist [7,8]. However, it may also exert agonistic effects on antinociception in some experimental animals [9-10]. Furthermore, research has demonstrated that activating the κ-opioid receptor has pain-relieving effects. However, the role of δ-opioid receptors in pain reduction remains little comprehended [11]

There has been no prior research comparing the use of intrathecal injection of hyperbaric Ropivacaine 0.75% with Fentanyl (25ug) and Butorphanol (100ug) as additional substances. In their work, Kumar et al. (2011) showed that the combined intrathecal administration of 25 μg of fentanyl and 25 μg of butorphanol, together with 12.5 mg of hyperbaric bupivacaine, successfully produces anesthesia for lower limb surgeries. [12] The intrathecal administration of bupivacaine and butorphanol provides a more extended duration of sensory blockade and superior pain relief when compared to the intrathecal administration of fentanyl and bupivacaine. In a previous study, the intravenous administration of butorphanol and fentanyl was compared, and it was discovered that the equianalgesic doses were 1 μg/kg for fentanyl and 20 μg/kg for butorphanol. Furthermore, Singh et al. (2006) investigate the impact of delivering a 25 μg dose of intrathecal fentanyl and butorphanol.[13]

In this investigation, we employed ropivacaine, a localized anesthetic that is recognized to possess a potency 30-40% lower than bupivacaine. In order to augment the anesthetic potency of ropivacaine, we chose to administer a larger dose of butorphanol(100 μg).

Our study revealed that butorphanol exhibited a comparable sensory and motor blockade start, as well as a comparable duration of sensory blockade (measured in minutes) up to L5. Nevertheless, the fentanyl group had a greater motor block bromage score.

Basunia et al. (2020) discovered that the fentanyl group experienced a faster start of sensory blockage (3.0836±0.2158 min) compared to the butorphanol group (3.1509±0.2464 min), but the difference was not statistically significant ($p>0.05$).[14]. Kumar et al. (2016) conducted research that showed that the time it took for the sensory block to begin was 8±1.4 minutes in the fentanyl group, whereas it took 8±3.2 minutes in the butorphanol group.[15] The extended duration reported in the subsequent research may be attributed to the much-reduced dosage of the spinal medications. Both groups in this investigation achieved a maximum sensory level of T6, which aligns with the findings of Reddy et al. The researchers administered a dose of 200 μg of intrathecal butorphanol and 3 mL of bupivacaine liberally in their investigation.[16] Singh et al (2016) conducted research that showed that the average length of time that the sensation-blocking effect lasted was substantially longer in patients who received a combination of 0.75% ropivacaine with buprenorphine or 0.75% ropivacaine with fentanyl, compared to those who simply received 0.75% ropivacaine.[13]

Our study found that the mean duration of analgesia was 273.75±13.34 minutes in the fentanyl group and 302.00±14.88 minutes in the butorphanol group. Furthermore, the butorphanol group had a notably extended duration of analgesia (measured in minutes) in comparison to the fentanyl group. Basunia et al. (2020) found that the butorphanol group had a substantially longer time to first request for emergency analgesia (378.41±10.25 min) compared to the fentanyl group (289.27±7.37 min). The combination of fentanyl and butorphanol, together with bupivacaine, effectively alleviated pain and induced anesthesia. Nevertheless, butorphanol demonstrated superiority in prolonging the time before further analgesics were required, aligning with the results reported by Kumar et al. (2011). The fentanyl group had a considerably shorter duration (308±14.9 minutes) until rescue analgesia was required compared to the butorphanol group (365.9±12.3 minutes). Both Reddy IR et al.[16] and Upasna B et al.[17] have revealed statistically significant findings in their respective research. Kim et al. (2009) found that the pain-relieving effect of a combination of 4 mg bupivacaine and 25 μ fentanyl in transurethral resection of the prostate (TURP) lasts around 7 hours.[18] Prior research indicates that the pain-relieving impact of intrathecal fentanyl often lasts for a duration of one to four hours [Hamber et al. 1999].[19] Research done by Singh et al. (2006) revealed that a lower percentage of patients who received intrathecal butorphanol needed further pain management compared to individuals who received intrathecal fentanyl.[20]

Our study found that bradycardia was seen in 7 participants, accounting for 17.50% of the sample. Hypotension was reported in 10 participants, representing 25.00% of the sample. Nausea was experienced by 5 participants, making up 12.50% of the sample. Vomiting was reported by 1 participant, accounting for 2.50% of the sample. At now, there is only one individual who is a member of the fentanyl group. Bradycardia was detected in 7 persons, accounting for 17.50% of the overall population. Eleven individuals, namely 27.5% of the sample, exhibited hypotension. Out of the sample, four individuals, which

accounts for 10.0% of the total, experienced nausea. Belonging to the butorphanol category. No instances of emesis were seen in the butorphanol group. Both groups had comparable outcomes in terms of negative consequences.

CONCLUSION;

In conclusion, our study demonstrates that both 25 µg fentanyl and 100 µg butorphanol, when administered intrathecally with 0.75% hyperbaric ropivacaine, provide effective and safe anesthesia for lower limb surgeries, with minimal adverse effects. The ropivacaine-butorphanol combination offers superior analgesic quality, significantly extending the duration of pain relief compared to the ropivacaine-fentanyl combination. Conversely, the ropivacaine-fentanyl combination provides slightly better quality and duration of motor block. These findings suggest that the choice between these combinations can be tailored based on the specific clinical requirements for analgesia and motor block, thereby enhancing patient care during lower limb surgical procedures.

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