Original Research Article

A prospective randomized double-blinded study comparing intrathecal nalbuphine vs intrathecal fentanyl added to 0.5% hyperbaric bupivacaine for perioperative anaesthesia and postoperative analgesia in patients undergoing hernioplasty

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Abstract

Background- Various adjuvants are added to the local anesthetics intrathecally, to prolongate the duration of anesthesia. Among the adjuvants the most commonly preferred are the opioids.Opioids like fentanyl, morphine, buprenorphine and nalbuphine have been administered intrathecally to fasten the onset time and increase the duration of sensorimotor blockade. In this study we compared the merits of intrathecal adjuvants fentanyl / nalbuphine when added to 0.5% hyperbaric bupivacaine in patients undergoing hernioplasty. **Aim**- The aim of the study was to compare the merits of intrathecal adjuvants fentanyl/nalbuphine hydrochloride when added to 0.5% hyperbaric bupivacaine in patients undergoing hernioplasty under spinal anaesthesia. **Methods-** Totally 120patients undergoing elective hernioplasty surgery were included in this study. They all were allocated into three groups of forty patients each randomly. Nalbuphine Group (A) 0.5ml of nalbuphine hydrochloride (500µg), Fentanyl group(B) 0.5ml of fentanyl (25µg), Control group (C) 0.5ml of Normal saline, were added as adjuvants to 3ml of 0.5% hyperbaric bupivacaine. Sensorimotor block onset time and duration, highest sensory level blockade and time to reach it, two segment regression of sensory level blockade and duration of analgesia were studied. **Results:** Onset time of a sensory block in Control group (C) 4.08 ±1.25 mins>Nalbuphine Group (A) 3.05 ±0.88mins >Fentanyl Group (B) 2.25 ±0.63 mins. Onset time of a motor block in Control Group (C) 3.43 ±0.93 mins>Nalbuphine Group (A) 2.33 ±0.69 mins> Fentanyl Group (B) 1.48 ±0.51 mins. Time to reach a highest sensory block in Control Group(C)14.54 ±3.54 mins>Nalbuphine Group (A)13.75 ±2.06 mins>Fentanyl Group(B) 11.68 ±2.44 mins. Duration of analgesia in Nalbuphine Group (A)5.15 ±0.350 hours>Fentanyl Group (B) 4.05 ±0.539 hours> Control Group (C) 2.64 ±0.349 hours. The onset of sensory and motor blockade, time to reach the highest sensory level was prolonged in the nalbuphine group than fentanyl group. The duration of sensory blockade, two segment regression of sensory block, and duration of analgesia were prolonged in the nalbuphine group than fentanyl group. The number of patients to reach highest sensory level T2-T4 was more in nalbuphine group. **Conclusion:** Comparing intrathecal adjuvants Nalbuphine and Fentanyl concludes that: Intrathecal Nalbuphine may be a good alternative to Fentanyl in surgeries like hernioplasty and in below umbilical surgeries which provides an extended sensorimotor blockade, and increased duration of analgesia without any adverse effects.

Key Word: Intrathecal, Nalbuphine, Fentanyl, Opioids

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INTRODUCTION

In 1898, August Bier first described "cocainization of the spinal cord". In Surgeries like hernioplasty the most preferred regional anaesthesia is spinal anaesthesia. Spinal anaesthesia produces dense sensorimotor and sympathetic blockade.Spinal anaesthesia reduces mortality and morbidity in high-risk surgical patients. Spinal anaesthesia is simple to perform and its quicker in onset with good sensorimotor blockade[1], and it provides very good analgesia and reduces stress response to

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surgery and intraoperative blood loss have made it as preferable anaesthesia in below umbilical surgeries like hernioplasty. Bupivacaine which is commonly used localanaesthetic, produces extended intense sensorimotor block with significant sympathetic blockade and very good surgical relaxation[2,3].Subarachnoid block with 0.5%hyperbaric bupivacaine usually lasts for 2 to 2.5 hours[4]. In regularly used dosage, it produces more unwanted side effects[5]: Minimizing the dosage of bupivacaine, limits its distribution of spinal block, and it causes comparably quicker recovery[6].Various adjuvants are added to the local anaesthetics intrathecally, to prolongate the duration of anaesthesia. Intrathecal adjuvants lower the requirement of local anaesthetic dose, and reduces unwanted hemodynamic effects of spinal anaesthesia and also provides satisfactory block[7,8].Among the adjuvants the most commonly preferred are the opioids. These adjuvants have "synergistic anti-nociceptive effect" along with intrathecal local anaesthetic both during intraoperative and postoperative periods by extending analgesia duration[9]. Opioids as intrathecal adjuvants added to local anaestheticsextend analgesia duration, enhances the quality of analgesia and reduces the requirement of postoperative analgesics[10].Opioids like morphine, fentanyl, buprenorphine and nalbuphine have been used intrathecally for rapidonset and to extend the duration of sensorimotor blockade. Nalbuphine acts viaκ receptors present in the spinal cord and brain when given intrathecally. It acts via kappa receptors and hence there is no adverse effects mediated by μreceptors.

MATERIALS AND METHODS

This Single-center, prospective, randomized double-blinded, interventional controlled study was done in Tirunelveli medical college hospital, at Department of Anaesthesiology and critical care from December 2017 to September 2018. The sample size was calculated using the formula $n=(u+v)2 \times(SD1^2+SD2^2)\div(\mu1-\mu2)$with at least 90 sample size needed to detect a difference with more than 80% power of study at 5% significance level.

Inclusion Criteria: 20 - 60 years of age, ASA physical status I or II, Patients planned for elective hernioplasty and given valid informed written consent.

Exclusion Criteria: Absolute contraindications for spinal anaesthesia, local site infection (at the subarachnoid block injection site), neurological / musculoskeletal disease, hemorrhagic diathesis, h/o allergy to local anaesthetics and Obese patients (obesity BMI > 30kg/m^2). 120 patients planned for elective hernioplasty surgery under Subarachnoid block were randomly allocated into 3 groups.

Randomization: 3 Groups by random number allotted by slips in the box technique Allocation and Intervention: 3 Groups (N = 40)

Nalbuphine Group A :15mg (3 ml) of 0.5% hyperbaric bupivacaine +nalbuphine 0.5 mg (0.5ml) - Total volume 3.5 ml. 10mg in one ml ampoule. 1 ml of nalbuphine added to 9ml of normal saline.After dilution each ml contains 1mg of nalbuphine. 0.5ml of nalbuphine is added to 0.5 % hyperbaric bupivacaine.

Fentanyl Group B: received 15mg (3 ml) of 0.5% hyperbaric bupivacaine + fentanyl 25 mcg (0.5ml) - Total volume 3.5 ml.

Control Group C: received 15mg (3 ml) of 0.5% hyperbaric bupivacaine + normal saline 0.5 ml (0.5ml)- Total volume 3.5ml.Patients planned for surgery were examined on the day before surgery. And also pre-operative assessment sheet, preoperative investigations were checked on the day before surgery. All the patients fasted overnight. Pre-medication[tablet ranitidine (150mg), tablet metoclopramide (10mg) and tab*let al*prazolam (0.5mg)] was given on the night before surgery. In the operating room, standard monitors like noninvasive blood pressure (NIBP), Electrocardiography (ECG) and pulse oximetry (SPO2) were connected and baseline values were recorded. After securing iv line with 18G cannula, patients have preloaded with10ml/kg of Ringer Lactate (RL) solution. Under strict aseptic precautions, patient in the right lateral decubitus position, using 25 G quincke's needle, lumbar puncture was performed at L3-L4 intervertebral space using the midline approach. Free flow of clear cerebrospinal fluid(CSF) was confirmed and drug was injected at 0.2ml/sec, according to the groups allocated as described above. Hemodynamic parameters (spo2, NIBP, pulse rate) were recorded at regular intervals intraoperatively and postoperatively.Onset time of sensorimotor blockade(sensory -T10 and motor - Bromage 3) time to reach highest level of sensory blockade, total duration of sensorimotor blockade, duration of analgesia, two-segment sensory level regression time, wererecorded. Hypotension (systolic blood pressure <90mmHg or < 20% from baseline) was treated with Inj.Ephedrine 6mg iv bolus, Bradycardia (HR < 60 beats/min) was treated with Inj. Atropine 0.6 mg iv bolus. The duration of analgesia was defined as the period from spinal injection to the first occasion when the patient complaints of pain (VISUAL ANALOGUE SCALE – 3) in the postoperative period. Visual Analog Scale(VAS) score of 4 or more, rescue analgesia (Inj.Tramadol 100mg im) was given in postoperative ward.

Statistical Analysis: Data were analyzed with SPSS version 16 and Microsoft Excel. Comparison of three groups wasdone by using one-wayANOVA. Descriptive

results were calculated using mean and standard deviation. P value of less than 0.05 was considered statistically significant.

RESULTS

All 120 patients with ASA physical status I/II who satisfied all inclusion criteria were randomly divided into three groups and underwent Hernioplasty under subarachnoid block. Mean age in three groups were around 44.18 years and was not statistically significant, mean height (p value=0.202) and mean weight (p value=0.652) were also not statistically significant. In my study, onset time of sensory blockade was earlier in fentanyl group (B) when compared to nalbuphine group. The mean onset time of sensory blockade (T10):earlier in fentanyl group (B) (2.25 ±0.63 mins) <Nalbuphine group (A) (3.05 ±0.88mins)< Control group(C) (4.08 ±1.25 mins). Comparison of mean time to achieve highest sensory level among three Groups is statistically significant (P value 0.002). Time to achieve highest sensory level of Fentanyl group(B) was (11.68 ±2.44 mins) much earlier than nalbuphine Group (A) (13.75 ±2.06 mins) and it is statistically significant (P value 0.003). The total number of patients achieved higher sensory level (T2 toT4) was more in Nalbuphine group (A) when compared to fentanyl Group (B) (T2 to T5). The mean time for two segment regression of sensory block in the nalbuphine group (A) was90.40 ±13.79 mins>fentanyl group B was 81.35 ±6.77 mins> control group (C) was 50.98 ±3.58 mins. Similar to sensory blockade the onset of motor blockade (fentanyl group(B)1.48±0.51 mins<nalbuphine group (A) 2.33 ±0.69 mins< control group(C) 3.43 ±0.93 mins)is much earlier in fentanyl group than nalbuphine group. Mean duration of motor blockade in the Nalbuphine group (A) 3.41 ±0.322 hours > Fentanyl group (B) 3.19 ±0.747 hours> control group(C) 1.97 ±0.358 hours, which was statistically significant(p-value<0.0001). Mean duration of motor blockade in nalbuphine group is higher than fentanyl group. The mean duration of analgesia in the Nalbuphine group (A) was found to be 5.15 ±0.350 hours> Fentanyl group (B) 4.05 ±0.539 hours> Control group(C) 2.64 ±0.349 hours, which was statistically significant (p-value<0.0001) between the three groups. Side effects observed during study were very minimal and most of the cases were stable in all the three groups.

Table 1: Distribution of Age, Height and Weight

Variables		Mean	SD	P value
Age	Group A	44.13	10.84	0.418
	Group B	45.83	9.22	
	Group C	42.58	12.60	
	Total	44.18	10.96	
Height	Group A	165.08	3.54	0.202
	Group B	165.28	3.40	
	Group C	163.98	3.49	
	Total	164.78	3.50	
Weight	Group A	63.98	5.06	0.652
	Group B	64.90	3.77	
	Group C	64.53	3.92	
	Total	65.13	4.44	

Table 2: Distribution of THSL, TRSL, MOT and SOT

Variables		Mean	SD	P value
THSL	Group A	13.75	2.06	0.002
	Group B	11.68	2.44	
	Group C	14.54	3.54	
	Total	12.92	2.87	
TRSL	Group A	90.4	13.79	<0.0001
	Group B	81.35	6.77	
	Group C	50.98	3.58	
	Total	74.24	19.19	
MOT	Group A	2.33	0.69	<0.0001
	Group B	1.48	0.51	
	Group C	3.43	0.93	
	Total	2.41	1.08	
SOT	Group A	3.05	0.88	<0.0001
	Group B	2.25	0.63	
	Group C	4.08	1.25	
	Total	3.13	1.21	

*THSL - Time to reach highest sensory level; *TRSL - Two segment regression of sensory level blockade; *MOT - Onset time of sensory block; *SOT – Onset time of sensory block

Table 2: Comparison between groups

Dependent Variables			Mean difference	P value
THSL	Group A	Group B	2.08	0.003
		Group C	-0.79	0.125
	Group B	Group A	-2.08	0.003
		Group C	-2.82	<0.0001
	Group C	Group A	0.79	0.125
		Group B	2.82	<0.0001
TRSL	Group A	Group B	9.05	<0.0001
		Group C	39.43	<0.0001
	Group B	Group A	-9.05	<0.0001
		Group C	30.38	<0.0001
	Group C	Group A	-39.43	<0.0001
		Group B	-30.38	<0.0001
MOT	Group A	Group B	0.85	<0.0001
		Group C	-1.10	<0.0001
	Group B	Group A	-0.85	<0.0001
		Group C	-1.95	<0.0001
	Group C	Group A	1.10	<0.0001
		Group B	1.95	<0.0001
SOT	Group A	Group B	0.8	0.001
		Group C	-1.03	<0.0001
	Group B	Group A	-0.8	0.001
		Group C	-1.83	<0.0001
	Group C	Group A	1.03	<0.0001
		Group B	1.83	<0.0001

*THSL - Time to reach highest sensory level; *TRSL - Two segment regression of sensory level blockade; *MOT - Onset time of sensory block; *SOT – Onset time of sensory block

Table 3: Comparison of the highest sensory level reached among three Groups

Group	HSL					Total	P value
	T2	T3	T4	T5	T6		
Group A	14	0	22	4	0	40	<0.0001
Group B	2	2	20	16	0	40	
Group C	0	0	1	8	31	40	

Table 4: Distribution of DMB and DOA

Variables		Mean	Std. Deviation	P value
DMB	Group A	3.41	.322	<0.0001
	Group B	3.19	.747	
	Group C	1.97	.358	
	Total	2.86	.815	
DOA	Group A	5.15	0.350	<0.0001
	Group B	4.05	.539	
	Group C	2.64	.349	
	Total	4.36	4.702	

*DMB - Duration of Motor block; *DOA - Duration of Analgesia

Table 5: Comparison of DMB and DOA between groups

Dependent Variable			Mean Difference	P value
DMB	Group A	Group B	.214	0.195
		Group C	1.439*	<0.0001
	Group B	Group A	-.214	0.195
		Group C	1.225*	<0.0001
	Group C	Group A	-1.439*	<0.0001
		Group B	-1.225*	<0.0001
DOA	Group A	Group B	1.090	<0.0001
		Group C	2.5	<0.0001
	Group B	Group A	-1.090	<0.0001
		Group C	1.410	<0.0001
	Group C	Group A	-2.5	<0.0001
		Group B	-1.410	<0.0001

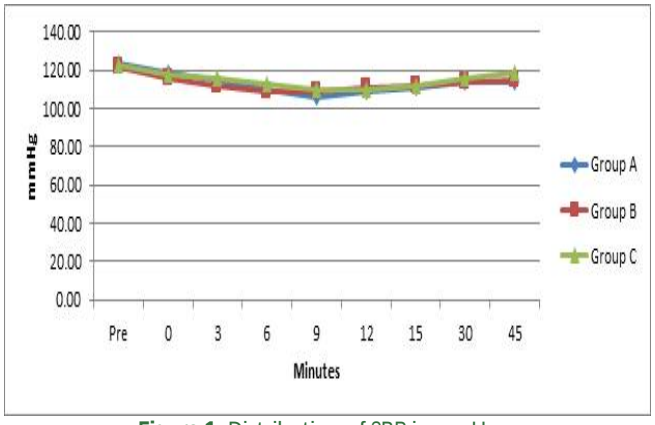

Figure 1: Distribution of SBP in mmHg

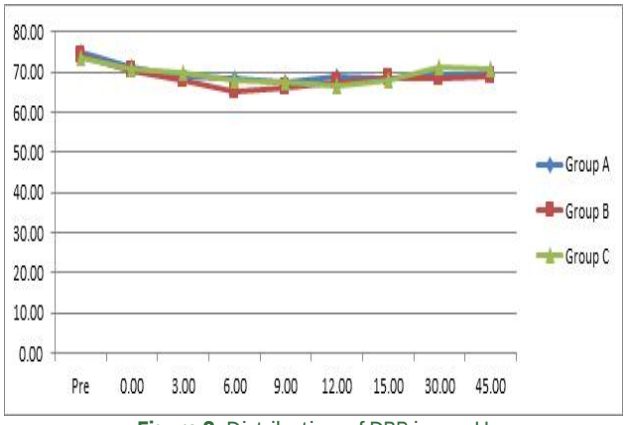

Figure 2: Distribution of DBP in mmHg

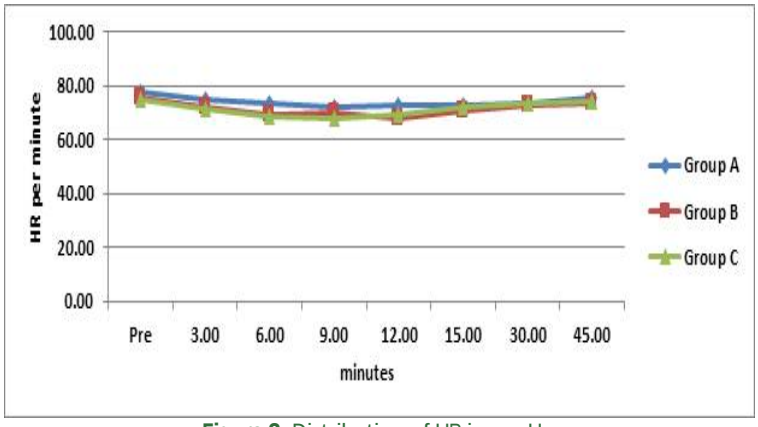

Figure 3: Distribution of HR in mmHg

DISCUSSION

Many researchers have been done so far mainly to improve the quality of subarachnoid block simply by varying drug regimens and technical methods. In order to extend the anaesthetic effects adjuvants are added to 0.5% hyperbaric bupivacaine when given intrathecally. Nalbuphine hydrochloride is both μ antagonist and κ agonist opioid. Nalbuphine extends the effects of local anaesthetics in intrathecal, epidural and also in peripheral nerve blocks and it has minimal respiratory depression and better hemodynamic stability. Various studies had been done using 25mcg of fentanyl added to 0.5% hyperbaric bupivacaine which administered intrathecally for various surgeries, including gynecological surgeries/lower limb surgeries /lower abdominal surgeries/caesarean section and revealed the efficacy and safety of intrathecally given fentanyl. Fentanyl and nalbuphine hydrochloride given intrathecally was in practice over many years and found to be safe and effective and has none urotoxic side effects when used intrathecally. Mukherjee *et al.*[11] performed a study to determine safety and optimal dose of intrathecal Nalbuphine hydrochloride. They concluded that 0.4mg of nalbuphine hydrochloride along with 0.5% hyperbaric bupivacaine significantly extends the duration of postoperative analgesia without any side effects. Hence we used 0.5mg of nalbuphine intrathecally. Early onset and earlier to achieve high sensory level of blockade by fentanyl group may be explained due to high lipid solubility of fentanyl which makes it to cross blood-brain barrier easily and also rapid tissue uptake. Similar result was obtained by the study conducted by Gurunath BB *et al.*[12] in 2018 and study conducted by Ravikiran J Thote *et al.*[13] However the study conducted by Hala Mostafa Gomaa *et al.*[14] concluded that no significant difference was noted between intrathecally given nalbuphine and fentanyl regarding to the sensory blockade. Higher sensory level and more prolongation of two segment regression of sensory blockade by intrathecal nalbuphine than intrathecal fentanyl was concluded by the studies conducted by Ravikiran J Thote *et al.*[13] Gurunath BB *et al.*[12], Shakooh *et al*[15], and by Jyothi B *et al.*[16] Study conducted by Ravikiran J Thote *et al.*[12], and the study conducted by Pallavi Ahluwalia *et al.*[17] concludes similar results. However, Hala Mostafa Gomaa *et al.*[14] concludes that there is no statistically significant difference in the duration of motor blockade between intrathecal nalbuphine and fentanyl. The results that obtained in our study reveals that duration of analgesia is much prolonged by intrathecal nalbuphine than fentanyl. Study conducted by Ravikiran J Thote *et al.*[13] also concludes that intrathecal nalbuphine prolongs the duration of analgesia than intrathecal fentanyl. Shehlashakooh *et al.*[15] study also concludes that sensorimotor blockade and postoperative analgesia was much prolonged with intrathecal nalbuphine group than plain bupivacaine group. Gurunath BB *et al.*[12] Study also concludes that the nalbuphine group had much-prolonged duration of postoperative analgesia than fentanyl group.

CONCLUSION

Comparing between Intrathecal Nalbuphine and Fentanyl concludes that: Intrathecal Nalbuphine may be a good alternative to Fentanyl in surgeries like hernioplasty and in below umbilical surgeries which provides prolonged sensorimotor blockade, and increased duration of analgesia without any adverse effects.

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