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## Review Article

# Efficacy of Intrathecal Nalbuphine Over Fentanyl as Adjuvant with Ropivacaine in Lower Abdominal and Lower Limb Surgeries

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Abstract: Background: Ropivacaine also showed the advantage of lesser motor blockade making it preferable when early mobilization is suggested. This helps to hasten the postoperative recovery [3]. Since its introduction into market in 1996, Ropivacaine has been put to extensive use in epidural, intrathecal and peripheral nerve blocks. Objectives: To measure, compare and analyse the below mentioned parameters at regular intervals among subjects undergoing lower abdominal and lower limb surgeries. Material & Methods: A prospective, randomized, comparative study. The study was conducted in the Department of Anesthesiology, Malla Reddy Institute of Medical Sciences a tertiary care centre in Hyderabad. All the patients who were undergoing the elective lower abdominal and limb surgeries in the department of anesthesiology during the study period. Study consisted of 60 cases. Simple random method. All the patients meeting the inclusion criteria were taken into the study. A pre-designed, pre-tested, semi structured and pre-coded proforma was used for recording all the findings. After obtaining Ethical clearance from the Institutional Ethical Committee, study was conducted. Results: Comparison of the Modified Ramsay Sedation Score between the two groups shows that Modified Ramsay Sedation Score at 30, 120, 150 and 180 mins is higher in GROUP-N and is statistically not significant with a p value of > 0.05. Comparison of the Modified Ramsay Sedation Score between the two groups shows that Modified Ramsay Sedation Score at 60 and 90 mins is higher in GROUP-N and is statistically significant with a p value of < 0.001. *Conclusion*: To conclude, Nalbuphine (500µg) seems to be an attractive alternative to 25µg Fentanyl as an adjuvant to spinal ropivacine in surgical procedures as it provides good quality of intraoperative analgesia, hemodynamically stable conditions, and excellent quality of postoperative analgesia as per our study.

**Keywords:** Nalbuphine, postoperative analgesia, Modified Ramsay Sedation Score.

### Introduction

When spinal anaesthesia was discovered during a miraculous experiment in 1885 by James Leonard Corning, he hardly would have known that it would evolve into one of the most sought-after techniques in the field of anaesthesia. Spinal Anaesthesia was introduced into clinical practice by KARL AUGUST BIER in 1898. It is the most preferred regional anaesthesia technique as it is easy to perform, avoids the problem of a difficult airway, avoids polypharmacy required for general anaesthesia, economical and produces rapid onset of anaesthesia and complete muscle relaxation with less side effects.

The aim of intrathecal local anaesthetics is to provide adequate sensory and motor block necessary for all lower abdominal surgeries. Three decades ago, few patients who were given bupivacaine developed life threatening arrhythmias, which were refractory to treatment. On recognizing this life- threatening cardiotoxicity of bupivacaine, the search for newer, safer local anaesthetic drugs began <sup>[1]</sup>. An important aspect of this cardiotoxicity is that it is related to the stereo specificity of bupivacaine with the 'S' isomer having very less cardio toxic potential compared to the 'R' form <sup>[2]</sup> Ropivacaine and levobupivacaine are the recent local anesthetic drugs that have significantly lower cardiotoxicity compared to bupivacaine

Ropivacaine also showed the advantage of lesser motor blockade making it preferable when early mobilization is suggested. This helps to hasten the postoperative recovery [3]. Since its introduction into market in 1996, Ropivacaine has been put to extensive use in epidural, intrathecal and peripheral nerve blocks [4]. Various adjuvants have been added to Ropivacaine to shorten the onset of block and to augment the clinical efficiency and duration of analgesia.

Fentanyl is an opioid agonist and acts on  $\mu$ -opioid receptors. Nalbuphine is a synthetic opioid analgesic with agonist- antagonist activity and acts as antagonist at  $\mu$ -receptors and agonist at k-receptors to provide reasonably potent analgesia. Nalbuphine, when used as an adjuvant to ropivacaine, has improved the quality of perioperative analgesia with fewer side effects. Nalbuphine has been used intrathecal by various investigators and is found to enhance the postoperative analgesia without any documentation of neurotoxicity. Morphine, fentanyl, and other  $\mu$ -opioids come under narcotics act, thus their free availability is a major concern in many hospitals in India, while nalbuphine is easily available and devoid of side effects such as nausea,

#### Material & methods

**Study Design:** A prospective, randomized, comparative study.

**Study area:** The study was conducted in the Department of Anesthesiology, Malla Reddy Institute of Medical Sciences a tertiary care centre in Hyderabad.

**Study Period:** Jan. 2021 – Dec. 2021.

**Study population**: All the patients who were undergoing the elective lower abdominal and limb surgeries in the department of anesthesiology during the study period.

**Sample size:** study consisted of 60 cases. **Sampling method:** Simple random method.

#### **Inclusion criteria:**

- 1. Patients aged between 18 and 60 years of either gender.
- 2. American Society of Anaesthesiologist (ASA) I &II grade.
- 3. Patients scheduled for elective surgeries.
- 4. Patients who are willing to give an informed written consent.

#### **Exclusion criteria:**

- 1. Patient refusal.
- 2. Patients having cardiovascular disorders, coagulation disorders, spinal deformities, neurological disorders.
- 3. Patients with history of allergy to study drugs.
- 4. Pregnant patients.

**Ethical consideration:** Institutional Ethical committee permission was taken prior to the commencement of the study.

#### Study tools and Data collection procedure:

All the patients meeting the inclusion criteria were taken into the study. A pre- designed, pre-tested, semi structured and pre-coded proforma was used for recording all the findings. After obtaining Ethical clearance from the Institutional Ethical Committee, study was conducted.

After taking informed consent, patients were posted for lower abdominal and lower limb surgeries and fulfilling the inclusion criteria were enrolled for the study. Documents providing information on the proposed study vomiting, pruritus, and respiratory depression with less chances of addiction. Hence the present study was undertaken to analyze the efficacy of intrathecal nalbuphine over fentanyl as adjuvant with ropivacaine in lower abdominal and lower limb surgeries.

**OBJECTIVES:** To measure, compare and analyze the below mentioned parameters at regular intervals among subjects undergoing lower abdominal and lower limb surgeries

- 1. Onset and duration of analgesia
- 2. Motor blockade
- 3. Hemodynamic parameters
- 4. Spo2 (oxygen saturation), respiratory rate
- 5. Postoperative period pain

and form for obtaining consent (consent form) were provided to the patient in the pre-anesthetic clinic. Pre anaesthetic assessment of each patient including detailed medical history such as diabetes mellitus, hypertension, pulmonary tuberculosis, allergy to drugs, bronchial asthma, epilepsy and bleeding disorders will be taken. Clinical examination includes general physical examination and recording of vital data as well as systemic examination of cardiovascular system, respiratory system, gastrointestinal tract, central nervous system and also airway and spine assessment will be done.

All the patients were advised overnight fasting. The following investigations were done: Haemoglobin, Blood cell count RBCs, WBCs & Platelets, Bleeding time and clotting time, Blood urea, Serum creatinine, Serum electrolytes, Blood grouping and Rh typing, Complete urine examination. Patients will be premedicated with injection Ondansetron 4mg and inj. Pantoprazole 40mg IV 1 hr before surgery. The patients were randomly allocated into two groups. The patients were randomly assigned into two groups: (30 in each group)

- Group A (n = 30) Patients received total of 4 ml ROPIVACAINE with 25 mcg FENTANYL
- Group B (n = 30) Patients received total of 4 ml ROPIVACAINE with 500 mcg of intrathecal NALBUPHINE

Before commencement of anaesthesia, patients were explained about the methods of sensory and motor blockade assessments. All patients were explained regarding the visual analogue scale (VAS) scoring system. The VAS consisted of a 10- cm horizontal paper strip with two end points: 0 = no pain and 10 = worst possible pain. Heart rate, Systolic Blood Pressure, Diastolic Blood Pressure, SP02 (Oxygen Saturation) and Respiratory Rate were monitored continuously and were recorded for 1 minute 3 minutes 5 minutes 10 minutes, every 10 minutes for the next 60 minutes and every 30 minutes till the end of surgery. Sedation was assessed by a categorical scale as used by Mostafa et al [5] and graded as: 1 - awake and alert, 2 - awake but drowsy, responding

to verbal stimulus, 3 - drowsy but arousable, responding to physical stimulus, and 4 - unarousable, not responding to physical stimulus. After completion of the surgery the patients were observed in the recovery room till the level

#### **STATISTICAL ANALYSIS:**

Data were analyzed using SPSS version 22.0 analysis between the groups was done using the unpaired sample t-test while within-group analysis was done using the paired sample t-test. Continuous variables were described using mean  $\pm$  standard deviation. Data for

of analgesia wears off to the spinal segment before shifting to the post- operative ward. The VAS score was serially assessed at every 30 min and till the patients complain of pain (VAS score >3)

categorical variables were compared using Chi-square test and Correlation was performed to examine the association between Continuous variables. P<0.05 was considered as significant.

#### **OBSERVATIONS & RESULTS:**

Table 1: Age & sex distribution among study participants

Group								P Value
		FENTA	FENTANYL		NALBUPHINE		Total	
		N	%	n	%	n	%	
Age (in	<=30	5	16.7	7	23.3	12	20.0	0.178
Years)	31 - 40	7	23.3	3	10.0	10	16.7	
	41 - 50	13	43.3	9	30.0	22	36.7	
	>51	5	16.7	11	36.7	16	26.7	
	Total	30	100	30	100	60	100	
Gender	Male	17	56.7	18	60	35	58.3	0.550
Gender	Female	13	43.3	12	40	25	41.7	

Table 2: ASA Grade

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				(	Group					
		FENTANYL		NALBUPHINE		Total				
		n	%	n	%	n	%			
ASA	1	27	90.0	28	93.3	55	91.7			
Grade	2	3	10.0	2	6.7	5	8.3			

**Table 3: Pre OP Vitals** 

Table 5. 11c O1 vitals								
		Group						
	FENTANYL		NALBUF					
	Mean	SD	Mean	SD				
Pre_OP_SBP	131	11	131	11	0.991			
Pre_OP_DBP	78	11	81	9	0.240			
Pre_OP_PR	78	10	79	9	0.722			
Pre_OP_RR	18	2	18	2	0.496			
Pre_OP_SPO2	100	0	100	0	-			
Means were compared using independent sample t test.								

Table 4: Time of onset Sensory and Motor

		Group						
	FENTA	FENTANYL						
	Mean	SD	Mean	SD				
Sensory Time of Onset	57.3	9.3	7.5	2.3	P<0.001			
Sensory Duration	123.6	10.6	150.8	10.1	P<0.001			
Motor Time of Onset	100.7	30.4	19.6	3.1	P<0.001			
Motor Duration	148.7	9.0	188.3	7.2	P<0.001			
Means were compared using independent sample t test.								

Onset of sensory block: Time of onset of Sensory block (sec) is delayed in GROUP F (mean value of Group F=57.3 and Group-N = 7.5) and is statistically significant with a p value of <0.001. Onset of motor block: Time of Onset of Motor block (sec) is delayed in GROUP F (mean value of Group F=100.7 and Group-N = 19.6) and is statistically significant with a p value of <0.001.

**Table 5: SYSTOLIC BLOOD PRESSURE** 

		P Value					
	FENTANYL			NALBUPHINE			
	n	Mean	SD	n	Mean	SD	
SBP_1Min	30	132	12	30	130	11	0.483
SBP_3Min	30	128	13	30	126	12	0.707
SBP_5Min	30	124	15	30	122	13	0.546
SBP_10Min	30	119	13	30	115	12	0.259
SBP_20Min	30	110	14	30	108	11	0.552
SBP_30Min	30	100	15	30	99	8	0.766
SBP_40Min	30	109	11	30	106	8	0.351
SBP_50Min	30	110	10	30	108	9	0.640
SBP_60Min	30	111	13	29	110	9	0.711
SBP_90Min	25	113	13	28	111	7	0.415
SBP_120Min	6	115	24	13	113	6	0.816
Means were compare	ed using indep	endent sample	e t test.				

Comparison of the SBP between the two groups shows that SBP at 0 mins (baseline), 1min, 5min, 10min, 20min, 30min, 40min, 50min, 60min, 90min, 120min, 150min, 180min is higher in GROUP-F and is statistically significant with a p value of < 0.05.

Table 6: DIASTOLIC BLOOD PRESSURE

		P Value					
		FENTANYI	J		NALBUPHINE		
	n	Mean	SD	n	Mean	SD	
DBP_1Min	30	77	10	30	81	9	0.136
DBP_3Min	30	77	10	30	81	9	0.136
DBP_5Min	30	73	9	30	75	7	0.341
DBP_10Min	30	69	9	30	72	8	0.120
DBP_20Min	30	67	8	30	71	8	0.122
DBP_30Min	30	64	8	30	67	7	0.241
DBP_40Min	30	65	6	30	67	6	0.223
DBP_50Min	30	65	5	30	67	6	0.273
DBP_60Min	28	66	5	29	67	6	0.328
DBP_90Min	23	67	6	28	68	6	0.377
DBP_120Mi	4	72	8	13	70	6	0.536
n							
Means were comp	ared using	independent	sample t tes	t.			•

Comparison of the DBP between the two groups shows that DBP at 0 (baseline), 1min, 5min, 10min, 20min, 30min, 40min, 50min, 60min and 90min mins is higher in GROUP F and is statistically not significant with a p value of > 0.05. Comparison of the DBP between the two groups shows that DBP at 120 mins is higher in GROUP N and is statistically not significant with a p value of > 0.05

**Table 7: MEAN ARTERIAL PRESSURE** 

		P Value					
	I	FENTANYL			NALBUPHINE		
	n	Mean	SD	n	Mean	SD	
MAP_1Min	30	96	9	30	97	8	0.430
MAP_3Min	30	94	9	30	96	8	0.352
MAP_5Min	30	90	9	30	91	8	0.769
MAP_10Min	30	85	8	30	87	7	0.601
MAP_20Min	30	82	8	30	83	7	0.418
MAP_30Min	30	76	8	30	77	7	0.495
MAP_40Min	30	80	6	30	80	5	0.742
MAP_50Min	30	80	4	30	81	6	0.598
MAP_60Min	30	78	11	29	82	5	0.116
MAP_90Min	25	79	11	28	82	5	0.104
MAP_120Min	6	70	22	13	84	5	0.037
Means were compa	ared using ind	ependent sam	ple t test.	•	•		•

**Table 8: Post OP Vitals** 

		P Value						
	FENT	FENTANYL		JPHINE				
	Mean	SD	Mean	SD				
Po_SBP_1MIN	100	15	99	8	0.766			
Po_SBP_30MIN	124	15	122	13	0.546			
Po_DBP_1MIN	65	6	67	6	0.223			
Po_DBP_30MIN	77	10	81	9	0.136			
Po_MAP_1MIN	77	7	78	6	0.568			
Po_MAP_30MIN	93	9	94	9	0.446			
Po_HR_1MIN	73	11	73	8	0.871			
Po_HR_30MIN	75	10	76	9	0.783			
Po_RR_1MIN	17	2	17	2	0.714			
Po_RR_30MIN	17	2	17	2	0.443			
Po_SPO2_1MIN	100	0	100	0	-			
Po_SPO2_30MIN	100	0	100	0	-			
Means were compared using independent sample t test.								

TABLE 9: COMPARISON OF MODIFIED RAMSAY SEDATION SCROTE BETWEEN TWO GROUPS

	Group	N	Mean	Std. Deviation	P Value
RS 30 Min	Nalbuphine	30	2.20	.610	0.078
	Fentanyl	30	2.00	.000	
RS 60 Min	Nalbuphine	30	3.10	.305	< 0.001
	Fentanyl	30	2.00	.000	
RS 90 Min	Nalbuphine	30	3.37	.490	< 0.001
	Fentanyl	30	2.20	.407	
<b>RS 120 Min</b>	Nalbuphine	30	2.20	.610	0.605
	Fentanyl	30	2.13	.346	
RS 150 Min	Nalbuphine	30	2.10	.305	0.309
	Fentanyl	30	2.03	.183	
RS 180 Min	Nalbuphine	30	2.10	.305	0.309
	Fentanyl	30	2.03	.183	

Comparison of the Modified Ramsay Sedation Score between the two groups shows that Modified Ramsay Sedation Score at 30, 120, 150 and 180 mins is higher in GROUP-N and is statistically not significant with a p value of > 0.05. Comparison of the Modified Ramsay Sedation Score between the two groups shows that Modified Ramsay Sedation Score at 60 and 90 mins is higher in GROUP-N and is statistically significant with a p value of < 0.001.

TABLE 10: COMPARISON OF VAS AMONG THE TWO GROUPS STUDIED

	Group	N	Mean	P Value
VAS 30 mins	Nalbuphine	30	.00	1
	Fentanyl	30	.00	1
VAS 60 mins	Nalbuphine	30	.00	1
	Fentanyl	30	.00	1
VAS 90 mins	Nalbuphine	30	.00	<0.001
	Fentanyl	30	.92	< 0.001
VAS 120 mins	Nalbuphine	30	.37	<0.001
	Fentanyl	30	1.95	< 0.001
VAS 180 mins	Nalbuphine	30	1.26	<0.001
	Fentanyl	30	2.76	< 0.001
VAS 240 mins	Nalbuphine	30	2.41	<0.001
	Fentanyl	30	3.63	< 0.001
VAS 300 mins	Nalbuphine	30	3.42	<0.001
	Fentanyl	30	4.67	< 0.001

Comparison of the Visual Analogue Scale between the two groups shows that Visual Analogue Scale at 30 and 60 mins is ZERO in both the groups and is statistically not significant with a p value of 1. Comparison of the Visual Analogue Scale between the two groups shows that Visual Analogue Scale at 90, 120, 180, 240 and 300 mins is higher in GROUP- F and is statistically significant with a p value of < 0.001.

#### **DISCUSSION:**

Spinal anaesthesia is the most frequently used regional anaesthesia technique as it is easy to perform, produces rapid onset of anaesthesia and complete muscle relaxation and is also economical. These advantages are sometimes offset by a relatively short duration of action and postoperative pain is an issue as well. The aim of Intrathecal local anaesthetic is to provide adequate sensory and motor block necessary for all lower abdominal surgeries. Local anaesthetics work by inhibiting voltage-gated sodium channels in the spinal cord by interfering with afferent and efferent sensory and motor impulses while Intrathecal Opioids activate opioid receptors in the dorsal grey matter of the spinal cord (substantia gelatinosa) to modulate the function of afferent pain fibres.

The combination of adjuvants to local anaesthetic is synergetic for producing the analgesia of prolonged duration without measurably increasing sympathetic or motor blockade, thus allows early ambulation of patients and reduction in dosages of local anaesthetics, hence the decline of their systemic side effects. Opioids selectively decrease nociceptive input from A delta and C fibres without affecting dorsal root axons or somatosensory-

evoked potentials. Various µ- agonists of opioids such as Morphine, tramadol, and Fentanyl are used as adjuvants to ropivacaine to prolong its clinical efficacy, improve the quality and minimize the requirement of postoperative analgesics, but they are associated with side effects of pruritus, nausea, vomiting, respiratory depression, constipation, and urinary retention. Fentanyl, a lipophilic opioid agonist, when used as an adjuvant, prolongs the duration of spinal anaesthesia. Intrathecally, Fentanyl exerts its effect by combining with opioid receptors in the dorsal horn of spinal cord.

Nalbuphine, agonist-antagonist, is a synthetic highly lipid-soluble opioid analgesic and possess an agonist action at the k-opioid receptor and antagonist action at the μ-opioid receptor to provide reasonably potent analgesia of visceral nociception. It has the potential to maintain or even enhance μ-opioid-based analgesia while simultaneously mitigating the μ-opioid side effects. Intrathecal Fentanyl is used commonly with heavy Ropivacine for spinal and epidural anaesthesia by many researchers. Yu et al <sup>[6]</sup> 2021 Nalbuphine as additives to local anesthetics can significantly prolong the two segments of sensory block and the average

duration of analgesia without increasing the incidence of adverse.

We conclude that Nalbuphine as additives to Ropivacaine significantly prolongs the two segments of sensory block. Contino et al [7] in 2021 Ropivacaine shows a clear advantage for spinal anesthesia during THA when considering rapid recovery. Its use should be strongly considered, especially in the ambulatory setting. We conclude that Ropivacaine shows a clear advantage for spinal anesthesia during THA when considering rapid recovery. Mavaliya et al [8] in 2020 concluded that nalbuphine significantly prolongs the duration of sensory block, duration of motor block, and duration of postoperative analgesia in comparison to fentanyl, when used as an intrathecal adjuvant to 0.75% ropivacaine in elective orthopedic lower limb surgeries, with minimal adverse effects. Our study concluded the same. Borah et al [9] in 2018 studied that Intrathecal nalbuphine can be a good adjuvant to subarachnoid block as it can prolong both sensory and motor blockade with minimal side effects. From our study, we can infer that when compared with 1.6 mg nalbuphine, both 0.4 and 0.8 mg nalbuphine can be used safely intrathecally with isobaric 0.75% ropivacaine in elective lower limb surgery as they both provide prolonged analgesia and a reliable motor block with equal efficacy but with lesser side effects. The same result was seen in this study.

Seetharam et al [10] in 2015 studied that the addition of fentanyl to ropivacaine significantly prolongs the duration of postoperative analgesia with clinically insignificant influence on hemodynamics and motor blockade with minimal side effects. Jagtap et al [11] in 2014 Intrathecal Ropivacine Fentanyl provides satisfactory anaesthesia with haemodynamic stability for major lower limb orthopaedic surgery. It provides similar sensory but shorter duration of motor block compared to BF which is a desirable feature for early ambulation, voiding, and physiotherapy. Our study shows Nalbuphine was alternative to fentanyl for prolonging duration of postoperative analgesia.

#### **CONCLUSION:**

To conclude, Nalbuphine (500µg) seems to be an attractive alternative to 25µg Fentanyl as an adjuvant to spinal ropivacine in surgical procedures as it provides good quality of intraoperative analgesia, hemodynamically stable conditions, and excellent quality of postoperative analgesia as per our study.

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