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Comparative study between intrathecal Nalbuphine and fentanyl as an adjuvant to Levobupivacaine in lower abdominal and lower limb surgeries

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ABSTRACT:
Background: Levobupivacaine has become popular for central neuraxial blocks in this century. The main advantage includes ease of technique and reliability. Nalbuphine is one of the synthetic Efficacy of Nalbuphine as an adjuvant to Levobupivacaine in spinal anaesthesia has not been strongly evidenced. In order to gain more evidence on this indication, this study was performed with the following objectives. **Objectives:** To compare the time of onset of sensory blockade, the height of sensory blockade, motor blockade as per Bromage scale, total duration of sensory blockade and motor blockade. **Methods:** A Randomized Controlled trail was conducted at Department of Anesthesiology At sri Siddhartha medical college for a period of 18 months among 81 subjects divided in to 3 groups by randomization. Patients in group FL received 3 ml of 0.5% Levobupivacaine with 25 µg of fentanyl. Patients in group NL received 3 ml of 0.5% Levobupivacaine with 800µg of Nalbuphine. Patients in Group L received 3ml of 0.5% Levobupivacaine alone. **Results:** In the study there was no significant difference in age, gender, ASA grade and anthropometric parameters b/w 3 groups. Vital parameters were within the normal range in all the 3 groups. Duration of Motor Block (2.29 ± 0.05 hrs), Duration of analgesia (4.64 ± 0.31 hrs) was significantly high for Group NL. Onset of Sensory (3.44 ± 0.89 min) and Motor block (3.96 ± 0.71 min) was faster in Group FL. There was significant difference in Time of onset of sensory blockade, the height of sensory blockade, motor blockade as per Bromage scale, total duration of sensory blockade, motor blockade between three groups. There was no significant difference in side effects b/w 3 groups. **Conclusion:** From the study it was concluded that Group NL had longer Duration of Motor Block and Duration of analgesia. Group FL had faster Onset of Sensory and motor block. Hence Nalbuphine and fentanyl as an adjuvant to Levobupivacaine had better response compared to Levobupivacaine alone.

KEYWORDS: Nalbuphine, Fentanyl, Levobupivacaine, Adjuvant, Intrathecal

I. INTRODUCTION :

In 1979, Wang and his colleagues first used intrathecal opioids for acute pain treatment. Since then, intrathecal opioid is widely used to increase the quality of Intraoperative anaesthesia, prolong the postoperative analgesia, traumatic and chronic cancer pain. Administration of intrathecal opioid along with local anaesthetics is to improve the quality of analgesia and to decrease the requirement of postoperative analgesics.[1,2]

Various opioids have been used intrathecally like morphine, fentanyl, buprenorphine and nalbuphine to fasten the onset and prolong the duration of sensory and motor blockade.

Nalbuphine is synthetically prepared opioid. It has both agonist and µ antagonist properties.[3] When given intrathecally it binds to kappa receptors in the spinal cord and brain. It produces analgesia and sedation via kappa receptors and hence there is no adverse effects mediated by µ receptors. Side effects like shivering, nausea, vomiting and urinary retention are infrequent with nalbuphine hydrochloride. Nalbuphine reaches ceiling effect at lower intrathecal dosage and so no need to increase the dosage.

Fentanyl is a lipophilic µ receptor opioid agonist. Intrathecal fentanyl as adjuvant to local anaesthetic has a rapid onset of action and significantly reduces visceral and somatic pain which have been proved in various studies. Although there are several studies that includes comparison of Nalbuphine and fentanyl as adjuvant, there is no particular study in patients undergoing Lower limb Surgery.[4,5]

Levobupivacaine has become popular for central neuraxial blocks in this century. The main advantage includes ease of technique and reliability. Nalbuphine is one of the synthetic Opioid analgesics with agonist–antagonist activity and acts as agonist at κ receptors to provide potent analgesia and antagonist at µ receptors. Efficacy of Nalbuphine as an adjuvant to Levobupivacaine in spinal anaesthesia has not been strongly evidenced. In order to gain more evidence on this indication, this

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study was performed with the following objectives. [6,7]

II. OBJECTIVE:

To compare the hemodynamic and post-operative analgesic efficacy of intrathecal nalbuphine with levobupivacaine, intrathecal fentanyl with levobupivacaine and intrathecal levobupivacaine alone.

III. MATERIALS AND METHODS:

A Randomized Controlled trail was conducted at the Department of Anaesthesiology at …… from …….. to ……..

The Sample Size Was estimated by using the difference in Mean Duration of motor block between Group A (receiving 15mg isobaric Levobupivacaine 0.5% (3ml), plus 25mcg Fentanyl) and Group B (received) 15mg isobaric Levobupivacaine 0.5% (3ml) plus 0.8mg Nalbuphine .from the study Ramesh Koppal et. al. [8] as 145.0 ± 4.0 min and 138.8 ± 9.9 min. Using these values at 95% Confidence limit and 80% power sample size of 24 was obtained in each group by using the below mentioned formula and Med calc sample size software. With 10% non-response sample size of 24 + 2.4 ≈ 26.4 = 27 cases will be included in each group. Hence a total of 81 study subjects were enrolled

81 subjects divided in to 3 groups by randomization. Patients in group FL received 3 ml of 0.5% Levobupivacaine with 25 µg of fentanyl. Patients in group NL received 3 ml of 0.5% Levobupivacaine with 800µg of Nalbuphine. Patients in Group L received 3ml of 0.5% Levobupivacaine alone. Time of onset of sensory blockade, the height of sensory blockade, motor blockade as per Bromage scale, total duration of sensory blockade, motor blockade and vital parameters were measured. Institutional ethical clearance was obtained and informed consent was taken prior to the start of the study.

Inclusion criteria:

- Asa I and II aged 18-60 yrs.;
- Patients undergoing elective lower abdominal surgeries;
- Bmi >18.5 to 25kg/m^2
- Patient who has given valid informed consent.

Exclusion criteria:

- Patients with a history of any cardiac or respiratory or cns disease.
- Patients with hepatic or renal dysfunction,
- Patients with gross spinal deformities
- Patients with raised intra cranial pressure
- Patient posted with bleeding diathesis
- Patients with known allergy to test drugs.

IV. METHODOLOGY:

81 ASA I and II patients scheduled for elective lower abdominal surgeries will be selected for study and were allotted into three groups namely Group NL, Group FL and Group L based on randomized number which was obtained by Computerized random number .

Patients in group LF will receive 3 ml of 0.5% levobupivacaine with 25 µg of fentanyl. Patients in group LN will receive 3 ml of 0.5% levobupivacaine with 800µg of nalbuphine. Patients in group L will receive 3ml of 0.5% levobupivacaine alone. total volume made up to 3.5ml with distilled water in all groups.

Vital Parameters, Time of onset of sensory blockade, the height of sensory blockade, motor blockade as per bromage scale , total duration of sensory blockade and motor blockade. Quality of analgesia (visual analogue score), two segment sensory regression time, time to first rescue analgesic and rescue analgesics in 24h was noted in all the groups

Patients will be advised overnight fasting – 6hrs for solids, 4hrs for semisolids and 2hrs for liquids. All patients will be given t. alprazolam 0.5 mg and t. ranitidine 150 mg on the previous night of surgery.

On arrival to operating room, iv line will be cited, and lactated ringer solution will be infused 4–6 ml/kg/I. All patients will be monitored with non-invasive blood pressure (bp), electrocardiograph (ecg), pulse oximeter (spo2) before giving spinal anesthesia.

Under all aseptic precautions after putting the patient in left lateral position, using 25-guage quincke spinal needle, spinal block will be performed at lumbar third and fourth interspace through a midline approach and the patient will be put to supine position.

The time of intrathecal injection is considered as 0.the parameters observed will be pulse rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure. Spo2 and respiratory rate were recorded every 2 min for 10 min and then every 10 min throughout the intraoperative period and at the end of surgery time of onset of sensory blockade, the height of sensory blockade, motor blockade as per bromage scale, total duration of sensory blockade and motor blockade, quality of analgesia (visual analogue score), two-segment sensory regression time, time to

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first rescue analgesic, and number of rescue analgesics in 24 h were also monitored.

The vital signs were recorded at time 0, 2, 5 min, then every 10 min for first hour and half-hourly until the end of surgery.

Chi-square test was used as test of significance for qualitative data. ANOVA (Analysis of Variance) was the test of significance to identify the mean difference between more than two groups for quantitative data. P value <0.05 was considered as statistically significant.

V. RESULTS :

A total of 81 study subjects were divided into three groups based on randomized number into Group NL , Group FL and Group L Respectively . In the study there was no significant difference in age, gender, ASA grade and anthropometric parameters b/w 3 groups. (Table 1) . Vital parameters like SBP, DBP, PR were within the normal range in all the 3 groups. (Table 2, Table 3, Table 4) . Duration of Motor Block (2.29 ± 0.05 hrs), Duration of analgesia (4.64 ± 0.31 hrs) was significantly high for Group NL. Onset of Sensory (3.44 ± 0.89 min) and Motor block (3.96 ± 0.71 min) was faster in Group FL. (Table 5, Table 6). There was significant difference in Time of onset of sensory blockade, the height of sensory blockade, motor blockade as per Bromage scale, total duration of sensory blockade, motor blockade between three groups. There was no significant difference in side effects b/w 3 groups. (Table 7)

Table 1: Profile of subject's comparison between three groups

		Group						P value
		Group NL		Group FL		Group L		
		Mean	SD	Mean	SD	Mean	SD	
Age		50.96	7.77	48.59	8.52	50.33	6.73	0.507
Height in CM		160.33	5.46	159.78	5.85	156.48	21.50	0.516
Weight in KG		61.81	6.50	61.37	7.01	59.22	9.53	0.429
		Group						P value
		Group NL		Group FL		Group L		
		Count	%	Count	%	Count	%	
Sex	Female	21	77.8%	19	70.4%	20	74.1%	0.825
	Male	6	22.2%	8	29.6%	7	25.9%	
ASA	1	23	85.2%	18	66.7%	19	70.4%	0.259
	2	4	14.8%	9	33.3%	8	29.6%	

Table 2: SBP comparison between three groups at different periods of follow-up

SBP	Group						P value
	Group NL		Group FL		Group L		
	Mean	SD	Mean	SD	Mean	SD	
Baseline	123.04	4.13	120.74	6.13	121.63	5.15	0.268
0 Min	118.81	4.91	122.33	5.23	121.93	3.53	0.012*
2 Min	112.67	2.66	113.11	2.50	115.26	3.10	0.002*
5 Min	108.22	3.00	108.52	1.72	110.22	3.11	0.016*
10 Min	104.81	2.90	104.15	1.99	106.00	3.59	0.066
20 Min	106.22	4.05	104.15	1.99	106.00	3.59	0.048*
30 Min	108.44	3.15	108.52	1.72	110.22	3.11	0.031*
40 Min	112.96	2.85	113.11	2.50	115.26	3.10	0.005*
50 Min	121.11	5.30	121.56	5.77	122.96	4.45	0.398

Table 3: DBP comparison between three groups at different periods of follow-up

DBP	Group						P value
	Group NL		Group FL		Group L		
	Mean	SD	Mean	SD	Mean	SD	
Baseline	72.33	6.79	97.48	121.89	74.59	10.24	0.357
0 Min	70.81	6.16	70.89	6.03	75.26	9.56	0.048*
2 Min	68.44	5.93	68.74	6.16	70.37	6.95	0.491
5 Min	65.85	5.65	65.63	5.98	68.07	6.98	0.286

10 Min	60.59	5.32	61.93	5.45	63.63	7.00	0.179
20 Min	61.48	5.34	61.93	5.45	63.63	7.00	0.383
30 Min	66.07	6.19	65.63	5.98	68.07	6.98	0.332
40 Min	68.30	6.07	68.74	6.16	70.37	6.95	0.460
50 Min	72.56	5.67	72.48	8.26	76.22	9.83	0.160

Table 4: PR comparison between three groups at different periods of follow-up

PR	Group						P value
	Group NL		Group FL		Group L		
	Mean	SD	Mean	SD	Mean	SD	
Baseline	75.19	7.62	76.00	10.60	73.74	8.49	0.647
0 Min	73.04	4.38	72.59	6.05	72.30	6.97	0.898
2 Min	72.59	4.19	75.85	6.25	74.48	8.40	0.188
5 Min	72.93	4.25	76.70	6.31	71.81	7.52	0.012*
10 Min	69.85	12.90	79.70	8.09	72.41	4.90	0.001*
20 Min	73.52	3.86	76.59	9.39	73.74	6.11	0.190
30 Min	74.26	2.51	77.19	8.44	75.59	6.98	0.258
40 Min	74.52	3.07	76.44	7.71	75.04	5.96	0.466
50 Min	74.26	3.53	76.67	6.15	77.11	5.27	0.094

Table 5: Highest Sensory Level comparison between three groups

		Group						P value
		Group NL		Group FL		Group L		
		Count	%	Count	%	Count	%	
Highest Sensory Level	T6	16	59.3%	17	63.0%	0	0.0%	<0.001*
	T7	11	40.7%	10	37.0%	16	59.3%	
	T8	0	0.0%	0	0.0%	11	40.7%	

Table 6: Outcome parameters comparison between three groups

	Group						P value
	Group NL		Group FL		Group L		
	Mean	SD	Mean	SD	Mean	SD	
Onset of Sensory block (Min)	4.85	0.91	3.44	0.89	5.85	0.60	<0.001*
Time for Highest Sensory Level (Min)	12.70	0.99	12.04	0.81	14.30	0.61	<0.001*
TSRSL in Min	94.15	3.78	89.85	2.41	89.74	1.93	<0.001*
Onset of Motor block (Min)	5.89	0.70	3.96	0.71	5.44	0.51	<0.001*
Duration of Motor Block (Hours)	2.29	0.05	2.24	0.03	1.96	0.21	<0.001*
Duration of analgesia (Hours)	4.64	0.31	4.28	0.08	2.97	0.27	<0.001*

Table 7: Side effects comparison between two groups

		Group						P value
		Group NL		Group FL		Group L		
		Count	%	Count	%	Count	%	
Side Effects	No	18	66.7%	16	59.3%	23	85.2%	0.278
	Bradycardia	2	7.4%	0	0.0%	0	0.0%	
	Hypotension	1	3.7%	4	14.8%	1	3.7%	
	Nausea	3	11.1%	2	7.4%	1	3.7%	
	Pruritis	0	0.0%	2	7.4%	0	0.0%	
	Shivering	1	3.7%	2	7.4%	1	3.7%	
	Vomiting	2	7.4%	1	3.7%	1	3.7%	

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VI. DISCUSSION:

Extensive research has been done over the years mainly to improve the quality of spinal anaesthesia simply by varying drug regimens and technical methods. Normally to prolong the anaesthetic effects adjuvants are added to hyperbaric bupivacaine 0.5% and given intrathecally. Adjuvants produce antinociceptive effect by acting perineurally or by acting at different receptor sites in the spinal cord.

Adjuvants mainly opioids are capable of producing early onset of sensory and motor blockade and also prolongs the postoperative analgesia. They also have sympathetic and motor sparing activities which allows early ambulation of patients postoperatively.

Mukherjee et al [9] performed a study to determine whether Nalbuphine hydrochloride is safe and whether it helps to prolongs analgesia by comparing it with control group and also to determine the optimum dose of intrathecal nalbuphine was 0.4mg of nalbuphine + 0.5% hyperbaric bupivacaine prolongs the duration of postoperative analgesia without any side effects.

The hemodynamic profile of the subjects in three groups in our study did not showed any significant changes and it was similar to the study findings of Hala Mostafa Gomma et al .[10]

In our study highest sensory level blockade was seen at the level of T 7 in Group NL and Group FL and T 8 in Group L. This was found to be statistically significant between three groups in our study . The Mean duration of Onset of Sensory Block and Time for highest sensory level attained between three groups in our study was found to be statistically significant in our study. Similar findings were also seen in the study done by Gurunath BB et al [11], Ravi Kiran J T et al.[12] Where as in another study done by Hala Mostafa Gomma et al .[10] there was no significant difference between intrathecal nalbuphine and fentanyl regarding to the sensory blockade.

The mean time for high sensory level and More prolongation of two segment regression of sensory block was seen more among Group NL than Group FL and Group L and it was statistically significant . Similae to our study in other studies done by Ravikiran J Thote et al [12], Gurunath B B et al [11] and Shehla Shakooh et al [13] and Jyothi et al [14] also opined that intrathecal nalbuphine had higher sensory blockade and two segment regression block than Fentanyl and control group.

The mean onset of motor block and duration of Motor block was found to be more among the subjects with intrathecal nalbuphine when compared to Fentanyl and control group and the association was found to be statistically significant between the three groups. The findings of our study was found to be similar to the findings of Pallavi A et al [15]and Ravikiran J thote et al[12]. However Hala Mostafa Gomaa et al.[10] concludes that there is no statistically significant difference in the duration of motor blockade between intrathecal nalbuphine and fentanyl.

The duration of Analgesia was found to be more in the nalbuphine group than Fentanyl and control group with significant statistical association . Study conducted by Ravikiran J Thote et al.,[12] also concludes that intrathecal nalbuphine prolongs the duration of analgesia than intrathecal fentanyl. Shehla shakooh,et al.,[13] study also concludes that sensory blockade ,motor blockade and post operative analgesia was much prolonged with intrathecal nalbuphine group than plain bupivacaine 92 group. Mukherjee et al., [9] study concluded that 0.4mg nalbuphine is the most effective intrathecal dose that increases postoperative analgesia with no side effects. Gurunath BB et al.[11] Study also cocludes that the nalbuphine group had much prolonged duration of postoperative analgesia than fentanyl group.

VII. 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 a prolonged sensory and motor blockade, and prolonged duration of analgesia without any adverse effect.

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