ORIGINAL RESEARCH

Comparative Evaluation of Different Doses of Nalbuphine as an Adjuvant in Patients Undergoing Surgery Under Sub Arachnoid Block with 0.5% Hyperbaric Bupivacaine: An Institutional Based Study

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ABSTRACT

Background: The combination of adjuvants to local anesthetic is synergetic for producing the analgesia of prolonged duration without measurably increasing sympathetic or motor blockade. The present study was conducted to compare the different doses of nalbuphine as an adjuvant in patients undergoing surgery under sub arachnoid block with 0.5% hyperbaric Bupivacaine.

Materials&Methods: Patients in Group A received 3 ml of 0.5% hyperbaric bupivacaine with 0.4mg Nalbuphine in 1ml Saline.Patients in Group B received 3 ml of hyperbaric 0.5% bupivacaine with 0.8mg of Nalbuphine in 1ml saline.The patients was observed for onset of sensory blockade; the height of sensory blockade, motor blockade as per bromage scale, total duration of sensory and motor blockade, quality of analgesia, two segment sensory regression time, time to first rescue analgesia and the number of rescue analgesics in 24 hrs. The data was analysed statistically using student t test, Chi-Square test. A P value less than 0.05 was considered statistically significant.

Results: Mean heart rate of patients in the two study groups was found to be statistically non- significant at 40- & 60-minutes time interval. Mean systolic blood pressure of patients in the two study groups was found to be statistically non- significant at 120 minutes time interval. Mean diastolic blood pressure of patients in the two study groups was found to be statistically non-significant at 20-40 minutes and after 60 minutes time interval. Mean blood pressure of patients in the two study groups was found to be statistically non- significant at 10-20 minutes, 50- & 90-minutes time interval. Mean respiratory rate of patients in the two study groups at was found to be statistically significant ($p<0.01$). Mean saturation level of patients in the two study groups was found to be statistically non- significant at 10-40 minutes and post 90 minutes time interval. Mean pain score of patients in the two study groups was found to be statistically non- significant after 90 minutes time interval. Mean Time for Motor Block, Mean duration of surgery between two study groups was found to be statistically significant. Mean time for sensory block between two study groups was found to be statistically non-significant.

Conclusion: The present study concluded that d 0.4 mg can be recommended as the optimal dose of nalbuphine if used intrathecally along with 3ml 0.5% hyperbaric bupivacaine in patientsundergoing various infra umbilical surgeries.

Keywords: Hyperbaric Bupivacaine, Infra Umbilical Surgeries, Intrathecal Nalbuphine

INTRODUCTION

Subarachnoid blockade is a common anesthetic technique for lower abdominal and lower limb surgeries. Adding adjuvant drugs to intrathecal local anesthetics improves the quality and duration of the sensory blockade and prolongs postoperative analgesia.

Intrathecal opioids are synergistic with local anesthetics, thereby intensifying the sensory block without increasing sympathetic block[1], and are the most commonly utilized spinal adjuvants to prolong postsurgical analgesia[2].Among various adjuvants, intrathecal opioid has provided an effective prolongation of postoperative analgesia after orthopedic surgical procedures. [3,4]The combination of adjuvants to local anesthetic 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 anesthetics, hence the decline of their systemic side effects.[5] Nalbuphine is used in almost all types of general and regional anesthetic techniques. Nalbuphine binds to kappa receptors distributed in the spinal cord and brain to produce analgesia. When used as an adjuvant to hyperbaric bupivacaine, it also improves the quality of perioperative analgesia with fewer side effects.[6] It is a mixed synthetic agonist-antagonist, which attenuates the μ-opioid effects and enhances the κ-opioid effects.[7]Nalbuphine is a mixed opioid agonist–antagonist which can prove to be particularly advantageous because of the potential to maintain or even enhance opioid-based analgesia while simultaneously eliminating the common μ-opioid side effects (nausea, emesis, pruritis, constipation, undesirable sedation, respiratory depression and the development of tolerance/dependence).[8-10] The present study was conducted to compare the different doses of nalbuphine as an adjuvant in patients undergoing surgery under sub arachnoid block with 0.5% hyperbaric Bupivacaine.

MATERIALS & METHODS

The prospective study was conducted among ninety patients admitted to Department ofAnaesthesiology, Heritage Institute of Medical Sciences,Bhadvar, Varanasifor elective surgery undergoing various infra umbilical surgery from year 2020 to 2022.American Society of Anaesthesiologists (ASA) I and II patients, age group of 15-55 years, patient with written valid consent, patient undergoing elective lower abdominal and orthopedic surgery were included in the study.Infection at the site, cardiac arrhythemias, heart blocks, bradycardia, allergic reaction to any anesthetic drug, ASA III and IV grade, patients with bleeding disorders, head injury, raised intracranial pressure were excluded from the study.The patients were allocated in two groups of 45 patients each.

- **Group A**: Receiving 0.4 mg nalbuphine in 1ml NS with 3ml 0.5% Hyperbaric Bupivacaine
- **Group B**: Receiving 0.8 mg nalbuphine with 1ml NS with 3ml 0.5% Hyperbaric Bupivacaine

Patient was premedicated with tablet alprazolam 0.25mg and tablet ranitidine 150mg orally the night before surgery and fasted for 6-8hours before procedure of spinal anesthesia.On the day of surgery after securing intravenous (18G) access in dorsum of the left hand, all the routine monitor was attached, patient was preloaded with Ringer's lactate solution 15 ml/kg over 10 min.Under all aseptic precautions after putting the patient in sitting position, using 25-guage Quincke spinal needle, spinal block was performed at lumbar third and fourth interspace through a midline approach and the patient was put to supine position after giving the drug. Patients in Group A received 3 ml of 0.5% hyperbaric bupivacaine with 0.4mg Nalbuphine in 1ml Saline.Patients in Group B received 3 ml of hyperbaric 0.5% bupivacaine with 0.8mg of Nalbuphine in 1ml saline.The time of intrathecal injection was considered as 0.SpO2, respiratory rate, pulse rate, blood pressure was recorded at 0, 5min, then every 10min for first hour and then every half hourly until end of surgery. The patients was observed for onset of sensory blockade; the height of sensory blockade, motor blockade as per bromage scale, total duration of sensory and motor blockade, quality of analgesia{visual analogue score},two segment sensory regression time, time to first rescue analgesia and the number of rescue analgesics in 24 hrs. The data was analysed statistically using student t test, Chi-Square test. A P value less than 0.05 was considered statistically significant.

RESULTS

After 10 minutes and further time intervals of follow up, it was observed that like at 60 minutes time interval the mean heart rate for group A (69.70±5.32) was lower than group B (72.5±5.93), similarly at other time intervals the difference was found to be statistically significant($p<0.01$), except at 40- & 60-minutes time interval($p>0.05$).After 5 minutes and further time intervals of follow up, it was observed that like at 60 minutes time interval the mean systolic blood pressure for group A(112.43±5.65mm/Hg) was lower than group B (99.5±5.21mm/Hg), similarly at other time intervals the difference was found to be statistically significant($p<0.01$), except at 120 minutes time interval($p=0.292$).At pre op the mean diastolic blood pressure for group A(75.5±6.78 mm/Hg) was lower in comparison of group B(92.1±8.49 mm/Hg) and also at further time intervals of follow up, the difference was found to be statistically significant($p<0.01$), except at 20-40 minutes and after 60 minutes time interval ($p>0.05$).At pre op the mean mean blood pressure for group A(90.82±6.44 mm/Hg) was lower in comparison of group B(94.82±6.31mm/Hg) and also at further time intervals of follow up, the difference was found to be statistically significant($p<0.01$), except at 10-20 minutes50 & 90 minutes time interval ($p>0.05$).It was observed that like at 60 minutes time interval the mean respiratory rate for group A(17.17±2.0) was higher than

group B (12.9±1.5), similarly at all time intervals the difference was found to be statistically significant($p<0.01$).It was observed that like at 60 minutes time interval the mean SPO2 for group A(100.0±0.0) was slightly higher than group B (99.6±0.81), similarly at all time intervals and the difference was found to be statistically significant($p<0.01$) except at 10-40 minutes and post 90 minutes time interval($p>0.05$).It was observed that like at 60 minutes time interval the mean SPO2 for group A (0.73±0.78) was lower than group B (0.3±0.65), similarly at all time intervals and the difference was found to be statistically significant ($p<0.01$) except after 90 minutes time interval ($p>0.05$).In group A rescue analgesia was not given to any patient whereas mean time for the same in group B was 392±103.70 minutes. The mean time for motor block for group A was 8.27±2.20 minutes whereas for group B, it was found to be 6.4±1.30 minutes, this difference was found to be statistically significant ($p<0.01$). The mean time for sensory block for group A was 4.27±1.41 minutes whereas for group B, it was found to be 4.1±0.84 minutes, this difference was found to be statistically non-significant ($p=0.581$).The mean duration of surgery for group A was 102.17±20.29 minutes whereas for group B, it was found to be 119±27.46 minutes, this difference was found to be statistically significant ($p<0.01$).

Table 1: Comparison of mean heart rate of patients in the two study groups at various time intervals

Time	Group	Mean	Std. Deviation	t test value	p value
Pre-OP	**A**	75.50	6.78	-.113	.910
	B	75.70	6.93		
0 Min	**A**	75.30	5.61	.337	.738
	B	74.10	18.71		
5 Min	**A**	73.00	5.02	-.311	.757
	B	74.10	18.71		
10 Min	**A**	71.17	6.11	-5.065	<0.01*
	B	78.50	5.05		
20 Min	**A**	69.73	4.66	-5.873	<0.01*
	B	77.00	4.92		
30 Min	**A**	70.70	5.96	-3.500	.001*
	B	76.80	7.46		
40 Min	**A**	71.43	7.50	-.587	.560
	B	72.50	6.55		
50 Min	**A**	68.73	5.11	-3.825	<0.01*
	B	74.20	5.93		
60 Min	**A**	69.70	5.32	-1.923	.059
	B	72.50	5.93		
90 Min	**A**	68.70	5.96	-2.121	.038*
	B	72.30	7.13		
120 Min	**A**	68.83	4.45	-10.596	<0.01*
	B	86.00	1.73		

*Statistically significant

Table 2: Comparison of mean systolic blood pressure of patients in the two study groups at various time intervals

Time	Group	Mean	Std. Deviation	t test value	p value
Pre-OP	**A**	129.50	11.39	1.058	.294
	B	126.70	8.96		
0 Min	**A**	124.57	8.19	-1.574	.121
	B	128.30	10.08		
5 Min	**A**	116.00	6.40	-5.642	<0.01*
	B	128.30	10.08		
10 Min	**A**	120.80	4.44	-1.992	.05*
	B	124.20	8.22		
20 Min	**A**	120.13	6.24	3.670	.001*

	B	113.40	7.88		
30 Min	**A**	117.03	6.06	4.005	<0.01*
	B	110.40	6.75		
40 Min	**A**	114.20	5.94	3.723	<0.01*
	B	100.40	19.42		
50 Min	**A**	112.07	5.55	3.680	.001*
	B	105.40	8.23		
60 Min	**A**	112.43	5.65	9.217	<0.01*
	B	99.50	5.21		
90 Min	**A**	110.27	4.96	2.989	.004*
	B	106.50	4.80		
120 Min	**A**	114.67	7.66	-1.098	.292
	B	117.67	2.65		

*Statistically significant

Table 3: Comparison of mean diastolic blood pressure of patients in the two study groups at various time intervals

Time	Group	Mean	Std. Deviation	t test value	p value
Pre-OP	**A**	75.50	6.78	-8.370	<0.01*
	B	92.10	8.49		
0 Min	**A**	73.00	5.02	-6.340	<0.01*
	B	83.40	7.45		
5 Min	**A**	71.17	6.11	-6.953	<0.01*
	B	83.40	7.45		
10 Min	**A**	70.70	5.96	-3.342	.001*
	B	77.20	8.83		
20 Min	**A**	69.70	5.32	-.202	.841
	B	70.00	6.15		
30 Min	**A**	68.70	5.96	.182	.856
	B	68.40	6.80		
40 Min	**A**	71.17	6.11	1.024	.310
	B	69.50	6.48		
50 Min	**A**	75.30	5.61	5.363	<0.01*
	B	68.20	4.59		
60 Min	**A**	68.73	5.11	.390	.698
	B	68.20	5.47		
90 Min	**A**	73.00	5.02	1.444	.154
	B	71.00	5.68		
120 Min	**A**	76.67	8.16	1.524	.151
	B	70.67	7.00		

*Statistically significant

Table 4: Comparison of mean blood pressure of patients in the two study groups at various time intervals

Time	Group	Mean	Std. Deviation	t test value	p value
Pre-OP	**A**	90.82	6.44	-2.429	.018*
	B	94.82	6.31		
0 Min	**A**	88.18	5.84	-6.953	<0.01*
	B	98.22	5.33		
5 Min	**A**	85.50	6.23	-3.774	<0.01*
	B	92.02	7.13		
10 Min	**A**	86.23	5.87	.508	.613
	B	85.51	5.13		
20 Min	**A**	85.34	6.20	1.606	.114
	B	82.72	6.43		

30 Min	**A**	87.12	6.07	2.525	.014*
	B	83.36	5.43		
40 Min	**A**	89.50	4.70	8.063	<0.01*
	B	78.40	5.90		
50 Min	**A**	80.87	6.00	.282	.779
	B	80.48	4.63		
60 Min	**A**	87.42	5.68	4.267	<0.01*
	B	81.33	5.38		
90 Min	**A**	27.63	32.06	-.624	.535
	B	32.92	33.56		
120 Min	**A**	93.33	9.01	-2.654	.010*
	B	99.47	8.91		

*Statistically significant

Table 5: Comparison of mean respiratory rate of patients in the two study groups at various time intervals

Time	Group	Mean	Std. Deviation	t test value	p value
Pre-OP	**A**	17.23	2.03	7.905	<0.01*
	B	13.40	1.71		
0 Min	**A**	17.17	2.78	6.333	<0.01*
	B	13.50	1.53		
5 Min	**A**	16.90	1.88	7.687	<0.01*
	B	13.50	1.53		
10 Min	**A**	16.66	2.30	7.091	<0.01*
	B	13.10	1.47		
20 Min	**A**	17.20	1.90	9.479	<0.01*
	B	13.00	1.51		
30 Min	**A**	16.96	2.19	7.711	<0.01*
	B	13.10	1.60		
40 Min	**A**	17.03	2.19	8.385	<0.01*
	B	12.80	1.69		
50 Min	**A**	17.13	2.34	8.266	<0.01*
	B	12.90	1.54		
60 Min	**A**	17.17	2.00	9.256	<0.01*
	B	12.90	1.54		
90 Min	**A**	17.37	1.99	9.721	<0.01*
	B	12.90	1.54		
120 Min	**A**	16.17	1.83	4.805	<0.01*
	B	12.67	1.00		

*Statistically significant

Table 6: Comparison of mean saturation level of patients in the two study groups at various time intervals

Time	Group	Mean	Std. Deviation	t test value	p value
Pre-OP	**A**	100.00	0.00	3.247	.002*
	B	99.60	0.67		
0 Min	**A**	100.00	0.00	2.693	.009*
	B	99.80	0.41		
5 Min	**A**	100.00	0.00	2.693	.009*
	B	99.80	0.41		
10 Min	**A**	99.87	0.43	.614	.542
	B	99.80	0.41		
20 Min	**A**	99.87	0.43	-1.682	.098
	B	100.00	0.00		
30 Min	**A**	99.90	0.31	-1.795	.078
	B	100.00	0.00		

40 Min	**A**	99.97	0.18	-1<0.01*	.321
	B	100.00	0.00		
50 Min	**A**	99.97	0.18	2.159	.035*
	B	99.70	0.65		
60 Min	**A**	100.00	0.00	2.693	.009*
	B	99.60	0.81		
90 Min	**A**	100.00	<0.01*0	NA	NA
	B	100.00	<0.01*0		
120 Min	**A**	100.00	0.00	1.115	.273
	B	99.70	0.65		

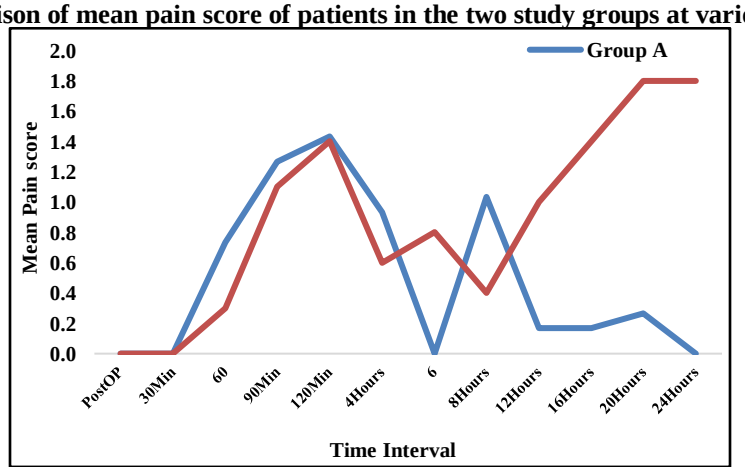
*Statistically significant

Table 7: Comparison of mean time rescue analgesia, motor & sensory block and duration of surgery of patients in the two study groups

Parameter	Group	Mean	Std. Deviation	t test value	p value
Time of rescue analgesia (Min)	**A**	0.00	0.00	NA	NA
	B	392.00	103.70		
Time for Motor Block (Min)	**A**	8.27	2.20	4.004	<0.01*
	B	6.40	1.30		
Time for Sensory Block (Min)	**A**	4.27	1.41	0.555	0.581
	B	4.10	0.84		
Duration of Surgery (Min)	**A**	102.17	20.29	2.701	0.009*
	B	119.00	27.46		

*Statistically significant

Chart 1: Comparison of mean pain score of patients in the two study groups at various time intervals



DISCUSSION

Nalbuphine when binds to μ receptors, competitively displaces other μ antagonists from the receptors without itself displaying any agonistic effect. When it binds to kappa receptors, it has agonistic effect. Hence, it is a mixed agonist-antagonist. It produces analgesia and sedation without μ side effects.[11]Comparison of mean heart rate of patients in the two study groups at various time intervals was found to be statistically significant(p<0.01), except at 40- & 60-minutes time interval(p>0.05). Comparison of mean systolic blood pressure of patients in the two study groups at various time intervals was found to be statistically significant(p<0.01), except at 120 minutes time interval(p=0.292). Comparison of mean diastolic blood pressure of patients in the two study groups at various time intervalswas found to be statistically significant(p<0.01), except at 20-40 minutes and after 60 minutes time interval (p>0.05). Comparison of mean blood pressure of patients in the two study groups at various time intervalswas found to be statistically significant(p<0.01), except at 10-20 minutes50 & 90 minutestime interval (p>0.05). Comparison of mean respiratory rate of patients in the two study groups at various time intervalswas found to be statistically significant(p<0.01). Comparison of mean SPO2 level of patients in the two study groups at various time intervals was found to be statistically

significant($p<0.01$) except at 10-40 minutes and post 90 minutes time interval($p>0.05$).

Nalbuphine exhibits ceiling effect for respiratory depression. Since respiratory depression was predominantly μ receptor-mediated and nalbuphine is a μ receptor antagonist, respiratory depression effect is expected to be attenuated by nalbuphine. Increasing the dosage from 0.8 to 2.4 mg did not cause any respiratory complications. This result correlates that of the studies done by Culebras et al.,[12] Tiwari et al.[13] Culebras et al., who conducted double-blind study in cesarean section with three different doses of nalbuphine 0.2,0.8, and 1.6 mg with 0.5% hyperbaric bupivacaine and compared with intrathecal morphine 0.2 mg with bupivacaine reported no differences were found with respect to maternal oxygen desaturation, Apgar scores, or neonatal umbilical blood gas values. There were no cases of newborn respiratory depression.[12]Khare A et al (2022)aimed to compare the effects of intrathecaldexmedetomidine and nalbuphine as an adjuvant to hyperbaric bupivacaine. Patients in both groups showed no significant difference in haemodynamic changes and incidence of side effects ($P > 0.05$).[14]Comparison of mean pain score level of patients in the two study groups at various time intervals was found to be statistically significant($p<0.01$) except after 90 minutes time interval($p>0.05$). Comparison of mean Time for Motor Block, Mean duration of surgery between two study groups was found to be statistically significant. Comparison of Mean time for sensory block between two study groups was found to be statistically non-significant. Patel, J. et al (2022)compared different doses of intrathecalnalbuphine as an adjuvant to bupivacaine in subarachnoid block in cesarean section. The parturient were randomly divided two groups of 30 each. Inj. Bupivacaine 2ml with Inj. Nalbuphine 0.75 mg (GROUP A) and 1 mg (GROUP B) diluted till 0.5 ml, making a total volume of 2.5 ml. Onset time of motor block was significantly prolonged in group A (3.93±0.59) as compared to group B (3.29±0.46). Duration of absolute analgesia (185.74±4.17) and effective analgesia in Group B (197.25±5.58) is higher as compared to group A, thus number of rescue analgesia required in 24hrs is more in Group A (2.03±0.72) as compared to group B (0.77±0.57).[15]Shah MS et al (2022)designed a study to comparatively evaluate the two different dosages of nalbuphine as intrathecal adjuvants on subarachnoid block (SAB) characteristics of 0.5% hyperbaric bupivacaine. Patients were randomized into three groups: group I received 15 mg of 0.5% hyperbaric bupivacaine, group II received 15 mg of 0.5% hyperbaric bupivacaine with 1.6 mg of nalbuphine, and group III received 15 mg of 0.5% hyperbaric bupivacaine with 2.4 mg of nalbuphine. Results showed that the onset time of the sensory block was 3.2 ± 1.0 minutes, 3.5 ± 1.6 minutes, and 3.1 ± 1.1 minutes in groups I, II, and III, respectively. The onset time of the motor block was 8.5 ± 1.0 minutes, 8.5 ± 1.1 minutes, and 8.2 ± 1.1 minutes in groups I, II, and III, respectively. The onset of sensory and motor blocks was comparable among the three groups with no statistically significant difference ($p > 0.05$). The total duration of analgesia was 117.8 ± 23.3 minutes, 166.8 ± 27.8 minutes, and 181.8 ± 25.9 minutes in groups I, II, and III, respectively, with a statistically significant difference. Few incidences of manageable hypotension, but no incidences of bradycardia or respiratory insufficiency, occurred. Five patients of the control group shivered, which was managed well by tramadol 50 mg and ondansetron 4 mg.[16]

CONCLUSION

The present study concluded that Intrathecalnalbuphine prolongs the duration of postoperative analgesia when used as an adjunct, and 0.4 mg is the most effective dose that prolongs early postoperative analgesia without increasing the risk of side-effects. We recommend 0.4 mg as the optimal dose of nalbuphine if used intrathecally along with 3ml 0.5% hyperbaric bupivacaine in patients undergoing undergoing various infra umbilical surgeries.

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