Original Article

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Anaesthesia Section

Effect of Different Doses of Intrathecal Nalbuphine as Adjuvant to Hyperbaric Bupivacaine on Characteristics of Subarachnoid Block in Pelvic and Lower Limb Orthopaedic Surgeries: A Randomised Clinical Study

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ABSTRACT

Introduction: Hyperbaric bupivacaine 0.5% is most commonly used amide local anaesthetic drug in spinal anaesthesia. Various additives have been used as an adjuvant to hyperbaric bupivacaine 0.5% to modify its anaesthetic properties. Nalbuphine, a mix opioid with high efficacy kappa receptors agonism has also been used as an adjuvant to hyperbaric bupivacaine 0.5% at different doses.

Aim: To compare and discover the effective dose of nalbuphine as adjuvant in subarachnoid block with hyperbaric bupivacaine in pelvic and lower limb orthopaedic surgeries in terms of onset and duration of sensory and motor block along with postoperative analgesia duration.

Materials and Methods: This randomised clinical study was conducted in the Department of Anaesthesia, Shrimati Bhikhiben Kanjibhai Shah Medical Institute and Research Centre (SBKS MIRC), Piparia, Vadodara, Gujarat, India over a period of 18 months from February 2023 to August 2024 on 80 patients belonging to 20-60 years of age, American Soceity of Anaesthesiology (ASA) Grade I or II, of either gender undergoing elective pelvic and orthopaedic surgeries. Patients were randomly divided into two groups having 40 patients each. Group A received hyperbaric bupivacaine 12.5 mg+0.4 mg nalbuphine (total 3 mL) and Group B received hyperbaric bupivacaine 12.5 mg + 0.8 mg nalbuphine (total 3 mL). Sensory and motor block characteristics like their onset time, time to achieve highest sensory level, time to achieve bromage 3, time of two segment regression, duration of sensory and motor block, duration of postoperative analgesia and time for requirement of first rescue analgesia dose were observed and assessed. Haemodynamic parameters along with intraoperative and postoperative side-effects were also observed.

Results: Both the study groups had similar demographics and haemodynamic parameters. Time of two segment regression of sensory block was significantly longer in Group B (135.25±11.49 min) than A (120.95±16.98 min) with statistically significant prolonged duration of sensory block in Group B (228.25±21.91 min) than A (206.75±15.21 min) ($p<0.0001$). Postoperative analgesia was also prolonged in Group B (294.75±19.15 min) than A (226.19±14.78 min) without significant increase the incidence of side-effects ($p\geq0.05$).

Conclusion: Study concluded that 0.8 mg nalbuphine as an adjuvant to 0.5% hyperbaric bupivacaine in subarachnoid block is more effective dose as it provides prolonged duration of sensory block and postoperative analgesia with good haemodynamic stability and minimal side-effects.

Keywords: Additive, Opioid, Postoperative analgesia, Spinal anaesthesia

INTRODUCTION

International Association for the Study of Pain (IASP) describes pain as "An unpleasant sensory or emotional experience connected with existing or prospective tissue damage, or characterised in terms of such harm." For ages, medical professionals have battled to discover effective solutions for both acute and chronic pain [1]. Early systemic opioid use for pain relief was initially successful but often led to side-effects like nausea, vomiting, respiratory depression, drowsiness, delayed bowel recovery, and hyperalgesia. To mitigate these issues, local anaesthetics have increasingly been used in perineural settings (intrathecal, epidural, and peripheral nerve) to reduce reliance on systemic opioids [2,3].

For lower limb and perineum surgeries, subarachnoid block is often preferred over general anaesthesia due to its safety, effectiveness, and avoidance of airway management issues. It reduces blood loss, venous thromboembolism, metabolic stress, and pulmonary complications, and allows better monitoring of the patient's mental state. It also offers faster onset, improved postoperative pain management, and lower costs compared to general anaesthesia, as it requires fewer drugs [4,5].

The most popular local anaesthetic for subarachnoid block, bupivacaine, has high potency, delayed onset of action, and a comparatively shorter duration of postoperative analgesic effect with dose ranging from 12 to 15 mg. It acts via binding intracellularly to voltage-gated sodium channels and thus blocking sodium influx into neurons and preventing depolarisation and subsequent initiation or propagation of a pain signal. Its systemic absorption is dependent on dosage and route of administration [6,7]. Due to its shorter duration action, various adjuvants have been added to local anaesthetics which helps to decrease the dose of local anaesthetics, improves quality and prolongs the duration of subarachnoid block with decreased toxicity and related complications. The commonly used adjuvant are opioids like morphine, fentanyl, buprenorphine and nalbuphine, α-2 receptor agonists like clonidine and

dexmedetomidine, N-methyl D-asparate (NMDA) receptor blocker such as ketamine & Gamma-aminobutyric Acid (GABA) receptor modulator such as midazolam [8-10].

Nalbuphine is a synthetic opioid that simultaneously stimulates κ and μ receptors. It enhances postoperative analgesia and prolongs pain relief when combined with local anaesthetics, offering effective pain management with minimal adverse effects. Unlike morphine and fentanyl, which are μ-receptor agonists, nalbuphine does not only agonise/antagonise μ receptors but acts as an agonist at κ receptors, which are crucial for pain modulation and are widely distributed in the brain and spinal cord. Nalbuphine's mixed agonist-antagonist properties reduce common side-effects like itching, nausea, urine retention, constipation, respiratory depression, and drowsiness [11].

Various studies conducted in past have tested different doses of nalbuphine for effectiveness as an adjuvant to 0.5% hyperbaric bupivacaine but there has been disparity in consensus regarding most effective dose [9,12,13]. So, after extensive literature search, current study has been designed and conducted to find most effective dose of nalbuphine in spinal anaesthesia with minimal side-effects with primary aim of comparing and spinal anaesthesia characteristics in terms of onset and duration of sensory and motor block along with postoperative analgesia duration in pelvic and lower limb orthopaedic surgeries. Secondary aim was to compare haemodynamic changes along with intraoperative and postoperative side-effects if, any.

MATERIALS AND METHODS

The present randomised clinical study was conducted in Department of Anaesthesia, Shrimati Bhikhiben Kanjibhai Shah Medical Institute and Research Centre (SBKS MIRC), Piparia, Vadodara, Gujarat, India. After approval from the Institutional Ethical Committee (SVIEC/ON/MEDI/BNPG21/NOV/22/105), the study was conducted over a period of 18 months February 2023 to August 2024 on patients undergoing elective pelvic and lower limb orthopaedic surgeries. Written and informed consent was obtained from all participants.

Inclusion criteria: Patients with ASA I and II, aged 20-60 years of either gender posted for elective pelvic and lower limb orthopaedic surgeries.

Exclusion criteria: Patients below 20 years or above 60 years, those refusing to participate, those with ASA III or higher, having contraindications to spinal anaesthesia, pregnant, having hepatic, renal, cardiac, or respiratory co-morbidities, bleeding disorders or coagulopathies, allergy to study drugs, seizure disorders, neurological disorders, neuropathies and patients with failed spinal anaesthesia converted to general anaesthesia were excluded from the study.

Sample size calculation: The sample size was calculated using Process Automation Software System (PASS) 15 {National Vital Statistics System (NVSS)}. A crossover pilot study was performed with 15 patients in each group which detected a predicted difference of 30 minutes in mean duration of motor block and postoperative analgesia amongst the two groups with type I error (α) of 0.05 and 0.8 power of study. This resulted in sample size of 76. To minimise the effect of data loss, dropouts (patient refusal or surgery cancellation for any reason) 80 patients (40 patients in each group) were recruited.

Study Procedure

Patients who met the inclusion criteria were divided into the following groups on the basis of randomised computer-generated sequence. Here, both the assessor and patients were blinded to the group allocation with the help of opaque sealed envelope method. Doses of nalbuphine as 0.4 mg and 0.8 mg for the study were derived from the study conducted by Mukherjee A et al., [12].

Group A: A 0.4 mg Inj. nalbuphine 0.5 mL {(0.2 mL taken from 1 mL BD syringe containing 2 mg nalbuphine + 0.3 mL Normal Saline (NS)} with Inj. hyperbaric bupivacaine 0.5% i.e., 12.5 mg (2.5 mL) intrathecally (Total volume=3 mL).

Group B: A 0.8 mg Inj. nalbuphine 0.5 mL (0.4 mL taken from 1 mL BD syringe containing 2 mg nalbuphine + 0.1 mL NS) with Inj. Hyperbaric bupivacaine 0.5% i.e., 12.5 mg (2.5 mL) intrathecally. (Total volume=3 mL).

After routine preoperative examination, investigations, adequate nil per oral status and written and informed consent, patients were shifted to operation theatre. Routine standard monitors were applied and baseline parameters like systolic blood pressure, diastolic blood pressure, pulse rate, respiratory rate and oxygen saturation were noted. Venous access was secured with 18-gauze intravenous cannula and preloading with 10 mL/kg of ringer lactate solution was started over 15-20 minutes.

Subarachnoid block was administered in the sitting position under strict aseptic and antiseptic precautions. Quincke's spinal needle of 25-gauze was inserted into the L3-L4 or L4-L5 intervertebral space. Once free flow of Cerebrospinal Fluid (CSF) flow was established, depending on the assigned study group, the respective drugs were injected intrathecally (2.5 mL of hyperbaric bupivacaine 0.5% and inj. nalbuphine (dose according to the group allocated). Following the injection, the patient was positioned supine and adjusted to achieve a sensory block up to the T6 segment and changes in systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, SpO_2 were noted at 0, 2, 5 minutes then every 10 minutes till 30 minutes and then every 15 minutes till end of the surgical procedure.

Sensory blockade was assessed by pin prick method using hypodermic needle.

- **Onset of sensory block** was defined as time from intrathecal injection to loss of pinprick sensation at L1 dermatome [12].
- **Time of onset of sensory analgesia (T10):** When sensory level reached T10, surgery was allowed to be started [12].
- **Highest level of sensory block** was considered till two consecutive levels of sensory block were same [12].
- **Time interval for two segment regression** was the time period taken to regress sensory blocks by two segments from highest level [12].

Duration of sensory block was time consumed for sensory regression to S2 dermatome [12].

Assessment was done at 2, 5, 10, 20, 30 minutes after injection and then 15 minutes interval till two successive levels of sensory block were same (i.e., level fixation) after which assessment was done every 15 minutes till surgery lasted and every 30 minutes till complete regression of sensory block.

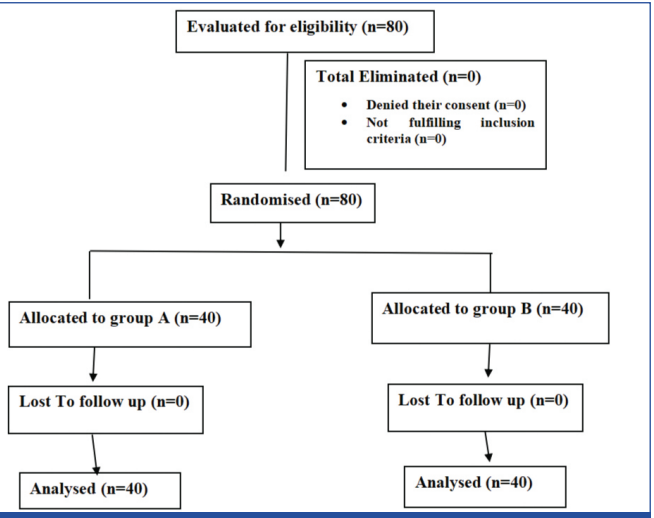
Motor blockade was assessed by Modified Bromage scale [13].

- **Onset of motor block** was defined as time from intrathecal injection to grade 3 motor block.
- **Duration of motor block** was considered as time from intrathecal injection to grade 0 motor block.

Assessment was done at 0, 5, 10, 15, 30 minutes after intrathecal drug injection and then every 15 minutes interval till the surgery lasted and every 30 minutes till complete regression of motor block occurred postoperatively.

- **Duration of rescue analgesia** was defined as time interval from intrathecal injection to the time rescue analgesia was demanded by patient (VAS score ≥4). Visual Analog Scale (VAS) [14] was used to assess intensity of pain. Inj. Diclofenac 75 mg was given for rescue analgesia. VAS score was assessed after shifting patient to postoperative ward half hourly till three hours, hourly till six hours and then at 8th hour and 12th hour.

Side-effects such as nausea, vomiting, hypotension, bradycardia, pruritic, sedation and respiratory depression were recorded and managed with appropriate medications. Hypotension was defined as fall in Systolic Blood Pressure (SBP) to less than 90 mmHg. Bradycardia was defined as decrease in heart rate greater than 20% from the baseline. Respiratory depression was defined as SpO_2 <90% on room air [12]. Intravenous infusion was maintained with Ringer's lactate, 5% dextrose and normal saline. At end of surgery, all patients were shifted to the recovery room and watched for Heart Rate (HR), Blood Pressure (BP), SpO_2 and Respiratory Rate (RR). Duration of sensory and motor block was assessed every 30 minutes till complete regression of both. The Consolidated Standards of Reporting Trials (CONSORT) flow diagram is given in [Table/Fig-1].



[Table/Fig-1]: The Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

STATISTICAL ANALYSIS

Data was collected and processed by Microsoft Excel 2019 (Microsoft® Corp., Redmond, WA). Analysis done using Statistical Package for Social Sciences for Windows, version 22.0 (IBM SPSS, Armonk, NY). Categorical variables were presented as percentage and frequency whereas the continuous variables were displayed as mean±standard deviation. The distribution of categorical variables was compared using either the Chi-square test or Fisher's-exact test. Continuous variables were compared using a student's t-test. A significance level of p-value < 0.05 was used to determine statistical significance.

RESULTS

All patients were able to complete the study without any surgery cancellation or drop outs. Demographic distribution (age, weight and gender), duration of surgery and ASA grading were comparable amongst both the groups and was statistically non significant (p≥0.05) [Table/Fig-2].

Intraoperative HR, SBP, DBP, SpO_2 and respiratory rate during surgery which were comparable amongst both the groups with no statistically significant difference at all time interval (p>0.05) and this has been depicted in [Table/Fig-3-7].

Parameters		Group A Mean±SD	Group B Mean±SD	p-value
Age (years)		39.23±13.25	34.58±10.78	0.0891 (NS)
Weight (kgs)		60.05±8.65	61.83±7.98	0.3417 (NS)
Gender n (%)	Female	31 (77.5%)	30 (75%)	1.0000 (NS)
	Male	9 (22.5%)	10 (25%)	
Duration of surgery (hours)		3.2±0.46	3.4±0.89	0.2787 (NS)
ASA grading n (%)	ASA I	15 (37.5%)	18 (45%)	0.6497 (NS)
	ASA II	25 (62.5%)	22 (55%)	

[Table/Fig-2]: Demographic data distribution comparison.
*p-value <0.05 was considered significant. Chi-square test was used to compare categorical data and student's t-test for continuous data; NS: Non significant

Heart rate	Group A Mean±SD	Group B Mean±SD	p-value
0 min	83.25±7.52	81.95±6.99	0.4257
2 min	81.15±6.73	80.8±7.03	0.7707
5 min	79.4±6.52	78.5±6.62	0.5419
10 min	78.7±5.5	77.7±5.83	0.4324
20 min	79±5.34	78.05±5.86	0.4211
30 min	78.45±5.61	77.55±4.7	0.4391
45 min	77.9±6.14	76.93±4.44	0.4206
60 min	78.2±6.16	77.45±4.27	0.5287
75 min	78.05±6.22	75.8±5.85	0.0996
90 min	77.6±6.05	75.7±5.43	0.1434
105 min	78.12±5.99	75.85±5.1	0.0718
120 min	77.53±6.51	75.79±5.27	0.1927
135 min	77±6.55	75.06±5.47	0.1545
150 min	76.63±7.92	76.65±5.04	0.9893
165 min	79.56±4.56	80±5.42	0.6955
180 min	79.43±5.74	79.8±6.29	0.7842

[Table/Fig-3]: Comparison of intraoperative heart rate.
*p-value <0.05 was considered significant; Student t-test was used for continuous data

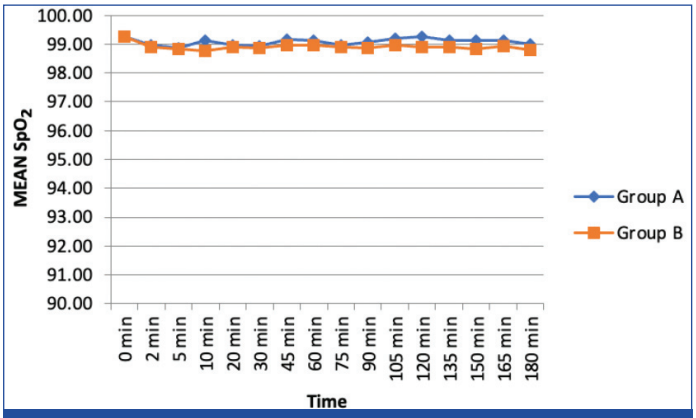
SBP	Group A Mean±SD	Group B Mean±SD	p-value
0 min	125.8±8.71	124.5±10.76	0.5543
2 min	121±8.1	120.85±9.53	0.9397
5 min	114.55±8.03	117±8.78	0.1966
10 min	111.85±7.15	112.6±8.43	0.6690
20 min	110.5±7.47	110.8±7.97	0.8626
30 min	110.7±7.72	109.1±8.24	0.3729
45 min	109.4±8.14	108.35±9.64	0.6001
60 min	110.65±8.63	108.9±9.58	0.3933
75 min	110.7±8.26	110±9.96	0.7332
90 min	110.75±7.7	110.75±8.77	1.0000
105 min	111.65±6.14	113.13±7.41	0.3337
120 min	111.47±6.03	113.85±7.59	0.1245
135 min	111.73±6.51	114.47±6.98	0.0733
150 min	114.38±8.98	116±6.63	0.3615
165 min	114.67±8.6	115.54±5.84	0.5981
180 min	116±7.57	118.2±5.61	0.1438

[Table/Fig-4]: Comparison of intraoperative SBP.
*p-value <0.05 was considered significant; Student t-test was used for continuous data

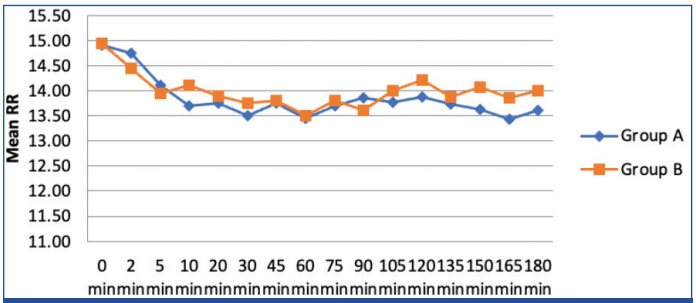
DBP	Group A Mean±SD	Group B Mean±SD	p-value
0 min	77.25±6.65	78.5±7.71	0.4398
2 min	76.9±7.23	76.85±6.97	0.9750
5 min	72.9±7.02	74.8±6.75	0.2209
10 min	73.15±3.65	73.45±6.59	0.7999
20 min	72.23±2.97	71.85±6.44	0.9662
30 min	72.45±2.92	71.2±6.12	0.2367
45 min	72.45±2.99	71.9±6.16	0.8608
60 min	72.6±2.84	72.05±5.56	0.7751
75 min	72.5±3	72.5±6.17	0.7604
90 min	73.25±3.41	73.3±5.93	0.9780
105 min	73.29±3.58	73.74±5.77	0.2377
120 min	73.93±3.91	74.62±6.18	0.1142

135 min	74.18±3.85	74.35±5.94	0.1000
150 min	74.38±3.52	74±5.19	0.6980
165 min	74.29±2.43	74.15±3.11	0.4410
180 min	75.6±4.1	75.2±4.92	0.0551

[Table/Fig-5]: Comparison of intraoperative DBP.
*p-value <0.05 was considered significant; Student t-test was used for continuous data



[Table/Fig-6]: Comparison of intraoperative SpO_2 in both groups.



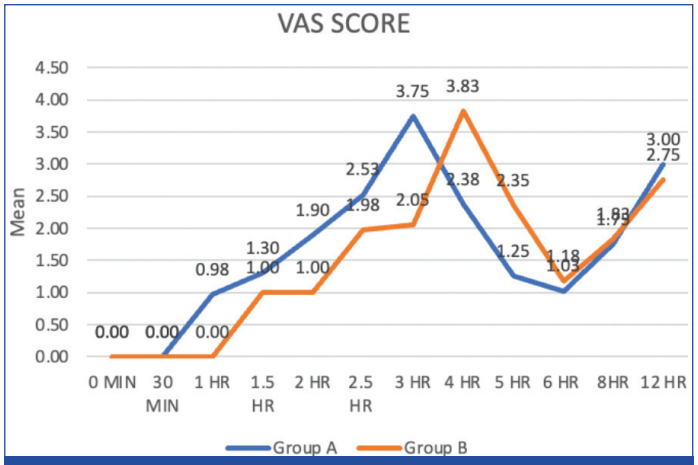
[Table/Fig-7]: Comparison of respiratory rate (per min) in both groups.

Time of onset of sensory and motor block and total duration of motor block was comparable in both groups (p-value=0.1862). While, time of two segment regression of sensory analgesia was longer in Group B (135.25±11.49 min) as compared to A (120.95±16.98 min) which was statistically significant (p-value <0.0001). Total duration of sensory analgesia was significantly longer in Group B (228.25±21.91 min) as compared to A (206.75±15.21 min) (p-value <0.0001). Need for rescue analgesia {Virtual Analogue Scale (VAS) ≥4} was significantly quicker in Group A (226.63±14.78 min) as compared to B (294.75±19.15 min) (p-value<0.0001) [Table/Fig-8].

Parameters (min)	Group A Mean±SD	Group B Mean±SD	p-value
Time of onset of sensory analgesia (L1)	2.58±0.57	2.41±0.57	0.1862 (NS)
Time of onset of sensory analgesia (T10)	5.13±0.61	5.01±0.84	0.4669 (NS)
Time to achieve highest level of sensory analgesia	7.68±0.56	7.58±0.59	0.4392 (NS)
Time of 2 segment regression of sensory analgesia	120.95±16.98	135.25±11.49	<0.0001 (S)
Time of onset of grade 3 motor block	5.61±0.58	5.54±0.69	0.6247 (NS)
Total duration of motor block	173±14.13	175.63±18.89	0.4828 (NS)
Total duration of sensory block	206.75±15.21	228.25±21.91	p<0.0001 (S)
Rescue analgesia (VAS ≥4)	226.63±14.78	294.75±19.15	p<0.0001 (S)

[Table/Fig-8]: Sensory and motor block assessment.
*Time duration recorded in minutes; p-value <0.05 was considered significant; Student t-test was used to compare continuous data; SD: Standard deviation; NS: Non significant; S: Significant

The VAS score was significantly low in Group B in postoperative period after two hours of shifting in postoperative ward till six hours (p-value<0.0001). Later VAS score was less in Group B but was statistically insignificant (p>0.05) [Table/Fig-9].



[Table/Fig-9]: Comparison of postoperative VAS score.
p-value at 2.5, 3, 4, 5 and 6 hours are statistically significant

Parameters	Group A n (%)	Group B n (%)	p-value
Nausea	1 (2.5%)	4 (10%)	0.1685
Vomiting	0	2 (5%)	0.1547
Hypotension	3 (7.5%)	7 (17.5%)	0.1790
Bradycardia	0	2 (5%)	0.3717
Respiratory depression	0	0	-
Sedation	0	0	-
Puritus	0	0	-

[Table/Fig-10]: Postoperative complications.

Seven patients had hypotension in Group B and three patients in Group A which was statistically insignificant and was managed by administering bolus of intravenous fluids and did not require any vasopressor support. None of the patients from both the groups suffered from statistically significant side-effects like nausea, vomiting, bradycardia, respiratory depression, sedation or pruritus at any time interval during the study period [Table/Fig-10].

DISCUSSION

In present prospective randomised clinical study, nalbuphine 0.8 mg added to 0.5% hyperbaric bupivacaine in subarachnoid block for pelvic and lower limb orthopaedic surgeries provided prolonged duration of sensory block and postoperative analgesia with good haemodynamic stability and minimal side-effects as compared to 0.4 mg nalbuphine. In 1991, Rawal N et al., studied behavioural and histopathologic effect following intrathecal administration of butorphanol, sufentanyl and nalbuphine in sheeps and concluded that nalbuphine was least irritating to neural tissue [15]. Large and small doses of nalbuphine that correspond to therapeutic epidural doses, when injected intrathecally appears to be relatively safer than others.

In present study, both the study groups were comparable in terms of demographic profile. There was no statistical difference in onset of sensory and motor blockade, time to reach highest sensory level, bromage 3 and duration of motor blockade. However, addition of 0.8 mg nalbuphine prolonged the duration of sensory blockade delayed two segment regression, prolonged postoperative analgesia and delayed the requirement of first rescue analgesia without any increase in statistically significant side-effects.

Various studies till date have compared different doses of intrathecal nalbuphine as an adjuvant to bupivacaine, a brief summary of those studies are represented in tabular format [Table/Fig-11] [9,12,13,16-24].

Studies which reciprocated results of current study found that 0.8 mg of nalbuphine was effective dose for prolonging postoperative analgesia [13,16-18]. While others found that higher doses of 1-1.6

S. No.	Author's name and year	Place of study	Sample size	Objectives	Parameter assessed	Conclusion
1	Ahmed F et al., [9] 2016	SMS Medical College, Jaipur, Rajasthan	100	Nalbuphine (0.8, 1.6, 2.4 mg vs control) Objective: Postoperative analgesia in abdominal hysterectomy	Sensory: Onset, highest level of sensory blockade, 2 segment regression time, duration of analgesia Motor: onset, duration, VAS, haemodynamic effects, side-effects	1.6 mg nalbuphine better than 0.8, 2.4 mg and control for said objective
2	Mukherjee A et al., [12], 2011	Calcutta National Medical College (CNMC), Kolkata, West Bengal	100	Intrathecal nalbuphine (0.2 mg vs 0.4 mg vs 0.8 mg vs control) Objective: To find optimum dose which prolongs analgesic effect with minimal side-effects.	Sensory: Onset, two-segment regression time, duration of postoperative analgesia. Motor- onset, duration Visual Analogue Scale (VAS) pain score side-effects	0.4 mg nalbuphine better than 0.2, 0.8 mg and control for said objective
3	Mahto S et al., [13], 2018	RIMS, Ranchi	120	Intrathecal nalbuphine 0.8 mg vs control Objective: Postoperative pain relief after lower abdominal surgery	Sensory: Onset, two-segment regression time, duration of postoperative analgesia. Motor- onset, duration Visual Analogue Scale (VAS) pain score side-effects	0.8 mg nalbuphine is safe and effective in providing prompt onset, adequate anaesthesia and prolonged analgesia
4	Ahluwalia P et al., [16], 2015	Teerththanker Mahaveer Medical College and Research Center, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh	70	Intrathecal nalbuphine 0.8 mg vs control Objective: To find optimum dose which prolongs analgesic effect with minimal side-effects in patients of lower abdominal surgeries under spinal anaesthesia	Sensory: Onset, duration of sensory block, postoperative analgesia, Motor: onset, duration blockade VAS, haemodynamic and side-effects	0.8 mg nalbuphine better than control for said objective
5	Jyothi B et al., [17], 2014	Karnataka Institute of Medical Sciences, Hubballi, Karnataka	100	Intrathecal nalbuphine (0.8, 1.6, and 2.4 mg vs control Objective: For postoperative analgesia in lower abdominal and orthopaedic surgeries	Onset of sensory block, Two segment regression time, haemodynamic changes, duration and quality of analgesia, and adverse effects	0.8 mg nalbuphine better than control for said objective
6	Shakooh S and Bhosle P [18], 2014	Bharati Vidyapeeth Deemed University Medical College, Pune, Maharashtra,	60	Intrathecal nalbuphine 0.8 mg vs control Objective: Postoperative pain relief after lower limb and lower abdominal surgeries	Sensory: Onset, two-segment regression time, duration of postoperative analgesia. Motor- onset, duration Visual Analogue Scale (VAS) pain score side-effects	Nalbuphine improves the spinal anaesthesia characteristics of bupicacaine 0.5% when added as additive without major adverse effects.
7	Raut Dessai S et al., [19], 2024	Jawaharlal Institute of Postgraduate Medical Education and Research, Wardha, Maharashtra	60	Nalbuphine 1.5 mg vs bupivacaine alone Objective: Prolongation of Postoperative Analgesia in Endoscopic Urological Surgeries for the	Sensory: Onset, two-segment regression time, duration of postoperative analgesia. Motor- onset, duration side-effects	Nalbuphine 1.5 mg provides faster onset of sensory and motor inhibition, delayed two-segment regression, and prolonged postoperative anaesthesia than bupivacaine alone.
8	Mohan S et al., [20], 2018	Navodaya Medical College, Raichur, Karnataka	60	Nalbuphine 0.8 mg vs 1.4 mg Objective: Postoperative analgesia in lower abdominal and lower limb surgeries	Sensory: Onset, highest level of sensory blockade, 2 segment regression time, duration of analgesia Motor: onset, duration, VAS, haemodynamic and respiratory changes, side-effects	Nalbuphine (1.4 mg) provides prolonged postoperative analgesia without increasing risk of side-effects
9	Gupta K et al., [21], 2017	Base Hospital Delhi Cantt, New Delhi	60	Nalbuphine 1 mg vs control Objective: Postoperative analgesia in lower limb orthopaedic surgery	Sensory: Onset, highest level of sensory blockade, 2 segment regression time, duration of analgesia Motor: onset, duration, VAS, haemodynamic and respiratory changes, side-effects	Nalbuphine 1 mg improves intraoperative analgesia without causing any undue and undesirable side-effects and complications.
10	Shah M S et al., [22], 2022	Hamdard Institute of Medical Sciences and Research, New Delhi	60	Nalbuphine 1.6 mg vs 2.4 mg as intrathecal adjuvants 0.5% hyperbaric bupivacaine.	Sensory: Onset, highest level of sensory blockade, 2 segment regression time, duration of analgesia Motor: onset, duration, VAS, haemodynamic and respiratory changes, side-effects	1.6 mg Intrathecal nalbuphine is better than 2.4 mg
11	Tiwari AK et al., [23], 2013	Sushruta Trauma Centre, Civil Lines, New Delhi	75	Intrathecal nalbuphine 0.2 mg vs 0.4 mg Objective: Prolongation of postoperative analgesia in lower abdominal, urologic and lower limb surgeries	Sensory: Onset, highest level of sensory blockade, 2 segment regression time, duration of analgesia Motor: onset, duration, VAS, haemodynamic and respiratory changes, side-effects	0.4 mg of nalbuphine is effective dose for achieving said objective
12	Singhal D et al., [24], 2018	ASCOMS, University of Jammu, Jammu and Kashmir	90	Nalbuphine 0.4 mg vs 0.8 mg) Objective: Prolongation of postoperative analgesia in Lower Abdominal and Lower Limb Surgeries-	Sensory: Onset, highest level of sensory blockade, 2 segment regression time, duration of analgesia Motor: onset, duration, VAS, haemodynamic and respiratory changes, side-effects	0.4 mg is the most effective dose that prolongs early postoperative analgesia without increasing the risk of side-effects
13	Present study	SBKS MIRC, Piparia, Vadodara, Gujarat	80	Nalbuphine 0.4 mg vs 0.8 mg) Objective: Effect on subarachnoid block characteristics in pelvic and lower limb surgeries	Sensory: Onset, highest level of sensory blockade, 2 segment regression time, duration of analgesia Motor: onset, duration, VAS, haemodynamic and respiratory changes, side-effects	0.8 mg Intrathecal nalbuphine provides most effective prolongation of postoperative analgesia without significant side-effects.

[Table/Fig-11]: Studies on intrathecal nalbuphine [9,12,13,16-24].

mg of nalbuphine provided significant prolongation of postoperative analgesia [9,19-22]. In contrast, few authors found even 0.4 mg of nalbuphine to be effective to improve spinal anaesthesia characteristics of 0.5% bupivacaine [12,23,24].

Intrathecal nalbuphine has also been compared to other opioids and non opioid adjuvants like buprenorphine, fentanyl, dexmedetomidine and morphine [25-28].

Kaushal S et al., and Narra G et al., compared intrathecal nalbuphine 0.8 mg with buprenorphine 60 µg and dexmedetomidine 5 µg respectively and found nalbuphine inferior [25,26]. While Pawar AB et al., and Gupta K et al., compared intrathecal nalbuphine with fentanyl 25 µg, and both found that nalbuphine was better and prolonged postoperative analgesia with minimal complications [27,28].

On comparing sensory block characteristics in current study, onset of sensory block and time to achieve highest level were comparable in both groups while time of two segment regression total duration of sensory blockade, postoperative analgesia and requirement of rescue analgesia were significantly prolonged in Group B. Similar sensory block characteristics were observed by some authors in their respective studies [17,18,24].

When motor block characteristics were compared, it was found that time of onset of Bromage grade 3 motor block, time of return of Bromage grade 0 motor block i.e., duration of motor block was comparable in both groups with no statistically significant difference. Similar observations were made by other authors. Those who compared nalbuphine with control group (Hyperbaric bupivacaine 0.5% alone) [9,12,13,16-19,21] found that nalbuphine significantly quickened the onset of motor block and prolonged the duration of the block. While those who studied different doses of intrathecal nalbuphine [9,12,17,20,22-24] found that there was no statistically significant difference with different doses for onset and duration of motor block.

There was no statistically significant difference in haemodynamic parameters between the two groups during surgery in this study. Similar findings in haemodynamic stability were seen by Raut Dessai S et al., [19]. While Singhal D et al., observed that 0.8 mg intrathecal nalbuphine led to statistically significant hypotension and bradycardia [24]. Overall, in present study, incidences of side-effects like nausea, vomiting were more in Group B than A but was statistically insignificant. None of the patients had pruritus and patients were cooperative and calm throughout the procedure with comparable Ramsay sedation score in both the groups. Supporting present findings, Singhal D et al., also found that incidences of nausea and vomiting were more with 0.8 mg nalbuphine compared to 0.4 mg [24]. While Raut Dessai S et al., did not observe significant side-effects with 1.5mg intrathecal nalbuphine [19].

Respiratory depression was not observed in any patient, probable explanation being the ceiling effect seen with nalbuphine as described by Romagnoli A and Keats AS and Gal TJ et al., [29,30]. Respiratory depression is primarily mediated by action on µ receptors and nalbuphine acts as a µ receptor antagonist, which might explain reduced risk of respiratory depression with nalbuphine. In all the studies mentioned and reviewed where higher dose of nalbuphine was used (from 0.8 to 2.4 mg), none of the patient suffered any respiratory issues.

Limitation(s)

Few limitations of this study are that it lacks a placebo group. As it included only ASA I and ASA II patients, effectiveness and safety of nalbuphine could not be assessed in ASA III and above patients in whom intraoperative haemodynamic stability is crucial. Also, present study was done in a single hospital, thus, its generalisability is confined.

CONCLUSION(S)

The present study concluded that intrathecal nalbuphine is a cost effective, easily available and safe adjuvant to 0.5% hyperbaric bupivacaine in subarachnoid block for pelvic and lower limb orthopaedic surgeries. At a dose of 0.8 mg, it is the more effective in prolonging postoperative analgesia with haemodynamic stability without increasing the risk of side-effects. Future studies can be done to assess effectiveness of nalbuphine at dose suggested by current study as additive in spinal anaesthesia for high risk patients.

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