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Original Article

Anaesthesia Section

Comparison between Intrathecal Hyperbaric Bupivacaine with Nalbuphine and Hyperbaric Bupivacaine with Fentanyl in Infraumbilical Surgeries: A Randomised Clinical Trial

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ABSTRACT

Introduction: Intrathecal adjuvants to local anaesthetics have been introduced to enhance clinical efficacy and prolong the duration of analgesia following infraumbilical surgical procedures, as spinal anaesthesia alone often provides inadequate postoperative pain relief. The addition of intrathecal opioids has been shown to effectively extend postoperative analgesia.

Aim: To compare the efficacy of intrathecal nalbuphine (0.4 mg) vs fentanyl (25 µg) as adjuvants to hyperbaric bupivacaine in infraumbilical surgeries.

Materials and Methods: The present triple-blinded randomised, clinical study was conducted at Dhiraj General Hospital, Vadodara, Gujarat, India, from February 2025 to June 2025. Sixty American Society of Anaesthesiologists (ASA) I-II patients undergoing elective infraumbilical surgeries were randomly allocated into two groups (n=30 each). Group A received bupivacaine (15 mg) with fentanyl (25 µg) and group B received bupivacaine (15 mg) with nalbuphine (0.4 mg) intrathecally. Primary outcomes included onset and duration of sensory/motor blockade and duration of analgesia. Secondary outcomes included haemodynamic parameters, sedation scores, and side-effects. Data were analysed using Statistical Package for Social Sciences (SPSS) version 20.0. Independent Student's t-test was used for continuous variables and Chi-square test for categorical variables. The $p<0.05$ was considered significant.

Results: Both groups had comparable demographic characteristics with no significant differences in age, weight, gender distribution, ASA grading, or surgery duration ($p>0.05$). Onset of sensory (4.07±1.12 vs 6.67±1.01 min, $p<0.001$) and motor blockade (6.73±1.00 vs 7.87±1.20 min, $p=0.009$) was faster in group A. Duration of analgesia was significantly longer in group B (404.76±25.23 vs 291.91±31.87 min, $p<0.001$). Group B required fewer rescue analgesics (2.03±0.95 vs 3.57±0.88, $p<0.001$). Pruritus occurred only in group A (13.3%), while bradycardia (23.3%) and hypotension (26.7%) were higher in group B.

Conclusion: Nalbuphine (0.4 mg) provides superior postoperative analgesia compared to fentanyl (25 µg) as an intrathecal adjuvant, making it an effective alternative for infraumbilical surgeries requiring prolonged pain relief.

Keywords: Local anaesthetic agent, Opioids, Postoperative analgesia, Spinal anaesthesia

INTRODUCTION

Lower limb orthopaedic surgeries are frequently associated with moderate to severe postoperative pain due to extensive tissue dissection, periosteal manipulation, and bone drilling. Effective pain management is crucial for patient comfort, early mobilisation, reducing deep vein thrombosis risk, improving functional outcomes, and shortening hospital stay. Inadequately managed acute postoperative pain can lead to delayed rehabilitation and chronic pain syndromes [1]. Spinal anaesthesia has become the mainstay technique for infraumbilical surgeries due to its rapid onset, reliability, and technical simplicity. Compared to general anaesthesia, it offers reduced metabolic stress response, decreased blood loss, reduced venous thromboembolism, and minimal pulmonary compromise [2]. Bupivacaine is commonly used but provides limited postoperative analgesia. Various adjuvants like opioids (morphine, fentanyl, nalbuphine), alpha 2 agonists (clonidine, dexmedetomidine), N-methyl-D-aspartate (NMDA) receptor antagonists (ketamine) and Gamma-Aminobutyric Acid (GABA) receptor agonists (midazolam) etc; have been added to enhance block quality and duration [3].

Fentanyl, a µ-opioid receptor agonist, enhances sensory blockade but causes pruritus, nausea, and respiratory depression [4]. Nalbuphine, a mixed opioid agonist-antagonist with κ-receptor efficacy and partial µ-antagonist properties, offers a safer alternative with a ceiling effect on respiratory depression [5]. Several studies have demonstrated the efficacy of intrathecal nalbuphine in various surgical settings, but the optimal dose of nalbuphine and its comparative efficacy against fentanyl remains a subject of ongoing research [6,7].

Recent evidence suggests that up to 30% of patients undergoing orthopaedic procedures develop persistent postoperative pain, emphasizing the importance of optimal perioperative analgesia [8]. Gupta K et al., has shown that intrathecal fentanyl doses ranging from 10-25 µg provide effective analgesia with acceptable side-effect profiles [4]. Recent advances in understanding spinal opioid mechanisms have revealed that κ-receptor activation produces analgesia through different pathways than µ-receptors, potentially offering advantages in certain clinical scenarios [9]. The existing literature lacks comprehensive comparisons between nalbuphine and fentanyl as intrathecal adjuvants, particularly evaluating sensory and motor blockade, analgesia, haemodynamic, sedation, Visual Analog Scale (VAS) pain scores, and side-effects, as well as their impact on postoperative recovery in patients undergoing infraumbilical surgeries [10].

The present study aimed to compare the efficacy of intrathecal nalbuphine (0.4 mg) versus fentanyl (25 µg) as adjuvants to hyperbaric bupivacaine in infraumbilical surgeries. The primary outcomes assessed were the duration of sensory block, duration of motor block, and duration of postoperative analgesia. Secondary

outcomes included the onset times of sensory and motor block, haemodynamic parameters, and the incidence of adverse effects.

MATERIALS AND METHODS

The present triple-blinded randomised clinical study was conducted in the Department of Anaesthesiology at Dhiraj General Hospital, SBKS Medical Institute and Research Centre, Vadodara, Gujarat, India after obtaining approval from the Institutional Ethics Committee (IEC No: SVIEC/ON/MEDI/SRP/MAY/25/74) from February 2025 to June 2025. The study was registered with Clinical Trial Registry-India (CTRI/2025/01/079600).

Sample size calculation: Sample size was calculated using the formula: $n = (Z\alpha/2+Z\beta)^2 \times (p_1(1-p_1) + p_2(1-p_2))/(p_1-p_2)^2$ Where $Z\alpha/2 = 1.96$ (95% confidence level), $Z\beta = 0.84$ (80% power). Based on previous studies [10,11] showing 30% difference in duration of analgesia (p_1=0.70, p_2=0.40), as clinically significant with an alpha error of 0.05 and power of 80%, the minimum sample size required was calculated to be 30 patients per group accounting for potential dropouts.

Inclusion criteria: Patients willing to provide written informed consent, with ASA grade I and II of either gender, scheduled for elective infraumbilical surgeries under spinal anaesthesia, aged between 18-60 years, with no known history of allergy to local anaesthetics or study drugs were included in the study.

Exclusion criteria: Patients with contraindication to spinal anaesthesia (patient refusal, increased intracranial pressure, coagulopathy, local site infection, severe spine deformity, severe thrombocytopenia, patients on anticoagulation therapy, haemodynamic instability), non-fasting status, known drug allergy, neurological disorders, ASA physical status grade III-V, significant comorbidities (cardiac, respiratory, or renal), and pregnancy were excluded from the study.

Study Procedure

Study population: Sixty patients of either gender, aged 18-60 years, belonging to American Society of Anaesthesiologists (ASA) physical status I or II, and scheduled for elective infraumbilical surgeries, were enrolled in the study.

Randomisation: Patients were randomly allocated into two groups using the chit (lottery) method [Table/Fig-1]: Computer-generated random numbers sealed in opaque envelopes were utilised to allocate the patients into:

- **Group A (n=30):** Received 3.0 mL (15 mg) of 0.5% hyperbaric bupivacaine with 25 µg (0.5 mL) of fentanyl, total volume 3.5 mL [11].
- **Group B (n=30):** Received 3.0 mL (15 mg) of 0.5% hyperbaric bupivacaine with 0.4 mg (0.04 mL) of nalbuphine and 0.46 mL of sterile normal saline, total volume 3.5 mL [10].

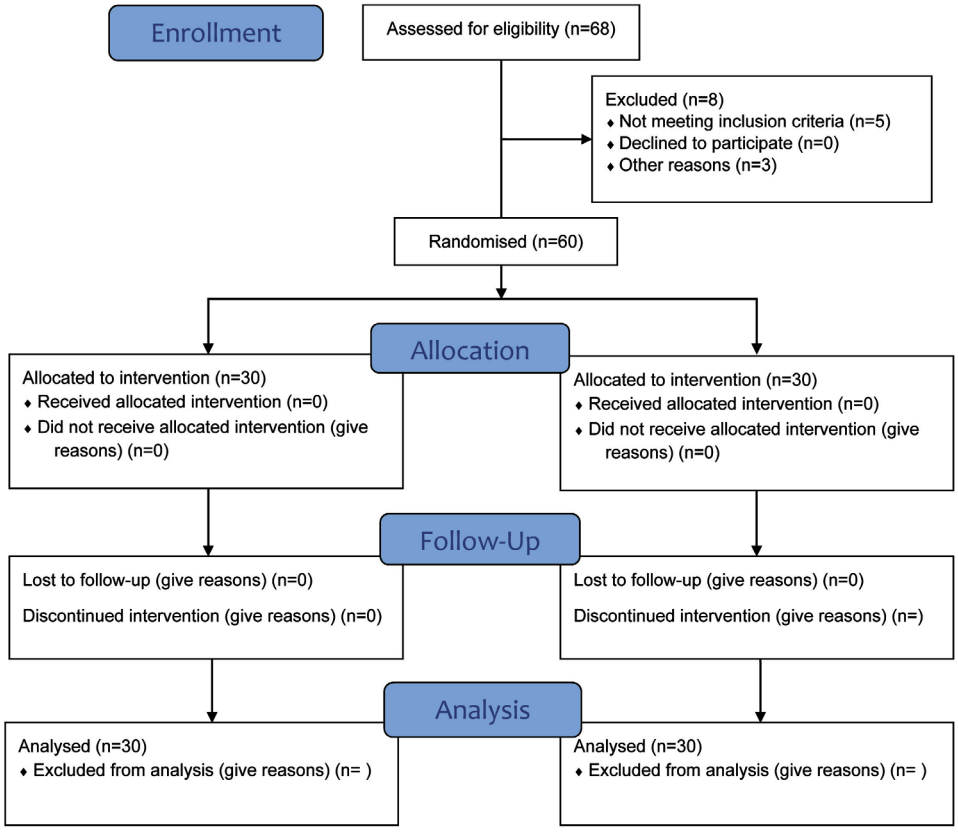
The syringes were prefilled with study drug solution by the main investigator. The Anaesthesiologist performing the block, the observer recording the data and the patients were blinded to the group allocation . The allocation sequence, enrolment and assignment to interventions was performed by the main investigator. The flow diagram of the study is depicted in [Table/Fig-1].

Anaesthetic technique: All patients were kept nil by mouth for at least eight hours before surgery. In the operating room, standard monitors {Electrocardiogram (ECG), non-invasive blood pressure, and pulse oximetry} were attached, and baseline vital signs were recorded. An 18G intravenous cannula was secured, and all patients received premedication with intravenous glycopyrrolate (0.004 mg/kg) and ondansetron (0.08 mg/kg). Patients were preloaded with 10 mL/kg of Ringer's lactate solution before spinal anaesthesia.

With the patient in sitting position, under aseptic conditions, lumbar puncture was performed at the L3-L4 or L4-L5 interspace using a 23G Quincke spinal needle. After confirming free flow of cerebrospinal fluid, the study drug was injected intrathecally according to group allocation. Patients were immediately positioned supine after the injection.

Assessment Parameters

Sensory block assessment: The level of sensory block was assessed by pinprick method using a hypodermic needle at 2, 5



[Table/Fig-1]: CONSORT flow diagram.

minutes after injection and at 5-minute intervals until two consecutive assessments showed the same level (fixation of level), after which assessments were done every 30 minutes.

Motor block assessment: Motor block was assessed using the modified Bromage scale:

- Bromage 0: Able to move hip, knee, and ankle;
- Bromage 1: Unable to move hip, able to move knee and ankle;
- Bromage 2: Unable to move hip and knee, able to move ankle;
- Bromage 3: Unable to move hip, knee, and ankle.

Motor block was assessed at baseline, 5, 10, 15, 30, 45, 60, 90, and 120 minutes after intrathecal injection, and then every 30 minutes until complete motor block regression.

Sedation assessment: Sedation was assessed using the Ramsay sedation scale at every 15 minutes postoperatively till the first dose of rescue analgesia was administered.

Haemodynamic monitoring: Heart rate, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), oxygen saturation, and respiratory rate were recorded at baseline, 2, 5, 10, 20, 30, 45, 60, 75, 90, 120, 150, and 180 minutes, and then every 30 minutes postoperatively until rescue analgesia was administered. Bradycardia (heart rate <60/min) was treated with intravenous atropine 0.6 mg. Hypotension (SBP decrease≥20% from baseline) was treated with intravenous mephentermine 6 mg. Respiratory depression was (defined as respiratory rate≤10 breaths/min or SpO_2 <95%) treated with oxygen 6L/min via facemask.

Pain assessment: Postoperative pain was assessed using the VAS from 0 (no pain) to 10 (worst imaginable pain) at 0, 10, 15, 30, and 60 minutes and then at 30-minute intervals until the patient received rescue analgesia. Duration of analgesia was defined as time from intrathecal injection to VAS score≥4. Rescue analgesia was provided with intravenous diclofenac sodium 75 mg when VAS score reached ≥4.

Side-effects: Adverse effects such as nausea, vomiting, pruritus, hypotension, bradycardia, respiratory depression, and shivering were recorded.

STATISTICAL ANALYSIS

Data were analysed using SPSS version 20.0. Independent Student's t-test was used for continuous variables and Chi-square test for categorical variables. p<0.05 was considered significant.

RESULTS

Both groups were comparable regarding demographic characteristics with no significant differences in age, weight, gender distribution, ASA grading, or surgery duration [Table/Fig-2].

Parameters	Group A (Fentanyl)	Group B (Nalbuphine)	t-value/χ^2	p-value
Age (years)	36.80±9.56	38.47±11.45	0.46	0.65
Sex (Male/Female)	17/13	13/17	0.14	0.71
Weight (kg)	70.13±9.14	67.40±7.72	0.89	0.38
ASA Grade (I/II)	19/11	18/12	0.17	0.68

[Table/Fig-2]: Demographic and baseline characteristics showing comparison of patient demographics between group A (Fentanyl) and group B (Nalbuphine).
Values are presented as mean±SD or numbers. Independent student's t-test (t-value reported) was used for statistical and Chi-square test (χ^2 value reported) for categorical variables p-value: p<0.05* statistically significant

The onset of both sensory and motor blockade was significantly faster in group A compared to group B (p<0.001). Two-segment regression time was significantly longer in group A (p<0.001). However, the duration of sensory blockade was significantly longer in group B, while motor blockade duration was longer in group A [Table/Fig-3].

Parameters	Group A (Fentanyl)	Group B (Nalbuphine)	t-value	p-value
Onset of sensory block at T10 (min)	4.07±1.12	6.67±1.01	8.67	<0.001*
Onset of motor block Bromage 3 (min)	6.73±1.00	7.87±1.20	2.73	0.009*
Two-segment regression (min)	164.60±14.17	142.87±14.58	5.51	<0.001*
Duration of sensory block (min)	200.07±13.08	227.47±18.54	6.16	<0.001*
Duration of motor block (min)	209.67±17.49	186.67±13.78	5.12	<0.001*

[Table/Fig-3]: Characteristics of spinal block comparing spinal block characteristics between group A (Fentanyl) and group B (Nalbuphine).
Values are presented as mean±SD or numbers. (t-value reported) was used for statistical analysis p-value: p <0.001** statistically highly significant; p<0.05* statistically significant

At baseline, all patients in both groups had a motor score of 0. The onset of motor block was significantly faster in group A, as evidenced by higher mean motor scores at 5, 10, and 15 minutes compared to group B (p<0.05). Complete motor blockade (score=3) was achieved by 30 minutes in both groups and maintained up to 90 minutes. Thereafter, regression of motor block commenced earlier in group B, with significantly lower mean motor scores at 120, 180, and 210 minutes (p<0.05), indicating faster motor recovery in group B than in group A [Table/Fig-4].

Time Point	Group A Mean±SD	Group B Mean±SD	t-value	p-value
Baseline	0	0	-	-
5 min	1.23±0.43	0.87±0.35	3.34	0.001
10 min	2.33±0.48	1.87±0.51	3.45	<0.001
15 min	2.97±0.18	2.63±0.49	3.23	0.001
30 min	3.00±0.00	3.00±0.00	-	1.000
45 min	3.00±0.00	3.00±0.00	-	1.000
60 min	3.00±0.00	3.00±0.00	-	1.000
90 min	3.00±0.00	3.00±0.00	-	1.000
120 min	2.67±0.47	2.27±0,52	2.97	0.004
180 min	1.73±0.45	1.27±0.45	3.59	<0.001
210 min	0.87±0.35	0.53±0.51	2.91	0.005

[Table/Fig-4]: Motor Block Progression (Bromage Scale) showing progression of motor block over time in both groups.
Values are presented as mean±SD or numbers. (t-value reported) was used for statistical analysis p-value: p<0.001** statistically highly significant

All patients in group B were adequately sedated (score≥3) compared to group A. Group B showed significantly prolonged analgesia duration (38.7% increase) with reduced rescue analgesic requirements compared to group A. Mean sedation scores assessed at 15-minute intervals were also significantly higher in group B [Table/Fig-5].

Parameters	Group A (n=30)	Group B (n=30)	t-value	p-value
Duration of analgesia (min)	291.91±31.87	404.76±25.23	14.31	<0.001
Time to first rescue analgesia (min)	324.40±31.22	426.35±27.68	12.78	<0.001
Number of rescue analgesics in 24 hours	3.57±0.88	2.03±0.95	6.23	<0.001
Sedation score (Ramsay scale)	3.00±0.68	4.00±0.82	4.89	<0.001

Table/Fig-5]: Analgesia characteristics comparing analgesic efficacy between group A (Fentanyl) and group-B (Nalbuphine).
Values are presented as mean±SD or numbers. (t-value reported) was used for statistical analysis p-value: p<0.001** statistically highly significant

At baseline, there were no significant differences between the two groups with respect to heart rate, SBP, or DBP. Heart rate and SBP remained comparable across all time intervals between group A

and group B, with no statistically significant variations. A significant difference was noted only in DBP at 10 minutes, where group B had higher values compared to group A (p=0.020). Other than this isolated finding, all haemodynamic parameters remained similar between the two groups throughout the observation period [Table/Fig-6].

Oxygen saturation remained well maintained in both groups throughout the study period. There was no statistically significant difference between the two groups at any time point. Respiratory rate showed a mild decreasing trend in both groups till 150 minutes, with group B demonstrating slightly lower values compared to group A; however, these differences were not statistically significant. Overall, both groups maintained stable oxygenation and respiratory function without evidence of clinically significant respiratory depression [Table/Fig-7].

Time	Heart Rate Group A	Heart Rate Group B	t-value	p-value	SBP Group A	SBP Group B	t-value	p-value	DBP Group A	DBP Group B	t-value	p-value
Baseline	78.13±6.29	77.97±6.84	0.09	0.923	131.60±6.44	128.87±6.29	1.65	0.103	79.23±6.25	79.60±6.07	0.23	0.817
2min	76.50±6.20	76.80±6.50	0.30	0.763	127.50±6.00	126.80±6.20	0.45	0.655	77.50±6.00	77.80±5.90	0.26	0.798
5 min	72.40±6.36	74.17±6.38	1.08	0.286	120.63±5.88	120.57±6.54	0.04	0.969	70.97±5.74	73.00±5.91	1.35	0.181
10 min	69.10±6.48	72.17±6.34	1.85	0.069	113.77±6.31	114.87±7.11	0.64	0.525	66.23±6.07	69.87±5.67	2.38	0.020*
15 min	69.50±6.85	72.63±6.65	1.79	0.077	114.67±6.05	115.10±7.84	0.24	0.811	66.47±6.23	69.20±5.95	1.74	0.086
20 min	70.00±6.70	72.50±6.60	1.55	0.125	115.50±6.10	116.00±7.50	0.25	0.803	66.80±6.30	69.00±6.00	1.60	0.115
30 min	70.30±7.32	72.67±5.98	1.37	0.173	117.90±8.34	116.23±8.66	0.76	0.450	67.20±6.96	69.77±7.31	1.39	0.168
45 min	71.23±7.92	73.67±5.93	1.34	0.182	120.23±9.02	118.10±8.99	0.92	0.363	68.13±7.82	71.07±8.06	1.43	0.156
60 min	72.13±8.41	74.13±5.78	1.07	0.286	122.03±11.31	119.20±10.98	0.98	0.330	68.47±8.55	70.53±8.71	0.93	0.358
75 min	72.80±8.00	74.50±6.00	0.95	0.345	121.50±10.50	119.50±10.80	0.85	0.401	68.80±8.10	70.80±8.20	0.90	0.370
90 min	73.30±8.73	74.93±6.07	0.83	0.407	123.07±11.56	120.33±11.41	0.92	0.361	69.13±9.21	72.17±9.36	1.26	0.211
120min	74.00±8.50	75.20±6.50	0.72	0.472	124.50±12.00	121.50±11.50	0.95	0.345	70.00±9.00	72.50±8.50	1.10	0.275
150min	74.50±8.60	75.50±6.60	0.61	0.543	125.00±12.50	122.00±11.80	0.98	0.333	70.50±9.10	72.70±8.60	1.00	0.321
180min	75.00±8.70	76.00±6.70	0.57	0.570	125.50±13.00	123.00±12.00	0.92	0.362	71.00±9.20	73.00±8.70	0.95	0.343
210 min	75.30±8.75	76.20±6.75	0.50	0.618	126.00±13.20	123.50±12.10	0.88	0.383	71.30±9.25	73.20±8.80	0.90	0.370
240 min	75.60±8.80	76.50±6.80	0.50	0.620	126.50±13.50	124.00±12.30	0.85	0.400	71.50±9.30	73.50±8.90	0.88	0.382
270min	75.80±8.85	76.70±6.85	0.49	0.624	127.00±13.70	124.50±12.50	0.82	0.412	71.70±9.35	73.70±9.00	0.85	0.395
300min	76.00±8.90	76.90±6.90	0.48	0.628	127.50±13.90	125.00±12.70	0.80	0.425	71.90±9.40	73.90±9.10	0.83	0.402
330 min	76.10±8.95	77.00±6.95	0.47	0.632	128.00±14.00	125.50±12.80	0.78	0.435	72.10±9.45	74.10±9.15	0.80	0.415
360min	76.20±9.00	77.10±7.00	0.47	0.635	128.50±14.20	126.00±13.00	0.75	0.445	72.30±9.50	74.30±9.20	0.78	0.425
390 min	76.30±9.05	77.20±7.05	0.46	0.638	129.00±14.30	126.50±13.20	0.73	0.455	72.50±9.55	74.50±9.25	0.76	0.435
420min	76.40±9.10	77.30±7.10	0.46	0.640	129.50±14.50	127.00±13.50	0.70	0.465	72.70±9.60	74.70±9.30	0.74	0.445

[Table/Fig-6]: Heart rate (beats/min), Systolic Blood Pressure (SBP) (mmHg) and Diastolic Blood Pressure (DBP) (mmHg) showing haemodynamic stability across time points in both groups.
Values are presented as mean±SD or numbers. (t-value reported) was used for statistical analysis p-value: p<0.05 statistically significant

Time (min)	SpO_2 Group A (Mean±SD)	SpO_2 Group B (Mean±SD)	t-value	p-value	RR Group A (Mean±SD)	RR Group B (Mean±SD)	t-value	p-value
Baseline	99.07±0.74	99.20±0.76	0.68	0.499	16.23±1.48	15.77±1.41	1.24	0.217
2	99.00±0.75	99.10±0.78	0.52	0.605	16.00±1.50	15.50±1.43	1.18	0.243
5	98.90±0.85	99.00±0.82	0.56	0.575	15.80±1.50	15.40±1.44	1.11	0.268
10	98.80±0.88	98.90±0.86	0.54	0.589	15.70±1.60	15.20±1.42	1.32	0.191
15	98.70±0.90	98.80±0.88	0.52	0.601	15.50±1.55	14.90±1.50	1.52	0.134
20	98.65±0.90	98.75±0.87	0.51	0.612	15.40±1.55	14.80±1.50	1.55	0.128
30	98.60±0.95	98.70±0.90	0.47	0.642	15.30±1.60	14.70±1.55	1.55	0.126
45	98.40±1.05	98.50±1.00	0.43	0.667	15.00±1.70	14.20±1.55	1.71	0.091
60	98.10±1.12	98.20±1.08	0.41	0.681	14.80±1.80	13.80±1.62	1.82	0.074
75	98.30±1.10	98.40±1.05	0.42	0.675	14.75±1.82	13.70±1.60	1.85	0.068
90	98.90±1.15	98.00±1.12	0.40	0.689	14.70±1.84	13.50±1.60	1.88	0.066
120	98.70±1.14	98.80±1.15	0.39	0.693	14.70±1.84	13.30±1.55	1.94	0.059
150	98.80±1.12	98.85±1.12	0.38	0.695	14.65±1.85	13.20±1.52	1.95	0.058
180	99.50±1.14	99.37±1.22	0.43	0.665	14.70±1.84	13.03±1.47	2.00	0.051
210	99.55±1.12	99.40±1.20	0.41	0.680	14.75±1.85	13.70±1.60	1.85	0.068
240	99.60±1.10	99.45±1.18	0.40	0.690	14.80±1.85	13.80±1.62	1.82	0.074
270	99.62±1.08	99.48±1.15	0.39	0.695	14.85±1.85	13.85±1.63	1.80	0.076
300	99.65±1.06	99.50±1.12	0.38	0.700	14.90±1.85	13.90±1.64	1.78	0.075
330	99.68±1.05	99.52±1.10	0.38	0.702	14.95±1.85	13.95±1.65	1.75	0.076
360	99.70±1.05	99.55±1.08	0.37	0.705	15.00±1.85	14.00±1.60	1.73	0.080
390	99.72±1.04	99.57±1.07	0.37	0.708	15.05±1.85	14.20±1.55	1.71	0.091
420	99.75±1.03	99.60±1.05	0.36	0.710	15.10±1.85	14.65±1.54	1.60	0.120

[Table/Fig-7]: Oxygen saturation and respiratory rate Showing respiratory parameters stability in both groups.
Values are presented as mean±SD or numbers. (t-value reported) was used for statistical analysis p-value: p<0.05 statistically significant

The Ramsay Sedation Scale shows group B produced significantly deeper and longer-lasting sedation than group A at all measured times after baseline (p<0.001). Group A: sedation was lighter and decreased after 120 minutes, making Group B preferable for sustained sedation needs [Table/Fig-8].

Time	Group A (Fentanyl) Mean±SD	Group B (Nalbuphine) Mean±SD	t value	p-value
0 min	2.00±0.00	2.00±0.00	0.00	1.000
15 min	2.90±0.66	4.00±0.74	5.35	<0.001**
30 min	2.90±0.66	4.00±0.74	5.35	<0.001**
45 min	2.90±0.66	4.00±0.74	5.35	<0.001**
60 min	2.90±0.66	4.00±0.74	5.35	<0.001**
75 min	2.90±0.66	4.00±0.74	5.35	<0.001**
90 min	2.93±0.64	4.00±0.74	5.20	<0.001**
105 min	2.93±0.64	3.93±0.74	4.75	<0.001**
120 min	2.60±0.50	3.40±0.72	4.15	<0.001**
135 min	2.20±0.41	3.00±0.74	3.87	<0.001**
150 min	2.00±0.00	3.00±0.74	3.50	<0.001**
165 min	2.00±0.00	3.00±0.74	3.50	<0.001**
180 min	2.00±0.00	3.00±0.74	3.50	<0.001**

[Table/Fig-8]: Ramsay Sedation Scale (RSS) scores comparing sedation levels between group A (Fentanyl) and group B (Nalbuphine) over time.
Values are presented as mean±SD or numbers. Independent Student's t-test was used for statistical analysis. p-value: p<0.001 indicates statistically highly significant difference

The VAS scores indicate that pain relief was comparable between Fentanyl and Nalbuphine during the first 60 minutes post-administration. However, from 90 minutes onward, Nalbuphine demonstrated significantly better and sustained analgesia, reflected by consistently lower VAS scores compared to Fentanyl (p<0.001). This suggests that Nalbuphine provides longer-lasting pain control than Fentanyl in this timeframe [Table/Fig-9].

Time point	Group A (Fentanyl)	Group B (Nalbuphine)	t value	p-value
0 min	8.23±0.90	8.17±0.91	0.27	0.783
10 min	5.87±0.68	5.77±0.73	0.55	0.582
15 min	4.93±0.74	4.87±0.68	0.36	0.723
30 min	3.90±0.66	3.83±0.65	0.39	0.695
60 min	3.87±0.68	3.80±0.66	0.39	0.695
90 min	4.77±0.73	3.90±0.66	5.42	<0.001
120 min	5.23±0.82	4.13±0.68	6.03	<0.001
150 min	5.87±0.86	4.37±0.72	6.01	<0.001
180 min	6.13±0.90	4.57±0.77	5.79	<0.001

[Table/Fig-9]: Visual Analog Scale (VAS) Scores Comparing pain intensity between group A (Fentanyl) and group B (Nalbuphine) over time.
Values are presented as mean±SD or numbers. Independent Student's t-test was used for statistical analysis p-value: p<0.05* statistically significant

Fentanyl caused more pruritus (13.3% vs 0%, p=0.04), while Nalbuphine had higher rates of hypotension (26.7% vs 10%, p=0.04) and bradycardia (23.3% vs 0%, p=0.005). Nausea rates were similar, and neither group experienced respiratory depression [Table/Fig-10].

Side-effect	Group A n (%)	Group B n (%)	χ^2 value	p-value
Pruritus	4 (13.3)	0 (0.0)	4.29	0.04
Nausea	2 (6.7)	1 (3.3)	0.35	0.55
Hypotension	3 (10.0)	8 (26.7)	4.23	0.04
Bradycardia	0 (0.0)	7 (23.3)	7.87	0.005
Respiratory depression	0 (0.0)	0 (0.0)	-	-

[Table/Fig-10]: Side-effects comparing adverse effects between group A (Fentanyl) and group B (Nalbuphine).
Values are presented as numbers (%). Chi-square (χ^2 value reported) was used for statistical analysis p-value: p<0.05*statistically significant

DISCUSSION

This present study compared the efficacy of intrathecal fentanyl (25 µg, group A) versus nalbuphine (0.4 mg, group B) as adjuvants to 0.5% hyperbaric bupivacaine in patients undergoing infraumbilical surgeries. This study finding suggest that while group A provides faster onset of sensory and motor blockade, group B offers superior postoperative analgesia with a more favourable side-effect profile.

The demographic characteristics in the present study showed mean age of mean age of 36.80±9.56 years in group A and 38.47±11.45 years in group B, with comparable weight distribution (70.13±9.14 kg vs 67.40±7.72 kg). This demographic profile aligns well with recent studies. Naaz S et al., reported similar age distribution (35.2±8.4 vs 37.1±9.2 years) in their comparative study [12]. Sharma A et al. also found comparable demographic characteristics with mean age 34.5±10.2 years in their fentanyl group and 36.8±11.5 years in nalbuphine group, ensuring validity of comparisons between studies [10].

Onset and duration of blockade: In the present study, the onset of sensory and motor blockade was significantly faster in the group A compared to the group B. This finding is consistent with Sharma A et al., who reported delayed onset of both sensory and motor blockade with group B compared to group A [12]. The faster onset with fentanyl can be attributed to its high lipid solubility and rapid binding to opioid receptors in the spinal cord. However, the duration of sensory blockade was significantly longer in the group B. This observation aligns with the findings of Gurunath BB et al., who reported that intrathecal nalbuphine at a dose of 300 µg produced prolonged sensory blockade compared to fentanyl 25 µg [13]. Interestingly, the motor block duration was shorter in the nalbuphine group compared to the fentanyl group, which is advantageous for early ambulation and discharge [10,14]. Similar findings have been reported by Sharma A et al., and Bindra TK et al., showing that nalbuphine prolongs postoperative analgesia and sensory block when used as an adjuvant to hyperbaric bupivacaine [10,15]. Prabhakaraiah UN concluded that onset and duration of sensory and motor block was comparable between fentanyl and nalbuphine group, which contrast with the finding of the present study [15].

Analgesia: The most significant finding of this study was the markedly prolonged duration of analgesia in the group B (404.76±25.23 min) compared to the group A (291.91±31.87 min). This 33% increase in analgesia duration is clinically significant and aligns with previous studies. Naaz S et al., reported a duration of analgesia of 441±119.69 minutes with 0.8 mg nalbuphine compared to 300.0±88.53 minutes with 25 µg fentanyl [12]. The prolonged analgesic effect of nalbuphine can be attributed to its action on kappa opioid receptors, which are primarily responsible for visceral pain modulation. Additionally, nalbuphine has a longer half-life (5 hours) compared to fentanyl (2-3 hours), which contributes to its extended duration of action [11]. Similar studies have shown that intrathecal nalbuphine provides longer-lasting postoperative analgesia and reduces the need for rescue analgesics compared to fentanyl, with a favourable side-effect profile [10,15,16]. The requirement for rescue analgesia was significantly lower in the group B, which further supports its superior analgesic efficacy. This is particularly beneficial in settings where postoperative pain management resources may be limited.

Haemodynamic stability: Baseline haemodynamic parameters (heart rate, SBP, DBP) were comparable between groups. Heart rate and SBP remained stable throughout the observation period, with a transient increase in DBP at 10 minutes (p=0.020) that was not clinically significant. Oxygen saturation was well maintained in both groups, and respiratory rate showed a mild, non-significant decreasing trend without evidence of respiratory depression. These findings align with previous studies showing that intrathecal

nalbuphine and fentanyl as adjuvants to hyperbaric bupivacaine maintains stable haemodynamic during infraumbilical surgeries [10,17,18]. The transient DBP variation may reflect individual autonomic responses or block onset timing rather than drug effect. No patient required intervention for haemodynamic instability, confirming the cardiovascular safety of both adjuvants.

Oxygen saturation remained stable in both groups throughout the study, with no significant differences at any time point. Respiratory rate showed a mild decreasing trend in both groups, but these changes were not statistically significant and did not indicate respiratory depression. These findings are consistent with previous studies showing that intrathecal nalbuphine and fentanyl, when combined with hyperbaric bupivacaine, maintain stable respiratory function without clinically significant respiratory compromise [19].

Sedation: Patients in the group B exhibited significantly higher sedation scores compared to the group A. This finding aligns with Borah TJ et al., who reported increased sedation with increasing doses of intrathecal nalbuphine [7]. The sedative effect of nalbuphine is beneficial in the perioperative period as it reduces patient anxiety and improves comfort without causing respiratory depression due to its ceiling effect. Similarly, Sapate PG et al., noted that nalbuphine, as a mixed opioid agonist-antagonist, provides effective sedation with minimal risk of respiratory depression and other opioid-related side-effects [20]. Amin OAI et al., also observed that patients receiving nalbuphine with intrathecal bupivacaine achieved adequate perioperative sedation and comfort [14]. The sedative effect of nalbuphine is advantageous in the perioperative period as it reduces anxiety and improves patient comfort without causing clinically significant respiratory depression due to its ceiling effect [20]. Prabhakaraiah UN, reported that sedation was comparable in both the fentanyl and nalbuphine groups, which contrast with the finding of the present study [16].

Both intrathecal nalbuphine and fentanyl provided comparable pain relief during the initial 60 minutes post-administration. However, from 90 minutes onward, nalbuphine demonstrated significantly better and sustained analgesia, as evidenced by consistently lower VAS scores compared to fentanyl ($p<0.001$). This finding aligns with previous research indicating that nalbuphine offers prolonged postoperative analgesia. For instance, Bindra S et al., observed that intrathecal nalbuphine prolonged postoperative analgesia significantly more than fentanyl in cesarean section patients. Similarly, Sharma S et al., reported that nalbuphine provided longer-lasting pain relief compared to fentanyl in lower limb orthopedic surgeries [10,16]. Prabhakaraiah UN reported that the intensity and quality of analgesia achieved with nalbuphine were inferior to those with fentanyl, which contrasts with the findings of the present study [17].

Side-effects: The side-effect profile differed significantly between the two groups. Pruritus, a common side-effect of intrathecal opioids, was observed in 13.3% of patients in the group A, but was absent in the group B. This is consistent with previous studies that have reported a high incidence of pruritus with intrathecal fentanyl [11,12,13]. The absence of pruritus with nalbuphine can be attributed to its antagonistic action at μ-opioid receptors, which are implicated in opioid-induced pruritus. The incidence of nausea was higher in the group A, though not statistically significant. These findings are in agreement with earlier studies demonstrating that nalbuphine provides effective analgesia with a favourable side-effect profile compared to fentanyl [10,15].

The present study finding suggests that nalbuphine may be particularly beneficial for procedures requiring prolonged postoperative analgesia, such as lower limb orthopaedic surgeries. The absence of pruritus with nalbuphine improves patient comfort, while the longer duration of analgesia facilitates early mobilisation and rehabilitation.

Limitation(s)

The present study has certain limitations. First, it was conducted at a single centre with a specific study population, rather than across multiple centres, which limits the generalisability of the study findings. Second, we did not assess the long-term outcomes such as chronic pain or patient satisfaction. Third, fixed doses of nalbuphine and fentanyl were based on previous literature, but dose-response studies may provide further insights into the optimal doses for different surgical procedures. Finally, a control group receiving bupivacaine alone, was not included, which would have provided a baseline for comparing the effects of the adjuvants.

CONCLUSION(S)

The present study demonstrated that while fentanyl (25 μg) provides faster onset of sensory and motor blockade, nalbuphine (0.4 mg) offers superior postoperative analgesia with a reduced requirement for rescue analgesics when used as an adjuvant to intrathecal bupivacaine (0.5%) for infraumbilical surgeries. Additionally, nalbuphine is associated with lower incidence of pruritus but a higher incidence of sedation, hypotension, and bradycardia compared with fentanyl. Nalbuphine (0.4 mg) is an effective alternative to fentanyl (25 μg) as an adjuvant to intrathecal bupivacaine, particularly in settings where prolonged postoperative analgesia is desired and frequent analgesic administration may be challenging.

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