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REVIEW ARTICLE
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A COMPARATIVE STUDY OF EFFECTS ON SUBARACHNOID BLOCK USING BUPIVACAINE WITH NALBUPHINE HYDROCHLORIDE AND BUPIVACAINE WITH FENTANYL FOR LOWER ABDOMINAL & LOWER LIMB SURGERIES

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Abstract

Background: Intrathecal adjuvants are commonly used to enhance the efficacy and duration of spinal anesthesia. Nalbuphine and fentanyl, when added to bupivacaine, offer distinct pharmacological profiles influencing onset, duration, and side effects.

Objective: To compare the effects of intrathecal bupivacaine with nalbuphine hydrochloride versus bupivacaine with fentanyl in patients undergoing lower abdominal and lower limb surgeries.

Methods: A prospective, randomized study was conducted on 100 patients allocated into two groups: Group N (bupivacaine + nalbuphine) and Group F (bupivacaine + fentanyl). Onset and duration of sensory and motor block, hemodynamic changes, duration of analgesia, and adverse effects were recorded and statistically analyzed.

Results: Group F showed a significantly faster onset of sensory (1.63 ± 0.69 min) and motor block (2.54 ± 0.58 min), whereas Group N had a significantly longer duration of analgesia (321.20 ± 48.66 min) and sensory block (248.68 ± 50.23 min). Adverse effects were fewer in the nalbuphine group. Hemodynamic parameters remained stable in both groups, with better systolic control in Group N.

Conclusion: While fentanyl ensures faster onset, nalbuphine provides prolonged analgesia with fewer side effects, making it a suitable intrathecal adjuvant for extended postoperative pain control.

Keywords: Intrathecal anesthesia, Nalbuphine, Fentanyl, Bupivacaine, Spinal block, Postoperative analgesia, Hemodynamic stability

INTRODUCTION

Central neuraxial blockade, particularly spinal (subarachnoid) anaesthesia, is among the most preferred regional anaesthesia techniques for lower abdominal and lower limb surgeries. Its popularity stems from its ease of administration, rapid onset, cost-effectiveness, and minimal physiological stress compared to general anaesthesia. It eliminates airway instrumentation-related complications and significantly reduces postoperative nausea, vomiting, and analgesic requirements [1].

Since its clinical introduction by Karl August Bier in 1898, spinal anaesthesia has evolved remarkably while retaining its dominance in various surgical settings including caesarean sections, orthopaedic procedures, and urological interventions [2]. One of the critical considerations in subarachnoid block is the selection of appropriate local anaesthetics and adjuvants to optimize the block's quality, onset, duration, and safety profile.

Bupivacaine, an amide-type long-acting local anaesthetic, is commonly used in spinal anaesthesia due to its potency and prolonged action. It is approximately three to four times more potent than lignocaine and provides satisfactory sensory and motor block. However, its onset is relatively slow, and higher doses may result in profound motor block or cardiotoxicity [3]. Therefore, to enhance its analgesic efficacy while minimizing adverse effects, the addition of opioid adjuvants has been explored extensively.

Intrathecal opioids synergistically potentiate the action of local anaesthetics by enhancing sensory blockade without significantly increasing sympathetic block. They allow for reduced doses of local anaesthetic, thus minimizing associated motor blockade and cardiovascular depression [4]. Among opioids, morphine and fentanyl are widely used, though morphine's delayed respiratory depression and regulatory restrictions limit its routine use. Fentanyl, a potent μ-opioid receptor agonist, is highly lipophilic, exhibits rapid onset, and enhances intraoperative analgesia with minimal rostral spread, reducing the risk of delayed respiratory depression [5].

However, opioids including fentanyl are associated with side effects such as pruritus, nausea, vomiting, urinary retention, and rare respiratory depression. Additionally, the Narcotic Drugs and Psychotropic Substances (NDPS) Act poses availability constraints for certain opioids in India. This has prompted exploration of alternative adjuvants with opioid-like properties but fewer regulatory hurdles.

Nalbuphine hydrochloride is a synthetic opioid agonist-antagonist that acts as a κ-receptor agonist and μ-receptor antagonist. This dual mechanism provides effective analgesia while mitigating typical μ-opioid-related side effects such as respiratory depression, pruritus, and nausea [6]. Nalbuphine's kappa agonism is associated with good analgesic efficacy, especially in visceral pain, and its ceiling effect on respiratory depression renders it a safer alternative [7]. Importantly, nalbuphine is not classified under the NDPS Act, making it more accessible in Indian clinical settings.

Several clinical studies have compared intrathecal nalbuphine and fentanyl as adjuvants to bupivacaine. While fentanyl offers faster onset of motor block and intraoperative analgesia, nalbuphine has shown superior postoperative analgesic duration with a reduced need for rescue analgesics [8]. Additionally, nalbuphine tends to have a more stable haemodynamic profile and a lower incidence of side effects compared to fentanyl, though the onset of sensory and motor blockade may be slightly delayed [9].

The current study has been designed to evaluate and compare the effectiveness of intrathecal 0.5% hyperbaric bupivacaine combined with either nalbuphine hydrochloride or fentanyl in patients undergoing lower abdominal and lower limb surgeries. The comparison encompasses critical parameters including time to onset and duration of sensory and motor blockade, postoperative analgesic duration, haemodynamic stability, and adverse event profile. The aim is to determine whether nalbuphine can be a viable, effective, and safer alternative to fentanyl in the context of spinal anaesthesia.

This comparative assessment is particularly relevant in the context of the ongoing search for optimal spinal adjuvants that provide effective perioperative analgesia without increasing complication rates or regulatory burdens. The findings of this study may guide anaesthesiologists in tailoring safer and more effective anaesthesia protocols for surgeries requiring lower limb and abdominal access [10].

MATERIALS AND METHODS

Study Design and Setting

This was a prospective, randomized, double-blind comparative study conducted in the Department of Anaesthesiology at a tertiary care hospital over a period of one year. The study protocol was approved by the Institutional Ethics Committee, and informed written consent was obtained from all participants prior to inclusion.

Sample Size and Randomization

A total of 100 patients, aged between 18 and 60 years, classified as American Society of Anesthesiologists (ASA) physical status I or II, undergoing elective lower abdominal or lower limb surgeries under spinal anaesthesia were enrolled. Patients were randomly allocated into two equal groups (n = 50 each) using a computer-generated randomization schedule:

- **Group N:** Received 3.0 mL of 0.5% hyperbaric bupivacaine with 0.4 mg nalbuphine hydrochloride (made up to 3.5 mL)
- **Group F:** Received 3.0 mL of 0.5% hyperbaric bupivacaine with 25 μg fentanyl (made up to 3.5 mL)

Inclusion Criteria

- Patients aged 18–60 years
- ASA physical status I and II
- Elective surgeries involving lower abdomen and lower limbs
- Written informed consent

Exclusion Criteria

- Patient refusal
- ASA physical status III and above
- Known allergy to local anaesthetics or study drugs
- Coagulopathy or bleeding diathesis
- Infection at the injection site
- Spinal deformities or neurological disorders
- Pregnancy or lactation

Anaesthesia Procedure

All patients were kept nil per oral as per standard guidelines and premedicated with 0.5 mg alprazolam the night before surgery. On arrival in the operating theatre, standard monitoring was initiated, including ECG, pulse oximetry, and non-invasive blood pressure. Intravenous access was secured, and patients were preloaded with 10 mL/kg of Ringer's lactate solution.

Under strict aseptic precautions, lumbar puncture was performed at the L3–L4 interspace using a 25G Quincke spinal needle in the sitting position. The respective study drug was administered intrathecally as per group allocation. The time of drug administration was noted as time zero.

Observations and Parameters

The following parameters were recorded:

- **Sensory block:** Onset time (pinprick method), highest level achieved, duration until regression to S1
- **Motor block:** Assessed using the Modified Bromage scale, including onset and duration
- **Hemodynamic parameters:** Heart rate, systolic and diastolic blood pressures recorded every 2 minutes for the first 10 minutes, then at regular intervals up to 120 minutes
- **Adverse effects:** Incidence of hypotension, bradycardia, nausea, vomiting, pruritus, shivering
- **Duration of effective analgesia:** Time from spinal injection to first requirement of rescue analgesia (VAS ≥ 4)

• **Rescue analgesia:** Injection Diclofenac sodium 75 mg IV was administered when required

Statistical Analysis

Data were compiled and analyzed using SPSS version 25 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) and compared using the independent t-test. Categorical data were analyzed using the Chi-square test. A p-value < 0.05 was considered statistically significant.

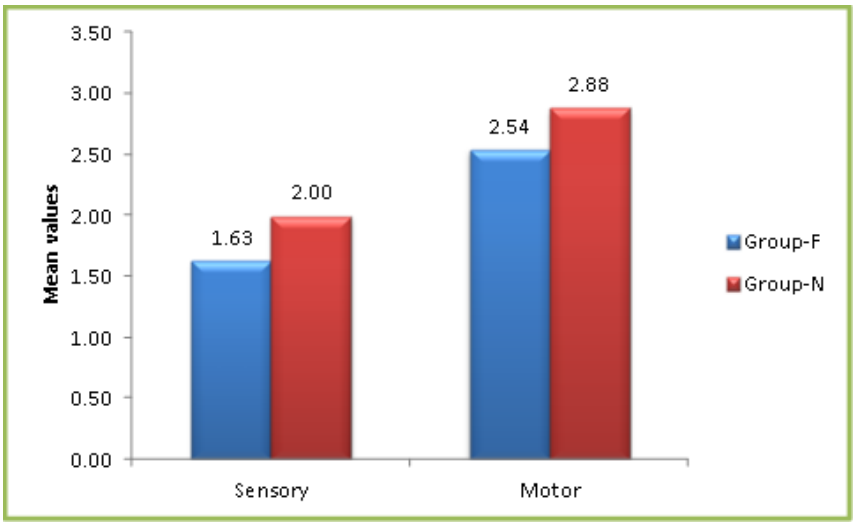
RESULTS

Table 1: Onset of Sensory and Motor Block

The mean onset of sensory block was significantly faster in the fentanyl group (1.63 ± 0.69 minutes) compared to the nalbuphine group (2.00 ± 0.53 minutes) ($p < 0.003$). Similarly, the onset of motor block was also faster in Group F (2.54 ± 0.58 minutes) than in Group N (2.88 ± 0.72 minutes), and this difference was statistically significant ($p < 0.01$). Graph 1

Table 1: Onset of Sensory Block and Motor Block in the Two Study Populations

Onset of Blockade (min)	Group-F (N=50) Mean ± SD	Group-N (N=50) Mean ± SD	p-value
Sensory	1.63 ± 0.69	2.00 ± 0.53	< 0.003
Motor	2.54 ± 0.58	2.88 ± 0.72	< 0.01



Graph 1: Onset Of Motor block and sensory block In the Two Study Populations

Table 2: Degree of Motor Block (Modified Bromage Scale)

Complete motor block (Modified Bromage Grade 3) was observed in all 50 patients in Group F and in 47 patients in Group N. Three patients in Group N demonstrated a partial motor block (Grade 2), whereas none in Group F did. However, the difference was not statistically significant ($p = 0.121$).

Table 2: Degree of Motor Block (Modified Bromage Scale) in Two Groups Studied

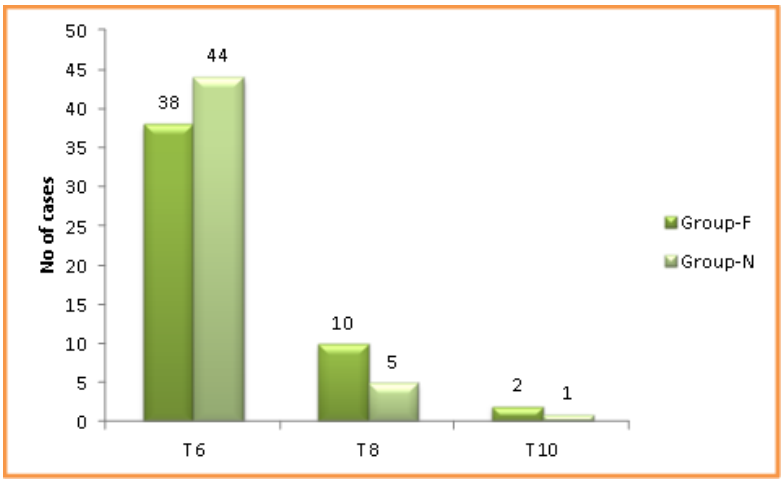
Degree of Motor Block (Modified Bromage Scale)	Group-F	Group-N	p-value (Fisher's Exact Test)
Able to move the foot only (Score 2)	0	3	0.121
Unable to move knee or foot (Score 3)	50	47	
Total	**50**	**50**	

Table 3: Highest Level of Sensory Blockade

The median sensory block level achieved was T6 in both groups. T6 was reached in 38 patients in Group F and 44 patients in Group N. Other block levels (T8, T10) were observed in fewer patients in both groups. There was no statistically significant difference in the distribution of peak sensory levels between the two groups ($p = 0.293$). Graph 2

Table 3: Highest Level of Sensory Blockade

Highest Level of Sensory Blockade	Group-F	Group-N	p-value (Chi Square Test)
T6	38	44	2.439, P < 0.293
T8	10	5	
T10	2	1	
Total	**50**	**50**	



Graph 2: Comparison of highest level of Sensory Blockade in the two study Populations

Table 4: Duration of Analgesia, Motor Block, and Sensory Block

The duration of analgesia was significantly longer in the nalbuphine group (321.20 ± 48.66 minutes) compared to the fentanyl group (297.72 ± 31.65 minutes) ($p = 0.005$). The duration of sensory block was also significantly longer in Group N (248.68 ± 50.23 minutes) versus Group F (229.22 ± 31.67 minutes) ($p = 0.023$). The duration of motor block was slightly longer in Group N (182.14 ± 30.85 minutes) than in Group F (180.50 ± 50.84 minutes), but this difference was not statistically significant ($p = 0.846$).

Table 4: Duration of Analgesia, Motor Block and Sensory Block (Min) in Two Groups of Patients Studied

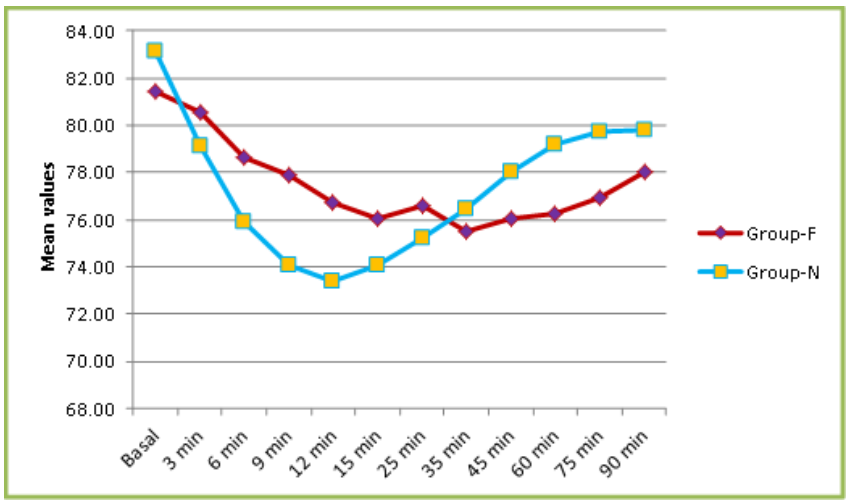
Parameter	Group-F (N=50) Mean ± SD	Group-N (N=50) Mean ± SD	p-value
Duration of Analgesia (min)	297.72 ± 31.65	321.20 ± 48.66	0.005
Duration of Motor Block (min)	180.50 ± 50.84	182.14 ± 30.85	0.846
Duration of Sensory Block (min)	229.22 ± 31.67	248.68 ± 50.23	0.023

Table 5: Heart Rate Trends

Baseline heart rate was similar between the groups, with Group F at 81.44 ± 12.94 bpm and Group N at 83.14 ± 11.22 bpm (p = 0.484). Heart rate gradually declined after spinal anaesthesia in both groups but remained within normal limits. No statistically or clinically significant differences in heart rate were observed at any time points between the two groups. Graph 3

Table 5: Comparison of Heart Rate (beats/min) in Two Groups of Patients Studied

Time Point	Group-F (N=50) Mean ± SD	Group-N (N=50) Mean ± SD	p-value
Basal	81.44 ± 12.94	83.14 ± 11.22	0.484
3 min	80.54 ± 13.64	79.08 ± 9.91	0.542
6 min	78.66 ± 14.35	75.94 ± 10.12	0.276
9 min	77.88 ± 15.19	74.06 ± 9.19	0.131
12 min	76.72 ± 14.34	73.38 ± 8.81	0.164
15 min	76.02 ± 12.73	74.06 ± 7.64	0.353
25 min	76.58 ± 13.64	75.22 ± 5.99	0.520
35 min	75.52 ± 12.89	76.42 ± 6.20	0.657
45 min	76.04 ± 11.90	78.04 ± 6.21	0.295
60 min	76.22 ± 12.27	79.18 ± 6.76	0.138
75 min	76.92 ± 13.03	79.74 ± 6.90	0.179
90 min	78.00 ± 12.87	79.76 ± 7.21	0.401



Graph 3: Heart Rate Measured at Different Time Points Among Study Participants

Table 6: Systolic Blood Pressure Trends

There was a measurable decline in systolic blood pressure post-spinal anaesthesia in both groups. Group F showed a slightly greater drop, with the lowest mean value of 105.20 ± 7.67 mmHg at 12 minutes. Group N had a minimum value of 108.78 ± 9.76 mmHg at the same time point. The fall in systolic blood pressure was statistically significant at 12, 25, 35, 75, and 90 minutes in favour of Group N (all $p < 0.05$), indicating better hemodynamic stability. Graph 4

Table 6: Comparison of Systolic Blood Pressure (mmHg) in Two Groups of Patients Studied

Time Point	Group-F (N=50) Mean ± SD	Group-N (N=50) Mean ± SD	p-value
Basal	115.24 ± 6.69	118.20 ± 8.78	0.061
3 min	110.98 ± 6.93	113.80 ± 10.88	0.125
6 min	108.12 ± 8.10	110.64 ± 9.07	0.146
9 min	106.46 ± 8.40	108.24 ± 9.64	0.327
12 min	105.20 ± 7.67	108.78 ± 9.76	0.044
15 min	106.32 ± 7.56	109.24 ± 9.32	0.089
25 min	107.94 ± 8.23	111.46 ± 8.79	0.041
35 min	108.90 ± 8.50	112.68 ± 8.09	0.025
45 min	111.32 ± 8.59	113.80 ± 8.14	0.142
60 min	111.60 ± 8.30	114.66 ± 7.57	0.057
75 min	111.66 ± 8.27	115.90 ± 6.71	0.006
90 min	112.58 ± 8.41	116.88 ± 6.93	0.006

Graph 4: Systolic Blood Pressure Measured at Different Time Points Among Study Participants

DISCUSSION

The present study was designed to compare the efficacy and safety of intrathecal bupivacaine combined with either nalbuphine or fentanyl for lower abdominal and lower limb surgeries. The findings suggest that while fentanyl provided a faster onset of block, nalbuphine offered longer-lasting analgesia with fewer side effects. These results align with and expand upon previously published research.

The demographic profile of the patients, including age, sex, ASA physical status, and type of surgery, was statistically comparable between the two groups, ruling out confounding influences. This homogeneity is crucial in validating the comparative outcomes, especially in a double-arm trial setting where balance in baseline characteristics enhances internal validity.

In terms of sensory and motor block onset, the current study demonstrated that the fentanyl group had a significantly faster onset compared to nalbuphine. Fentanyl, being highly lipophilic, rapidly penetrates neural tissues, thus reducing the time to block establishment [11]. This rapid onset is consistent with findings by Pert and Snyder, who established the presence and action of opiate receptors in nervous tissue [12].

However, nalbuphine showed superiority in the duration of analgesia, sensory block, and motor block. This extended analgesic effect can be attributed to nalbuphine's κ-receptor agonism, which enhances spinal analgesia without significantly compromising hemodynamic stability [13]. The prolonged sensory blockade is particularly beneficial in surgeries where postoperative pain management is critical. A similar pattern was observed by Bindra et al., who reported that intrathecal nalbuphine provided superior postoperative pain relief compared to fentanyl [14].

The findings related to hemodynamic parameters are particularly noteworthy. Although both drugs were hemodynamically stable, nalbuphine exhibited a lesser reduction in systolic blood pressure at multiple time intervals post-block. This is of clinical importance, especially in patients at risk of hypotension under spinal anesthesia. Comparable outcomes were reported by Gurunath and Madhusudhana, who noted better cardiovascular stability with nalbuphine [15].

Adverse effects were less frequent in the nalbuphine group. Pruritus, nausea, vomiting, and shivering were more prevalent with fentanyl, in agreement with its known μ-opioid receptor–mediated side effects. Nalbuphine, being a mixed agonist-antagonist, tends to block these undesirable μ-mediated effects while maintaining analgesia via κ-receptors [16-18]. This pharmacodynamic characteristic explains the better tolerability observed in our cohort. Jaisinghani et al. reported similar findings, where nalbuphine groups had lower incidence of opioid-induced adverse effects [16].

Motor block duration was statistically similar between the two groups, suggesting that neither drug excessively prolonged motor blockade. This is a desirable property, as early ambulation postoperatively is beneficial for patient recovery. The Modified Bromage score findings in our study support the clinical safety of nalbuphine in this context.

Another important aspect is the time to first rescue analgesic, which was significantly delayed in the nalbuphine group. This reduces the postoperative analgesic requirement and enhances patient satisfaction. The reduced analgesic consumption in nalbuphine patients is not only clinically meaningful but also economically advantageous in high-volume surgical centers. Singh et al. noted that nalbuphine extended the time to first analgesic request compared to fentanyl [17].

In summary, the present findings suggest that although fentanyl ensures a quicker block onset, nalbuphine offers more prolonged analgesia with minimal adverse effects. The choice between the two adjuvants should be guided by the clinical scenario—fentanyl may be more suitable for short procedures where rapid onset is desired, while nalbuphine may be preferred for longer surgeries requiring extended postoperative pain control.

The limitations of this study include the single-center design and the modest sample size. A larger multicenter randomized control trial may provide further validation. In addition, qualitative patient feedback on postoperative comfort and satisfaction could strengthen the conclusions [19,20].

CONCLUSION

This study concludes that both nalbuphine and fentanyl, when used as adjuvants to intrathecal bupivacaine, are effective for lower abdominal and lower limb surgeries. Fentanyl offers a faster onset of sensory and motor block, while nalbuphine provides significantly longer postoperative analgesia with fewer adverse effects. Hemodynamic stability was better maintained with nalbuphine, and it was associated with a reduced requirement for rescue analgesics. Therefore, nalbuphine may be preferred for procedures requiring extended pain relief, whereas fentanyl remains suitable for shorter surgeries. The choice of adjuvant should be tailored based on surgical duration and individual patient factors.

REFERENCES

1. Parameshwara G. Spinal, epidural to combined spinal epidural analgesia, the history of central neuraxial block. Indian J Anaesth. 2001;45(6):406–12.
2. Dureja GP, Jayalaxmi TS. Colloid preloading before spinal and epidural anaesthesia. Hosp Today. 2000;5(11):601–3.
3. Barasch PG, Collen BF. Clinical Anaesthesia. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2006. p. 700–6.
4. Henderson DJ, Faccenda KA, Morrison LM. Transient radicular irritation with intrathecal plain lignocaine. Acta Anaesthesiol Scand. 1998;42:376–8.
5. Colin VJ. Principles of anaesthesiology. 3rd ed. Philadelphia: Lea & Febiger; 1993. p. 1445–52.
6. Raghuraman MS. Intrathecal nalbuphine – will it gain wider acceptance? Egyptian J Anaesth. 2017;33(3):289–93.
7. Shakooh S, Bhosle P. Intrathecal nalbuphine an effective adjuvant for post operative analgesia. Innov J Med Health Sci. 2014;4(2):79–82.
8. Gomaa HM, Mohamed NN, Zoheir HAH, Ali MS. Comparison between postoperative analgesia after intrathecal nalbuphine with bupivacaine and intrathecal fentanyl with bupivacaine after cesarean section. Egyptian J Anaesth. 2014;30:405–10.
9. Larson MD. History of anaesthetic practice. In: Miller RD, editor. Miller's Anaesthesia. 6th ed. Philadelphia: Churchill Livingstone; 2005. p. 3–52.
10. Brill S, Gurman M, Fisher A. A history of administration of local analgesics and opioids. Eur J Anaesth. 2003;20:682–9.
11. Pert CB, Snyder SH. Opiate receptor: demonstration in nervous tissue. Science. 1973;179:1011–4.
12. Sicard A. Les injections medicamenteuses extra-durales par voie sacrococcygienne. Compt Rend Soc Biol. 1901;53:396–8.
13. Lamotte C, Pert CB, Snyder SH. Opiate receptor binding in primate spinal cord: distribution and changes after dorsal root section. Brain Res. 1976;112:407–12.
14. Bindra TK, Kumar P, Jindal G. Postoperative analgesia with intrathecal nalbuphine versus intrathecal fentanyl in cesarean section: A double-blind randomized comparative study. Anesth Essays Res. 2018;12(2):561–5.
15. Gurunath BB, Madhusudhana R. Postoperative analgesic efficacy of intrathecal fentanyl compared to nalbuphine with bupivacaine in spinal anesthesia for lower abdominal surgeries. Anesth Essays Res. 2018;12:535–8.
16. Jaisinghani RN, Kanase NV, Dhulkhed VK, Dimble K, Gandhi S. A prospective randomized double blind comparative study of 0.8 mg nalbuphine hydrochloride and 25 mcg fentanyl as adjuvants to 0.5% hyperbaric bupivacaine in subarachnoid block in lower limb surgeries. Int J Med Health Res. 2018;4(4):26–31.
17. Singh J, Agarwal A, Vatal A. Intrathecal nalbuphine an effective adjuvant for post operative analgesia: A comparative study with fentanyl. Int J Contemp Med Res. 2017;4(1):39–42.
18. Bisht S, Rashmi D. Comparison of intrathecal fentanyl and nalbuphine: A prospective randomized controlled study in patients undergoing total abdominal hysterectomy. Anaesth Pain Intensive Care. 2017;21(2):194–8.
19. Singh N, Kumar S, Tyagi RK. A clinical comparative study of intrathecal nalbuphine versus intrathecal fentanyl added to 0.5% hyperbaric bupivacaine for perioperative anaesthesia and analgesia in lower abdominal surgeries. IOSR J Dent Med Sci. 2017;16(3):33–40.
20. Naaz S, Shukla U, Srivastava S, Ozair E, Asghar A. A comparative study of analgesic effect of intrathecal nalbuphine and fentanyl as adjuvants in lower limb orthopaedic surgery. J Clin Diagn Res. 2017;11(7):UC25–8.