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Research Article

A COMPARISON OF EFFICACY OF EPIDURAL BUTORPHANOL AND FENTANYL FOR POST-OPERATIVE PAIN ANALGESIA IN LOWER ABDOMINAL AND LOWER LIMB SURGERIES UNDER EPIDURAL ANESTHESIA: A PROSPECTIVE RANDOMIZED DOUBLE-BLINDED STUDY

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ABSTRACT

Objective: Lower doses of epidural opioids can achieve post-operative analgesia for infraumbilical surgeries. A study was conducted to compare the efficacy of epidural butorphanol and fentanyl for post-operative analgesia, onset, duration, and side effects in infraumbilical surgeries.

Methods: A study was conducted on 80 adult patients, both male and female, aged between 20 and 60 years, having American Society of Anesthesiologists Physical Status I and II, who were undergoing lower abdominal and lower limb surgeries under epidural anesthesia. The patients were randomly divided into two groups: Group A and Group B. Both groups were given injections of bupivacaine 20 mL of 0.5% epidurally. In the post-operative period, when the patient's Visual Analog Scale score was more than 4, Group A was administered butorphanol 2 mg followed by top-up doses of 0.5 mg, and Group B was administered fentanyl 50 µg followed by top-up doses of 15 µg, which were diluted to 10 mL in normal saline. Along with cardiorespiratory parameters, the study also noted onset, duration, quality of analgesia, and the number of epidural doses in 24 h. The statistical analysis was done using Student's t-test and two-tailed Fisher's exact test or Chi-square (χ^2) test, and a significant value of $p<0.05$ was considered.

Results: In comparing the post-operative analgesia between both groups, it was found that Group B had significant early onset of analgesia (2.600±0.4557 vs. 6.087±0.7501), shorter duration of analgesia (200.08±26.257 vs. 366.25±42.829), a higher number of epidural doses administered (3.75±1.171 vs. 2.98±0.733), lower quality of analgesia (2.55±0.504 vs. 3.18±0.636), and a greater incidence of vomiting (30.0% vs. 2.5%) when compared to group A.

Conclusion: Superior analgesia with higher sedation can be achieved through epidural butorphanol, while fentanyl has a quicker onset of analgesia but a higher tendency for vomiting. Our conclusion is that both options, fentanyl and epidural butorphanol, are safe and effective for achieving post-operative pain relief.

Keywords: Epidural anesthesia, Butorphanol, Fentanyl, Postoperative analgesia.

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INTRODUCTION

Epidural anesthesia is a technique that may be used as a primary surgical anesthetic and for post-operative pain management. An optimal method of epidural analgesia for major surgical procedures should deliver efficient pain management while causing minimal adverse reactions and ensuring high levels of patient contentment. It would also obtund central sensitization and pain-induced organ dysfunction, improving outcomes. The use of epidural analgesia for pain relief was revolutionized by the use of epidural opioids after the discovery of opioid receptors in the dorsal horn of the spinal cord. Both pre-synaptic and post-synaptic effects of opioids occur in the dorsal horn, which impacts the modulation of nociceptive input. However, opioids do not cause any motor or sympathetic blockade. Butorphanol is a lipophilic narcotic with weak µ-receptor agonist and antagonist activity, as well as potent κ-receptor agonism [1]. Its potent analgesic and sedative effects do not cause respiratory depression. Butorphanol is commonly administered to manage pain after surgery and during childbirth [2,3]. Fentanyl, characterized by its high lipid solubility, functions as a potent µ-receptor agonist and is a phenylpiperidine derivative. It exhibits a rapid onset and short duration of action. Few studies have compared the use of butorphanol and fentanyl for surgeries and post-operative analgesia managed with epidural anesthesia.

METHODS

After approval from the Hospital Ethical Committee with written informed consent, this prospective randomized double-blinded study was conducted in the Department of Anaesthesiology Base Hospital Delhi Cantt.

Inclusion and exclusion criteria

Adult patients of age between 20 and 60 years, either sex, and American Society of Anesthesiologists (ASA) Physical Status Classification I and II, who received epidural anesthesia for lower abdominal and lower limb surgery, were included in the study. Patient refusal, spinal deformity, bleeding diathesis, sepsis, and significant cardiorespiratory and hepatic, renal, and neurological disease were excluded from the study.

Sample size calculation

After discussion with a statistician and considering a Type I error of 0.05 and a Type II error of 0.1 to yield a power of 80%, a total sample size of 80 patients was calculated and divided into two groups of 40 patients each using the computer-generated random table.

Procedure

The pre-anesthetic checkup was done for all included patients, relevant details related to history and examination were recorded and necessary

investigations were done. All the patients were kept nil per oral 6 h before surgery. The Visual Analog Scale (VAS) was introduced to the patients to make them familiar with it and taught them to rate the pain on the VAS scale. The VAS consisted of a 10 cm line, marked at 1 cm each where the mark "0" means no pain, and mark "10" represents the worst possible pain. The numbers marked by the patient were taken as units of pain intensity. A trained anesthesia technician prepared the study drugs and the anesthesiologist performing the epidural block and recording the observations was kept blinded during the study period. Tablet ranitidine 150 mg and alprazolam 0.25 mg were given orally as premedication 2 h before the surgery. In the operation theater, the patient was connected to a multichannel monitor with ASA Standard Monitoring such as electrocardiography, heart rate (HR), non-invasive blood pressure, pulse oximetry (SpO_2), temperature, and respiratory rate (RR) were carried out and recorded. Peripheral venous access with an 18G cannula was secured. The patients were pre-loaded with Ringer's lactate 10 mL/kg over 15–20 min before the epidural block. The epidural space was identified in the L3-4 intervertebral space using the loss of resistance technique by 18G Tuohy's needle with proper positioning under aseptic precautions. The epidural catheter was threaded 2–3 cm inside the epidural space and fixed. A 3 mL test dose of 2% lignocaine with adrenaline 1:2,00,000 was injected through the catheter and observed for inadvertent placement. After confirming the correct placement of the catheter, epidural anesthesia was activated with a 20 mL bolus dose of 0.5% bupivacaine. The onset of analgesia, level of sensory blockade (maximum sensory level after 30 min), motor blockade (Bromage scale), and duration of surgery were noted. The onset of analgesia (sensory block) is defined as the time interval between administering local anesthetic (0.5% bupivacaine) epidurally and loss of sensation to blunt pinprick. The level of sensory blockade is the maximum sensory dermatome level after 30 min of administering the local anesthetic (0.5% bupivacaine) in the epidural space. Motor blockade in the lower limb was assessed using a modified Bromage scale.

- 0 = no paralysis, able to lift extended leg at the hip
- 1 = unable to raise the extended leg, able to flex the knee but not lift the extended leg
- 2 = unable to flex the knee, able to move the foot only
- 3 = unable to flex the ankle. Unable to move even the foot.

The onset time of motor blockade was defined as the interval between administration of local anesthetic (0.5% bupivacaine) epidurally to the point in which the Bromage score of 3 was achieved, respectively. The duration of motor blockade was defined as the time interval between administration of local anesthetic (0.5% bupivacaine) epidurally to the point where Bromage score 0 was reached (Table 1).

Data collection

Post-operative analgesia was assessed by VAS score and if VAS score was >4, Group A patients received butorphanol 2 mg epidurally followed by top-up doses of 0.5 mg if required and Group B patients were administered fentanyl 50 µg epidurally followed by top-up doses of 15 µg if required (VAS >4) for the relief of post-operative pain. VAS score was noted initially at 5, 10, 15, 30, 45, and 60 min, then hourly for 8 h followed by 4-hourly monitoring for 24 h. The timing of incremental top-ups, the interval between epidural top-ups, and the total dose given in 24 h were recorded. If analgesia was inadequate even after two consecutive incremental epidural top-up doses given 20–30 min apart, patients were given rescue analgesia in the form of injection of diclofenac sodium 75 mg intramuscular and were excluded from the study. Hemodynamic parameters monitoring was done before activating epidural anesthesia and subsequently at 5, 10, 15, 30, 45, 60, and 90 min and the end of the surgery. After the surgery, the patient was shifted to the recovery room. Side effects such as sedation, pruritus, nausea, vomiting, respiratory depression, and hypotension were also noted.

The sedation was assessed after giving the study drug-based ASA as follows:

- No sedation, the patient was wide awake
- Mild sedation, the patient is awake but drowsy
- Moderate sedation, sleepy but arousable
- Severe sedation, unarousable.

Statistical analysis

Data were expressed as mean±standard deviation and percentages. The data were analyzed using Statistical Package for the Social Sciences (SPSS) 20.0 Appropriate univariate and bivariate statistical analyses were carried out using the Student's t-tests for the continuous variables and two-tailed Fisher's exact test or Chi-square (χ^2) test was used for categorical variables. $p<0.05$ was considered statistically significant. $p<0.0001$ was considered highly significant.

RESULTS

A total of 80 patients who underwent lower abdominal and lower limb surgeries were enrolled in the study and were randomly divided into two groups. The demographic characteristics in both groups exhibited marked similarities and did not show any statistically significant difference ($p>0.05$) (Table 2).

Duration of surgery is comparable in both groups ($p>0.05$).

Epidural fentanyl provided a significantly faster onset of pain relief than with epidural butorphanol ($p<0.001$).

Duration and quality of analgesia are significantly longer and better for butorphanol than in the fentanyl group ($p<0.001$).

A number of epidural top-ups required in the initial 24 h is significantly more in the fentanyl group ($p<0.001$) (Table 3).

Pre-operative HR, systolic blood pressure, diastolic blood pressure (DBP), and SpO_2 were also comparable in the groups. Throughout the study period, the mean values of hemodynamic parameters remained comparable between the groups ($p>0.05$) (Table 4).

The frequency of nausea and pruritis is higher in Group B (12.5% both) compared to Group A (5% and 2.5%, respectively), which are comparable in both groups ($p>0.05$).

Sedation is significantly higher in Group A compared to Group B ($p<0.001$) and episodes of vomiting were higher in Group B as compared to Group A ($p<0.001$) (Table 5).

DISCUSSION

Post-operative pain is an acute pain, which starts with the surgical trauma and usually ends with tissue healing. Better analgesia is achieved

Table 1: Quality of analgesia

Pain score	Pain relief
0	No pain relief
1	Poor pain relief
2	Fair pain relief
3	Good pain relief
4	Excellent pain relief

Table 2: Demographic profile of the patients in both groups

Demographic characteristics	Group A (n=40)	Group B (n=40)
Age (years) (Mean±SD)	45.40±9.94	43.55±10.12
Sex (Male: Female)	19:21	22:18
Weight (kg) (Mean±SD)	58.32±7.98	56.77±8.38

Data are presented as Mean±SD, Ratio, n: Number of participants

Table 3: Characteristics of epidural butorphanol and fentanyl

Parameters	Group A (n=40) (Mean±SD)	Group B (n=40) (Mean±SD)	p-value
Duration of surgery (min)	117.37±28.622	104.88±21.378	t=2.213; *P*>0.05 (NS)
Onset of analgesia (in min) Mean±SD)	6.087±0.7501	2.600±0.4557	t=25.130; P<0.001** (HS)
Duration of analgesia (in min) Mean±SD	366.25±42.829	200.08±26.257	t=20.921; P<0.001** (HS)
No epidural dosage in 24 h (Mean±SD)	2.98±0.733	3.75±1.171	t=−3.547; P<0.001** (HS)
Quality of analgesia (Mean±SD)	3.18±0.636	2.55±0.504	t=4.872; P<0.001** (HS)

**p<0.001 is highly significant, Mean±SD, t value-T test

Table 4: Comparison of hemodynamic parameters

Time interval	Hemodynamic parameters	Group A	Group B	p-value
		Mean±SD	Mean±SD	
0 min	Heart Rate	82.00±2.68	83.20±2.67	p>0.05(NS)
	Systolic blood pressure	121.40±8.66	120.60±6.32	p>0.05(NS)
	Diastolic Blood Pressure	80.45±7.49	81.10±6.75	p>0.05(NS)
	Oxygen Saturation(Spo_2)	97.68±1.46	98.70±1.18	p>0.05(NS)
5 min	Heart rate	82.15±7.45	82.40±5.42	p>0.05(NS)
	Systolic blood pressure	122.23±6.72	121.43±5.97	p>0.05(NS)
	Diastolic blood pressure	79.75±6.48	80.40±5.99	p>0.05(NS)
	Oxygen Saturation(Spo_2)	97.35±1.14	98.38±1.17	p>0.05(NS)
10 min	Heart rate	79.53±6.87	81.33±6.21	p>0.05(NS)
	Systolic blood pressure	122.93±6.50	120.38±5.54	p>0.05(NS)
	Diastolic blood pressure	81.08±6.91	81.85±6.21	p>0.05(NS)
	Oxygen saturation (Spo_2)	97.93±1.31	98.08±1.14	p>0.05(NS)
15 min	Heart rate	76.95±5.18	81.45±4.82	p>0.05(NS)
	Systolic blood pressure	123.35±6.15	120.80±5.99	p>0.05(NS)
	Diastolic blood pressure	81.18±6.86	81.50±6.51	p>0.05(NS)
	Oxygen saturation (Spo_2)	98.03±1.39	98.05±1.15	p>0.05(NS)
30 min	Heart rate	78.03±5.60	80.73±5.27	p>0.05(NS)
	Systolic blood pressure	122.28±6.25	121.73±4.89	p>0.05(NS)
	Diastolic blood pressure	79.85±6.38	80.50±5.93	p>0.05(NS)
	Oxygen saturation (Spo_2)	97.78±1.39	98.33±1.05	p>0.05(NS)
45 min	Heart rate	77.98±5.74	82.18±4.86	p>0.05(NS)
	Systolic blood pressure	122.75±6.16	122.05±5.63	p>0.05(NS)
	Diastolic blood pressure	80.55±7.36	81.13±6.75	p>0.05(NS)
	Oxygen saturation (Spo_2)	97.78±1.23	98.40±0.98	p>0.05(NS)
1 h	Heart rate	75.85±5.22	79.50±7.01	p>0.05(NS)
	Systolic blood pressure	121.25±7.61	120.00±6.45	p>0.05(NS)
	Diastolic blood pressure	79.80±6.62	80.50±5.94	p>0.05(NS)
	Oxygen saturation (Spo_2)	97.88±1.36	98.70±1.07	p>0.05(NS)
2 h	Heart rate	75.53±4.87	80.53±5.70	p>0.05(NS)
	Systolic blood pressure	120.85±7.45	120.60±5.66	p>0.05(NS)
	Diastolic blood pressure	81.55±7.07	81.65±6.76	p>0.05(NS)
	Oxygen saturation (Spo_2)	97.85±1.42	98.55±1.26	p>0.05(NS)
4 h	Heart Rate	75.00±4.50	79.90±4.44	p>0.05(NS)
	Systolic blood pressure	121.58±6.18	120.23±6.06	p>0.05(NS)
	Diastolic blood pressure	81.05±7.49	81.50±7.15	p>0.05(NS)
	Oxygen saturation (Spo_2)	97.80±1.29	98.60±1.06	p>0.05(NS)

Data are presented as Mean±SD, NS: Non-significant

Table 5: Comparison of side effects of epidural butorphanol and fentanyl groups

Side effects	Group A (n=40)	Group B (n=40)	Significance
Nausea (%)	2 (5.0)	5 (12.5)	t=1.20; P>0.05(NS)
Pruritis (%)	1 (2.5)	5 (12.5)	t=1.73; P>0.05(NS)
Sedation (%)	22 (55.0)	0 (0.0)	t=6.99; P<0.001**(HS)
Vomiting (%)	1 (2.5)	12 (30.0)	t=3.59; P<0.001**(HS)

Data are presented as percentage (%),**p<0.001 – Highly significant (HS), P>0.05 – Non-significant (NS), t value – Student's t-test

with lower doses of opioid medications when these are administered in extradural space as compared to intramuscular or intravenous routes of administration. Adverse effects associated with narcotics are post-operative nausea and vomiting, pruritis, respiratory depression, and urinary retention.

Fentanyl was chosen for the study due to advantages such as no neurolytic preservatives, being highly lipophilic, better retained within the epidural space, having a short half-life, and being stable in salt solutions for more than 72 h. Butorphanol tartrate is an agonist-antagonist opioid analgesic. It has an agonistic activity on the kappa receptor and either antagonist or partial agonist on the mu receptor. The use of butorphanol in epidural space has been employed successfully for the relief of pain in the post-operative period. It is relatively safer than pure agonist opioids because of its ceiling effect on, lower addiction potential respiratory depression, lesser nausea, vomiting, pruritus, and urinary

retention. In our study, patients in Group A reported delayed onset and longer duration of analgesia, with mean values of 6.08±0.75 min and 366.25±42.82 min, respectively, compared to Group B, with mean values of 2.60±0.45 min and 200.08±26.25 min, respectively (p<0.001). Our findings are similar to the study conducted by Parikh *et al*. [4] who evaluated epidural butorphanol versus morphine for post-operative analgesia in patients undergoing open nephrectomy. Patients in the butorphanol group received 0.04 mg/kg butorphanol epidurally whereas the morphine group received 0.06 mg/kg morphine epidurally. The duration of analgesia was significantly better in the morphine group compared to the butorphanol group (p<0.05). The duration of post-operative analgesia is comparable to our study (339.13±79.57 min vs. 366.25±42.82 min). Pokharel *et al*. [5] conducted a study to observe the effectiveness and safety of low-dose epidural butorphanol for post-operative analgesia after cesarean section and reported that bupivacaine with low-dose butorphanol 0.5 mg as an adjuvant provided better and prolonged analgesia compared to bupivacaine alone and with 0.75 mg butorphanol adjuvant. Jose *et al*. [6] compared the efficacy and safety of epidural buprenorphine and butorphanol tartrate for post-operative analgesia. Group A received 1 mL (0.3 mg) of buprenorphine, Group B received 1 mL (1 mg) of butorphanol tartrate epidurally. The butorphanol analgesia duration was comparable with our study (342.53±47.42 vs. 366.25±42.82 min). Malik *et al*. [7] compared the safety and effectiveness of post-operative analgesia using epidural butorphanol 2 mg and epidural fentanyl 50 μg. The duration and quality of analgesia with the butorphanol group were better than the fentanyl group. A smaller number of epidural top-ups were required in the butorphanol group compared to the fentanyl group in the post-operative period. Similarly in our study, the quality of analgesia was better in the butorphanol group compared to the fentanyl group (p<0.05). Patients in the butorphanol group required less epidural dosage in 24 h compared to the fentanyl group (p<0.05). The two groups' hemodynamic parameters such as pulse rate, systolic, DBP, RR, and oxygen saturation levels were comparable at different time intervals during the 24-h observation period (p>0.05). Palacios *et al*. [8] conducted a randomized double-blind comparative study for post-operative analgesia in cesarean section. They concluded that epidural butorphanol of 1 mg, 2 mg, and 4 mg has a rapid onset of pain relief as compared to morphine 5 mg (p<0.05). Lytle *et al*. [9] reported the use of fentanyl (50 μg) epidurally provided effective postoperative analgesia with minimal side effects which is comparable with our study. Sharma *et al*. [10] studied the effect of Epidural butorphanol 2 mg and fentanyl 75 mcg for post-operative analgesia using combined spinal epidural anesthesia technique in lower abdominal and lower limb surgeries. They reported faster onset analgesia with the fentanyl group and longer duration of analgesia in the butorphanol group. Banerjee and Pattnaik [11] compared epidural butorphanol, fentanyl, and nalbuphine for post-operative analgesia in lower abdominal surgeries. Duration of post-operative analgesia was longer in the butorphanol group and onset of analgesia was quick in the fentanyl group similar to our study. Kaur and Bajwa [12] compared epidural butorphanol and fentanyl as adjuvants in lower abdominal surgeries. They concluded that delayed onset and prolonged duration of postoperative analgesia in the butorphanol group compared to the fentanyl Group. Birajdar *et al*. [13] compared epidural nalbuphine and fentanyl with bupivacaine for post-operative analgesia in lower limb surgeries. Epidural fentanyl has a faster onset of action compared to nalbuphine and has a longer duration of post-operative analgesia compared to nalbuphine (p=0.05%). Venkatraman and Sandhiya [14] evaluated the efficacy of epidural butorphanol tartrate in post-operative analgesia in the immediate post-operative period and reported a prolonged duration of analgesia with excellent quality of analgesia with epidural butorphanol. Chandra and Babu [15] compared Epidural butorphanol, nalbuphine, and fentanyl for post-operative analgesia in lower abdominal surgeries and found an early onset of analgesia in the fentanyl group and a longer duration of post-operative analgesia in the butorphanol group similar to our study.

In our study, the proportion of patients experiencing nausea, pruritus, sedation, and vomiting in Group A and Group B were (5.0% vs. 12.5%), (2.5% vs. 12.5%), (55.0% vs. 0% p<0.001), and (2.5% vs. 30% p<0.001), respectively. Hunt *et al*. [1] and Naulty *et al*. [16] reported a higher incidence of sedation with epidural butorphanol.

Ackerman *et al*. [17] and Palacios *et al*. [8] reported incidence of pruritus was 7% versus 1.4% with butorphanol epidurally, respectively. Lytle *et al*. [9] reported incidence of pruritis was 4% with fentanyl and nausea was 25.5% with epidural butorphanol.

CONCLUSION

We have found that epidural administration of butorphanol provides longer-lasting and denser analgesia with fewer side effects such as nausea, vomiting, pruritus, and sedation, compared to fentanyl. However, the onset of analgesia was delayed with butorphanol. Sedation was the most notable side effect in the butorphanol group, which was statistically significant at p<0.05 compared to epidural fentanyl. Epidural fentanyl provided a rapid onset of analgesia, albeit with slightly higher incidences of nausea and pruritus, which were not statistically significant at p>0.05. Vomiting was significantly higher in the fentanyl group compared to the epidural butorphanol group (p<0.05). In conclusion, both butorphanol and fentanyl are safe and effective drugs for post-operative epidural analgesia, with minor side effects.

AUTHORS CONTRIBUTION

All authors contributed to manuscript preparation.

CONFLICTS OF INTEREST

No conflict of interest.

AUTHORS FUNDING

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REFERENCES

1. Hunt CO, Naulty JS, Malinow AM, Datta S, Ostheimer GW. Epidural butorphanol-bupivacaine for analgesia during labour and delivery. Anesth Analg. 1989;68:323-7.
2. Bharti N, Chari P. Epidural butorphanol-bupivacaine analgesia for postoperative pain relief after abdominal hysterectomy. J Clin Anesth. 2009;21:19-22.
3. Shrestha CK, Sharma KR, Shrestha RR. Comparative study of epidural administration of 10 ml of 0.1% bupivacaine with 2 mg butorphanol and 10 ml of 0.25% plain bupivacaine for analgesia during labour. JNMA J Nepal Med Assoc. 2007;46:1-6.
4. Parikh GP, Veena SR, Vora K, Parikh B, Joshi A. Comparison of epidural butorphanol versus epidural morphine in postoperative pain relief. Middle East J Anaesthesiol. 2014 Feb;22(4):371-6.
5. Pokharel K, Rahman TR, Singh SN, Bhattarai B, Basnet N, Khaniya S. The efficacy and safety of low-dose epidural butorphanol for postoperative analgesia following cesarean delivery. JNMA J Nepal Med Assoc. 2008 Apr-Jun;47(170):57-61
6. Jose DE, Ganapathi P, Anish Sharma NG, Shankaranarayana P. Postoperative pain relief with epidural buprenorphine versus epidural butorphanol in laparoscopic hysterectomies: A comparative study. Anesth Essays Res. 2016 Jan-Apr;10(1):82-7.
7. Malik P, Manchanda C, Malhotra N. Comparative evaluation of epidural fentanyl and butorphanol for postoperative analgesia. J Anaesth Clin Pharmacol. 2006;22(4):377-82.
8. Palacios QT, Jones MM, Hawkins JL, Adenwala JN, Longmire S, Hess KR, *et al*. Post-caesarean section analgesia: A comparison of epidural butorphanol and morphine. Can J Anaesth. 1991;38(1):24-30.
9. Lytle SA, Goldsmith DM, Neuendorf TL, Lowry ME. Postoperative analgesia with epidural fentanyl. J Am Osteopath Assoc. 1991;91(6):547-50.
10. Sharma S, Naik S, Jamale PB, Dhulkhed VK, Prasoon A. A comparison of epidural butorphanol 2mg and fentanyl 75 mcg for postoperative analgesia using combined spinal epidural anaesthesia technique: A randomized double-blind clinical study. Int J Med Health Res. 2018 Apr;4(4):97-101.
11. Banerjee S, Pattnaik SK. A comparative study between epidural butorphanol, nalbuphine and fentanyl for postoperative analgesia in

lower abdominal surgeries. Asian J Pharm Clin Res. 2017;10(5):383-8. doi: 10.22159/ajpcr. 2017.v10i5.16802
12. Kaur J, Bajwa SS. Comparison of epidural butorphanol and fentanyl as adjuvants in the lower abdominal surgery: A randomized clinical study. Saudi J Anaesth. 2014;8:167-71.
13. Birajdar SB, Peerzade SF, Shabeer Ali K, Sultana SS, Mohammed Afzal A. A comparative study between epidural nalbuphine and fentanyl with bupivacaine for post operative analgesia in lower limb surgeries. Int J Adv Res. 2023;11(4):1008-22.
14. Venkatraman R, Sandhiya R. Evaluation of efficacy of epidural butorphanol tartarate for post-operative analgesia. Int J Pharm Pharm Sci. 2015;7(2):52-4.
15. Chandra AS, Babu BV. A comparative Study between epidural butorphanol, nalbuphine, and fentanyl for post-operative analgesia in lower abdominal surgeries: A prospective randomized double-blinded trial. J Med Sci Clin Res. 2019;7(12):518-26.
16. Naulty JS, Johnson M, Burger GA, Datta S,Weiss JR, Morrison J. Epidural fentanyl for post cesarean delivery pain management. Anesthesiology. 1983;59:415.
17. Ackerman WE, Juneja MM, Kaczorowski DM, Colclough GW. A comparison of the incidence of pruritus following epidural opioid administration in the parturient. Can J Anaesth. 1989;36:388-91.