ORIGINAL ARTICLE

Effect of Epidural Dexmedetomidine and Fentanyl Infusion for Postoperative Analgesia in Patients Undergoing Upper Abdominal Surgeries: A Randomized, Double-blind Study

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Abstract

Background: Effective perioperative pain management is critical for patients undergoing major upper abdominal surgeries. Epidural analgesia, a cornerstone of regional anesthesia, is widely used to manage pain in these surgical cases. Fentanyl and dexmedetomidine are commonly used additives to local anesthetics for epidural analgesia. This trial aims to compare the two additives.

Settings and design: The study was a double-blind, randomized controlled study conducted in a tertiary care hospital.

Materials and methods: The trial included patients aged 18–65 of either gender who had planned upper abdominal surgery. The patients received an epidural infusion of 0.1% bupivacaine with either dexmedetomidine or fentanyl for postoperative analgesia. Outcome variables included static and dynamic pain on the visual analogue scale (VAS), analgesic consumption, and hemodynamic variables. Each group had 34 patients.

Observations: The demographic variables were comparable between the groups. At various time points, the static and dynamic VAS score for pain were significantly lower in the dexmedetomidine group. The analgesic consumption was also lower in the dexmedetomidine group. Hemodynamic variables and complications were similar between the groups.

Conclusion: Dexmedetomidine, as an adjuvant to epidural bupivacaine, is better than fentanyl in patients undergoing upper abdominal surgery.

Keywords: Dexmedetomidine, Bupivacaine, Fentanyl, Epidural analgesia, Pain management, Local anesthetics, Postoperative pain.

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Introduction

Effective perioperative pain management is critical for patients undergoing major upper abdominal surgeries, as it significantly impacts postoperative recovery and overall patient comfort.[1] Epidural analgesia, a cornerstone of regional anesthesia, is widely used to manage pain in these surgical cases. Delivering local anesthetics directly to the epidural space provides potent pain relief, reduces the need for systemic opioids, and minimizes associated side effects. The choice of adjuncts combined with local anesthetics in epidural analgesia can further enhance analgesic efficacy and reduce adverse effects.

Bupivacaine, a long-acting local anesthetic, is commonly used for epidural analgesia due to its reliable and prolonged analgesic properties.[2,3] To potentiate its effects, it is often combined with other pharmacological agents such as opioids or α-2 adrenergic agonists. Fentanyl, a potent opioid, and dexmedetomidine, a selective α-2 adrenergic agonist, are two such adjuncts frequently used in clinical practice. Fentanyl provides strong analgesia through its action on mu-opioid receptors but is associated with dose-dependent adverse effects like respiratory depression and pruritus.[4] Dexmedetomidine, on the other hand, offers analgesia and sedation through central and peripheral mechanisms without the respiratory depression seen with opioids.

In this study, we compared the effectiveness of dexmedetomidine and fentanyl as an additive to local anesthetic in epidural infusion for postoperative analgesia in patients after upper abdominal surgery. The objective of the trial was to establish a better adjunct between dexmedetomidine and fentanyl to bupivacaine for postoperative epidural analgesia in patients after upper abdominal surgery.

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Conflict of interest: None

Materials and Methods

This prospective, double-blind, randomized controlled study was done at King George's Medical University, Lucknow, from December 2022 to April 2023. The study protocol was approved by the intuitional ethics committee (Reference number: ECR/262/Inst/UP/2013/RR-19), and the trial was registered with the Clinical Trial Registry of India (Registration number: CTRI/2022/07/043764). All the recruited patients gave informed and written consent for the study.

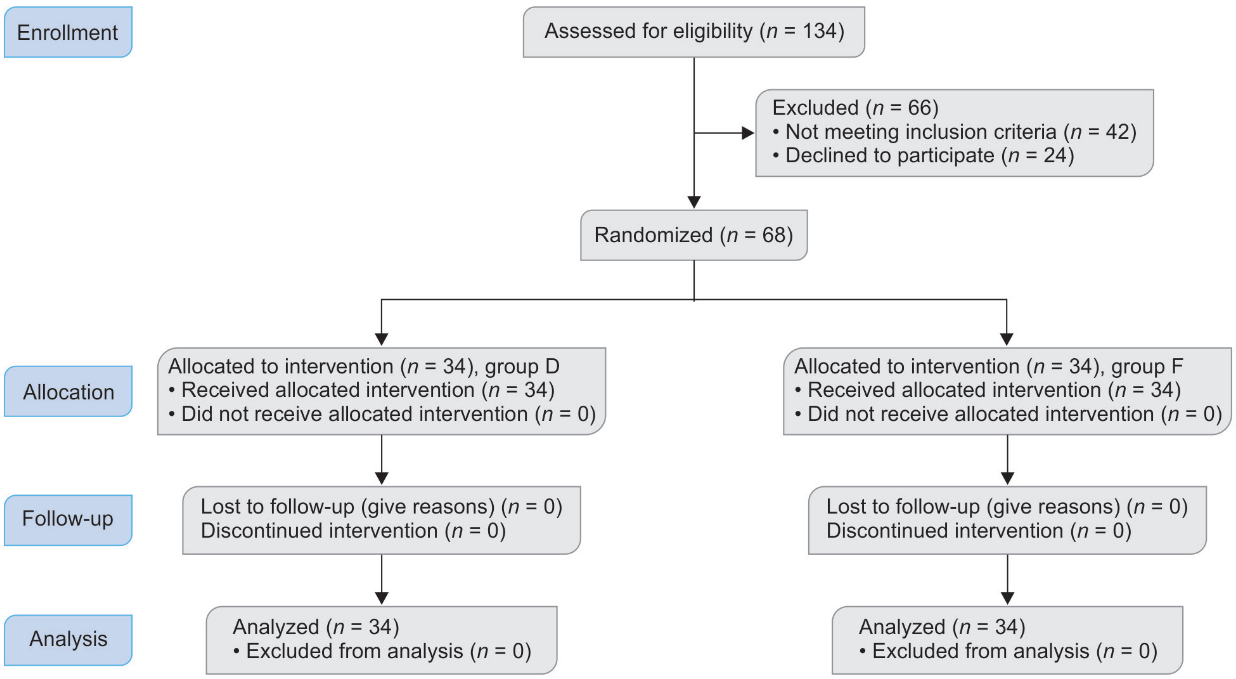

Fig. 1: CONSORT diagram showing the patient flow in the study

Patients of either gender of age between 18 and 65 years scheduled for major upper abdominal surgery under general anesthesia and belonging to ASA physical status I–III were included in the trial. Patients with a history of cardiovascular disease, respiratory disease, bleeding disorders, infection at the epidural placement site, spinal anomalies, and allergy to study medications or α-adrenergic agonists were excluded from the study.

The randomization sequence was decided by computer-generated random numbers. Allocation concealment was achieved using an opaque sealed envelope technique. The envelope containing the study medication group was opened by an anesthesia technician in a room adjacent to the operation theater where no one else was present. The technician mixed the study medication with bupivacaine in identical syringes so that the anesthetist and the observer were unaware of the drug in the syringe. The patient was also unaware of the study group allocation. The allocation sequence was generated by the first author, recruitment was done by the second author, and groups were assigned by the third author.

The recruited patients were divided by the above-mentioned technique into either of the following two groups: Group F received bupivacaine and fentanyl in epidural, and group D received bupivacaine and dexmedetomidine in epidural. In both groups, the concentration of bupivacaine was 0.1%. In group F, fentanyl was added to bupivacaine in 2 µg/mL concentration. In group D, the concentration of dexmedetomidine was 0.5 µg/mL. In both groups, the infusion was continued for 24 hours.

After the patients arrived in the operating theater, monitors were applied: Pulse oximeter, non-invasive blood pressure, and electrocardiogram. At least one intravenous access was secured, and one liter of intravenous fluid was given. The patients were then placed in a sitting position. The epidural catheter was placed between T8 and T9. After successful catheter placement, 6 mL drug solution was given as a bolus, and continuous infusion was started at 6 mL/hour. If any patient had hypotension [mean arterial pressure (MAP) < 65 mm Hg], 5 mL/kg of IV fluid was given; if responding the epidural infusion was continued at the same rate. If there was a persistent drop in MAP < 65 mm Hg, the infusion was stopped and restarted when MAP became normal. If there was bradycardia (<50 beats/min) along with hypotension intravenous injection atropine was given, infusions stopped, and these patients were excluded from the study. Injection paracetamol 1 gm IV was given if pain on the visual analogue scale (VAS) was >3 during the study period. The surgery started after giving an epidural bolus dose. Pain intensity on the VAS was the primary outcome measure. Secondary outcome measures were heart rate (HR) MAP, percentage of patients needing rescue analgesia, and side effects.

The study had a predetermined power of 0.9, and type I error of 0.05. To detect a difference in mean VAS of 0.53, with a variance of 0.324 and 0.562, 34 patients were needed in each group.[5] Our study had a sample size of 34 participants in each group. Data were managed and analyzed using statistical software SPSS version 24 (Chicago, IL, USA). The continuous quantitative data are compared using student's *t*-test and presented in mean with standard deviation. The categorical data are represented as number and percentages and were analyzed using Chi-square test. Ordinal data were analyzed using the Mann–Whitney *U*-test. A two-sided $p < 0.05$ was considered significant for all the statistical tests.

Results

Figure 1 shows the patient's flow through the trial. Table 1 shows the baseline and demographic characteristics of the patient. All the characteristics were statistically similar between the groups. Table 2 compares resting pain between the groups. Resting pain was significantly higher in group F at baseline and at 6 hours after extubation. Table 3 compares dynamic pain between the groups. Dynamic pain was significantly higher in group F at baseline, 1 hour, and 6 hours after extubation. At baseline, rescue analgesia was needed in 3 (8.82%) patients of group D and 10 (29.41%) patients

Table 1: Demographic and baseline data of the patients

Variable	*Group D (n = 34)*	*Group F (n = 34)*	*p-value*
Mean age (years)	53.9 ± 5.52	52.85 ± 6.43	$t = 0.7225$ $p = 0.4726$
Sex (M/F)	23/11	22/12	$\chi^2 = 0.0657$ $p = 0.7977$
BMI (kg/m^2)	20.9 ± 5.2	21.3 ± 4.8	$t = 0.3296$ $p = 0.7428$
ASA grade I/II/III	11/20/3	10/20/4	$\chi^2 = 0.1905$ $p = 0.9092$
Operation time (minutes)	230.52 ± 61.43	220.35 ± 50.42	$t = 0.7462$ $p = 0.4582$
Type of operation			
Whipple's surgery	7 (20.58%)	5 (14.70%)	$\chi^2 = 0.0162$
Gastrectomy	5 (14.70%)	4 (11.76%)	$p = 1.000$
Radical cholecystectomy	5 (14.70%)	6 (17.64%)	
Hydatid cystectomy	4 (11.76%)	5 (14.70%)	
Biliary stricture removal	5 (14.70%)	4 (11.76%)	
Surgical debulking of pseudomyxoma peritonei	3 (8.82%)	4 (11.76%)	
Small bowel resection	5 (14.70%)	6 (17.64%)	

Table 2: Visual analogue scale (VAS) score (Static) of enrolled patients

VAS score (Static)	*Group D (n = 34)*		*Group F (n = 34)*		
	Mean	*SD*	*Mean*	*SD*	*p-value*
Baseline (extubation)	0.94	1.16	2.15	1.35	$t = 3.964$ $p < 0.0001$*
1 hour	0.24	0.42	0.35	0.54	$t = 0.9376$ $p = 0.3519$
2 hours	0.06	0.24	0.09	0.28	$t = 0.4743$ $p = 0.6368$
4 hours	0.03	0.17	0.03	0.17	$t = 0.000$ $p > 0.9999$
6 hours	0.06	0.24	0.35	0.48	$t = 3.151$ $p = 0.0024$*
12 hours	0.03	0.17	0.03	0.17	$t = 0.000$ $p > 0.9999$
18 hours	0.00	0.00	0.00	0.00	–
24 hours	0.00	0.00	0.00	0.00	–

*Statistically significant

Table 3: Visual analogue scale score (Dynamic) of enrolled patients

VAS score (Dynamic)	*Group D (n = 34)*		*Group F (n = 34)*		
	Mean	*SD*	*Mean*	*SD*	*p-value*
Baseline (extubation)	1.91	1.04	3.12	0.80	$t = 5.377$ $p < 0.0001$*
1 hour	1.91	1.04	3.12	0.80	$t = 5.377$ $p < 0.0001$*
2 hours	0.85	0.55	1.53	0.61	$t = 4.828$ $p < 0.0001$*
4 hours	0.44	0.55	0.38	0.54	$t = 0.4539$ $p = 0.6514$
6 hours	0.15	0.43	0.21	0.47	$t = 0.5492$ $p = 0.5847$
12 hours	0.03	0.17	0.09	0.28	$t = 1.068$ $p = 0.2894$
18 hours	0.00	0.00	0.00	0.00	–
24 hours	0.00	0.00	0.00	0.00	–

*Statistically significant

in group F ($\chi^2 = 4.660$, $p = 0.0309$). At 1 hour, rescue analgesia was needed in 4 (11.76%) patients in group D and 13 (28.24%) patients in group F ($\chi^2 = 6.353$, $p = 0.0117$). At the remaining time points, rescue analgesia was not needed in any patient. Sedation scores were higher in group D at baseline (Table 4). Postoperative HR and blood pressure are shown in Figures 2 and 3. They were statistically similar at all the time points. Side effects are shown in Figure 4 and were statistically similar between the groups.

Table 4: Sedation score (Ramsay) of enrolled patients

Sedation score (Ramsay)	*Group F (N = 34)*		*Group D (N = 34)*		
	Mean	*SD*	*Mean*	*SD*	*p-value*
Baseline (extubation)	1.91	0.45	2.35	0.64	$t = 3.279$ $p = 0.0016$*
1 hour	2.00	0.00	2.00	0.00	–
2 hours	2.00	0.00	2.00	0.00	–
4 hours	2.00	0.00	2.00	0.00	–
6 hours	2.00	0.00	2.00	0.00	–
12 hours	2.00	0.00	2.00	0.00	–
18 hours	2.00	0.00	2.00	0.00	–
24 hours	2.00	0.00	2.00	0.00	–

*Statistically significant

Discussion

Regional analgesia is an important part of perioperative pain management.[6–9] Epidural analgesia is the most commonly used regional analgesic technique, especially in patients undergoing major upper abdominal surgeries. Epidural analgesia has become

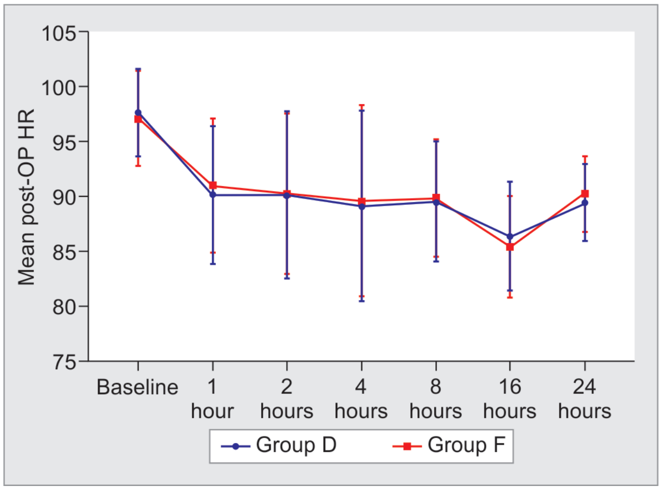

Fig. 2: Postoperative heart rate (HR) of enrolled patients

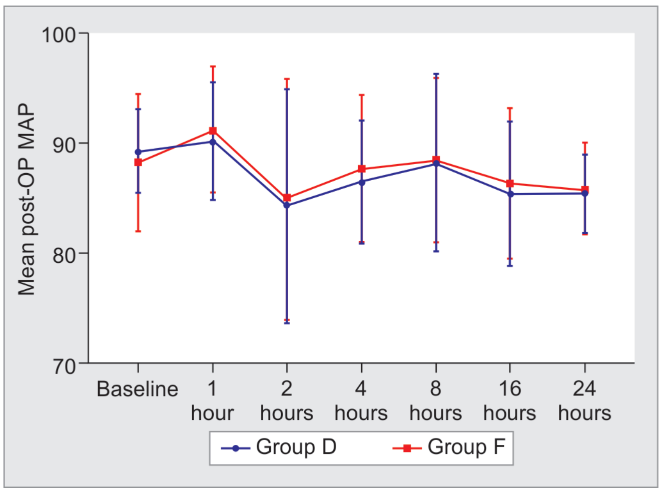

Fig. 3: Postoperative MAP of enrolled patients

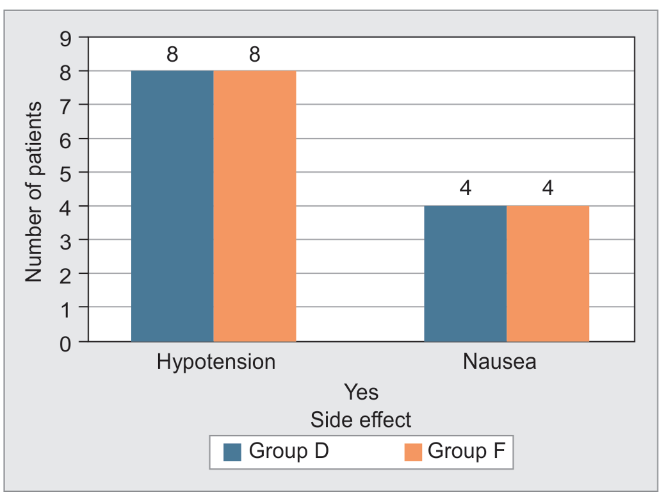

Fig. 4: Graphical distribution of side effects in enrolled patients

an integral part of postoperative care. This technique offers numerous benefits in managing pain after surgery, enhancing patient recovery, and improving overall outcomes. One of the primary benefits of epidural analgesia is its superior pain control. Compared to systemic analgesics like opioids, epidural analgesia provides more effective pain relief, especially for major abdominal, thoracic, and lower limb surgeries. Delivering medication directly to the spinal nerves, blocks pain signals more efficiently, allowing patients to experience less discomfort. Effective pain management is crucial in the postoperative period as it can significantly reduce stress responses to surgery, thereby enhancing recovery. Moreover, epidural analgesia minimizes the reliance on systemic opioids, which are often associated with numerous adverse effects. Opioids, while effective for pain relief, can lead to adverse effects such as nausea, vomiting, constipation, respiratory compromise, and the potential for addiction. By reducing the need for systemic opioids, epidural analgesia helps mitigate these risks, leading to a more comfortable and safer recovery for patients. Epidural analgesia also promotes earlier mobilization, which is a key factor in postoperative recovery. Effective pain control enables patients to participate in physical therapy and ambulation sooner, reducing the risk of complications such as deep vein thrombosis (DVT), pulmonary embolism, and muscle atrophy. Early mobilization is particularly important for elderly patients and those with comorbid conditions, as it can significantly improve their overall prognosis and reduce hospital stay duration. Additionally, epidural analgesia has been shown to improve pulmonary function. After major abdominal or thoracic surgeries, patients often experience impaired lung function due to pain, which can lead to shallow breathing and an increased risk of pneumonia. Epidural analgesia facilitates deeper breathing and better cough effort, helping to maintain optimal lung function and prevent pulmonary complications. Cardiovascular stability is another advantage of epidural analgesia. By providing consistent and effective pain relief, it reduces the stress response to surgery, which can cause fluctuations in blood pressure and HR. This is particularly beneficial for patients with cardiovascular diseases, as it minimizes the risk of cardiac events in the postoperative period. Effective pain control alleviates patient discomfort, facilitates postoperative recovery, and reduces the incidence of chronic pain syndromes.

Various pharmacological agents are used in epidural analgesia to enhance pain relief and minimize side effects.[6,7] Among these, bupivacaine, a long-acting local anesthetic, is commonly combined with adjuncts like opioids or α-2 adrenergic agonists to potentiate analgesic effects.[9] This trial aimed to compare the efficacy and safety of two combinations: Bupivacaine with fentanyl and bupivacaine with dexmedetomidine in patients undergoing major upper abdominal surgeries.

We observed that the mean VAS score (static) at baseline was statistically lower in group D compared to group F. The VAS score (dynamic) at baseline was significantly higher in group F than in group D. At 1 and 2 hours, a significant difference in the same was observed. The sedation score was also higher initially in dexmedetomidine as compared to the fentanyl group. Significantly more rescue analgesia was required in the fentanyl group as compared to dexmedetomidine.

Dexmedetomidine is a selective α-2 receptor agonist with a much higher affinity for the α-2 receptors than the α-1 receptors. The ratio of this affinity is 8 times that of clonidine.[10,11] The analgesic effects of dexmedetomidine are due to both central and peripheral mechanisms. In the central nervous system, dexmedetomidine acts at the α-2 receptor in the locus coeruleus and reduces the sympathetic outflow, causing analgesia and sedation. Dexmedetomidine also blocks the pre-synaptic C-fibers as well as the post-synaptic dorsal horn neurons. Fentanyl is an opioid analgesic and produces analgesia by acting on μ opioid receptors. Being an opioid, it causes dose-dependent respiratory depression, pruritis, urinary retention, and constipation. Dexmedetomidine, on the other hand, is devoid of such effects. Dexmedetomidine causes minimal respiratory depression.

Other authors have compared dexmedetomidine and fentanyl as adjuvant to local anesthetics in epidural analgesia and anesthesia. The observations of our trial concur with the findings of these trials.

Akhondzadeh compared dexmedetomidine with fentanyl as an additive to neuraxial ropivacaine in postoperative patients after orthopedic surgery.[12] They found that compared to fentanyl, dexmedetomidine hastened the speed of block onset and provided better pain relief in terms of the intensity pain and duration of pain relief. Side effects were similar between the groups. In a systemic review and meta-analysis by Qian et al., it was observed that patients receiving dexmedetomidine had a faster onset of anesthesia and longer duration of analgesia.[13] This study included 672 patients and compared dexmedetomidine to fentanyl. Alansary and Elbeialy compared dexmedetomidine and fentanyl as additive to bupivacaine in patients under general anesthesia.[14] They found that dexmedetomidine provided better pain control than fentanyl in the postoperative period. Our findings of better analgesia with dexmedetomidine are similar to the findings of these trials. In other types of surgeries also, dexmedetomidine is superior to fentanyl as an additive to epidural local anesthetics.[15–18]

Our study included patients undergoing only upper abdominal surgery. This is a limitation as the findings of the trial may not be generalizable to other types of surgery.

Conclusion

Compared to fentanyl, the addition of dexmedetomidine to bupivacaine produces better pain relief in the postoperative period in patients undergoing upper abdominal surgery under general anesthesia.

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