Original Article

Continuous Epidural versus Transdermal Fentanyl for Postoperative Analgesia after Total Abdominal Hysterectomy: A Randomised Comparative Study

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Abstract

Background: This study evaluated and compared the effectiveness and safety profiles of fentanyl administered through a transdermal patch versus continuous epidural infusion for postoperative pain control in patients who had undergone total abdominal hysterectomy (TAH). **Material and Methods:** This was a prospective observational comparative randomized study carried out among 42 ASA I–II patients of age 18 to 60 years who underwent TAH at a tertiary hospital in South India (June 2021–November 2022). Patients were randomly allocated into Group E (epidural fentanyl infusion) and Group T (transdermal fentanyl patch). Hemodynamic stability and pain were assessed 2–24 hours postoperatively. Ramsay and Bromage scores were used for assessing sedation and motor block. SPSS v25 was used for analyzing data, and $p < 0.05$ was considered significant. **Results:** There were significantly lower VAS scores in Group E at 6, 8, and 12 hours ($p = 0.019$, <0.0001, <0.0001, respectively), indicating better analgesia. Epidural drug consumption was higher in Group T (123.67 ± 4.41 mL vs. 113.81 ± 3.63 mL, $p < 0.0001$). Rescue analgesic requirement and incidence of nausea or vomiting were similar across groups. Hemodynamically, patients were stable in both groups postoperatively. Ramsay and Bromage scores were comparable, showing no excessive sedation or motor block. **Conclusion:** Both routes provided effective analgesia, but continuous epidural fentanyl yielded superior pain control, reduced drug requirement, and higher patient satisfaction, making it the preferred postoperative analgesic technique following TAH.

Keywords: analgesia, epidural, fentanyl, hysterectomy, nausea, Visual analogue scale, vomiting.

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Introduction

Total abdominal hysterectomy (TAH) is a major common surgical procedure performed at all levels of hospitals and carries a significant risk of postoperative morbidity with postoperative pain. From an anesthetist's point of view, control of postoperative pain remains important since it may affect the quality of life, mobilization, and resumption of daily activities. Moreover, control of postoperative pain allows for better comfort, outcomes, and early discharge.[1]

The use of epidural analgesia has been widely adopted, with the exceptions of patients having coagulopathy, raised intracranial tension, local sepsis, or personal refusal. Opioids remain a popular choice for postoperative analgesia, among which fentanyl has been the most common choice, with other categories of drugs being ropivacaine, bupivacaine, levobupivacaine, tramadol, ketamine, and meperidine.[2]

Fentanyl remains the most widely utilized among various opioid analgesics. It is preferred instead of morphine and other opioids because of its favorable physicochemical characteristics. As a synthetic opioid, fentanyl is estimated to be 80–300 times more potent than morphine, with an analgesic index nearly four times higher. It is a synthetically produced compound with a relatively small molecular size and high solubility in both lipid and water. These properties contribute to its potent analgesic effect and make it a suitable candidate for administration through the transdermal route.[3,4]

Against the continuous epidural fentanyl infusion, transdermal fentanyl patches have been introduced and approved by the USFDA, especially for patients resistant to opioids or needing round-the-clock opioid medications. Though transdermal fentanyl has not been advised for acute postoperative pain due to the risk of severe respiratory depression and, in some cases, mortality, studies have shown that transdermal fentanyl demonstrates superiority over placebo in providing relief from postoperative pain among patients undergoing major abdominal surgeries, including total abdominal hysterectomy.[5]

Literature search shows that the superiority of transdermal

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fentanyl patches over continuous epidural fentanyl infusion has not been proven, and no study has been conducted so far among patients undergoing TAH.

Thus, the present study was conducted to compare transdermal fentanyl with epidural fentanyl for postoperative pain control among patients who underwent major abdominal surgeries, i.e., total abdominal hysterectomy. The results may help determine whether transdermal fentanyl holds superiority over continuous epidural fentanyl in terms of efficacy and safety, thereby supporting its potential use in routine clinical practice.

Materials and Methods

A randomized, prospective, observational comparative study was carried out in patients ofaged8 to 60 years, with an ASA physical status of I–II and a BMI ranging from 20 to 35 kg/m², who were scheduled to undergo TAH in a single centre in South India from June 2021 to November 2022. Patients with known allergies to the study drugs, cognitive dysfunction, or uncontrolled comorbidities were excluded. Ethical clearance for the study was taken from the Institutional Ethics Committee (MOSC/IEC/531/2021; dated 08/01/2021), and the trial was prospectively registered with the Clinical Trials Registry of India under the registration number CTRI/2021/05/033653.

Sample Size

The sample size determination was guided by the methodology described in the study conducted by Nidhi et al,[6], who observed that the VAS scores at 12 hours and 24 hours in the transdermal fentanyl patch group were 6.07 ± 0.740 and 6.60 ± 0.770, respectively, while in the epidural fentanyl group they were 4.03 ± 1.066 and 5.90 ± 0.845, respectively. Based on these reference parameters, and considering a study power of 80% with a 5% level of significance, the required sample size was estimated to be 21 participants per group, resulting in a total of 42 subjects. After explaining the study, informed consent was obtained on the day before surgery.

Randomisation and group allotment

A total of forty-two patients were randomly assigned to either Group E (epidural fentanyl infusion) or Group T (transdermal fentanyl patch) using a closed, opaque envelope technique to ensure allocation concealment. The randomization sequence was prepared in advance, and envelopes were opened sequentially at the time of patient enrollment. Owing to the inherent differences in the mode of drug administration, blinding of the patients and investigators was not feasible, and therefore, the study was conducted as an open-label trial. But bias was minimised with standard randomisation.

Randomization was performed using a computerized random number generation method. The random number–generating function RANDBETWEEN(1,2) was used to allocate participants into one of the two study groups. If the generated number was 1, the participant was assigned to Group E, and if 2 was generated, the participant was assigned to Group T. Randomization was continued until one group reached the predetermined sample size of 21 participants; thereafter, the remaining participants were allocated to the other group to ensure equal sample sizes in both groups.

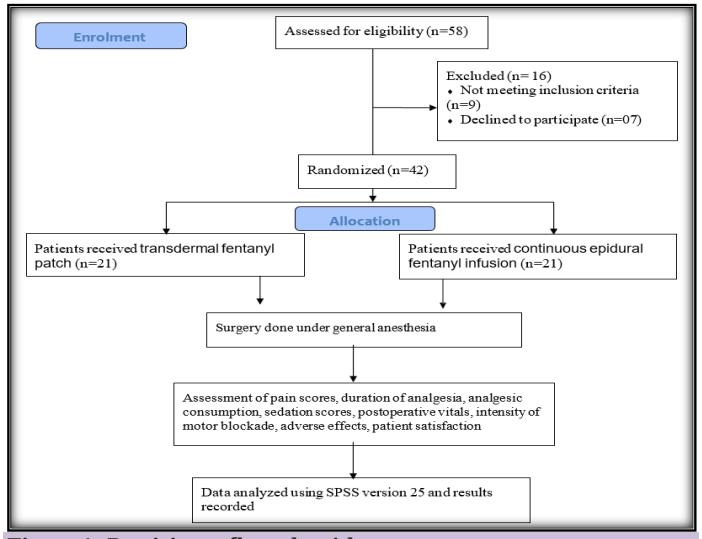

Figure 1: Participant flow algorithm

[Figure 1] shows the study flow chart.

Premedication consisted of alprazolam 0.5 mg, pantoprazole 40 mg, and ondansetron 4 mg administered both the night prior to surgery and again on the morning of the procedure. Patients were advised to fast for 6 hours for solid food and 2 hours for clear liquids. Upon arrival in the operating room, an intravenous line was secured, and standard ASA monitoring was initiated, including pulse oximetry (SpO_2), non-invasive blood pressure (NIBP), electrocardiography (ECG), and end-tidal carbon dioxide ($EtCO_2$) monitoring. The bladder was catheterized. Surgery was performed under general anesthesia.

On arrival in the operating room, premedication was administered with intravenous midazolam 1 mg. The epidural catheter was inserted prior to induction of general anesthesia. Using an 18G Tuohy needle, the epidural space was identified by the loss-of-resistance-to-air technique. A 20G flexible epidural catheter was then threaded 3–4 cm into the epidural space in a caudal direction and secured in place. After confirming absence of blood or cerebrospinal fluid on aspiration, a test dose of 3 ml of 2% lignocaine containing adrenaline 1:200,000 was administered.

General anaesthesia was induced with midazolam 1 mg, fentanyl 2 µg/kg, and propofol 2 mg/kg intravenously. Endotracheal intubation was facilitated by using rocuronium 1 mg/kg IV. Maintenance of anesthesia was carried out with sevoflurane in a mixture of oxygen and air (1:2) with controlled positive pressure ventilation. A continuous intravenous fentanyl infusion was initiated 30 minutes after induction at a rate of 0.5 µg/kg/hr and discontinued 30 minutes before the end of surgery. All patients were administered 1 g acetaminophen intravenously before the fentanyl infusion was withdrawn. Intravenous ondansetron 4 mg was administered after the surgery.

Epidural infusions in both groups were started 15 minutes before the completion of surgery with a 10 ml bolus of 0.15% ropivacaine + 2 µg/ml fentanyl in group E and 0.15%

ropivacaine in group T, followed by an epidural infusion at 5–8 ml/h. Additionally, a transdermal fentanyl patch of 25 µg/h was placed before induction of anaesthesia in group T so that effective analgesia occurred at the end of the surgical procedure.

At the completion of surgery, Extubation was carried out routinely in all patients after reversal of neuromuscular blockade using neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg intravenously. No additional pharmacological agents were administered at extubation to blunt sympathetic responses. Hemodynamic stability was maintained by ensuring adequate depth of anesthesia during emergence, gentle suctioning, and smooth extubation techniques. Any episodes of tachycardia or hypertension were managed as per institutional protocol.

Postoperative monitoring included recording heart rate, blood pressure, and SpO_2, along with assessment of pain using the Visual Analogue Scale (VAS) at rest at 2, 4, 6, 8, 12, 18, and 24 hours following surgery. A score of three or more was considered breakthrough pain and was treated with intravenous tramadol 50 mg and a diclofenac suppository. If pain remained inadequately controlled, an additional 5 ml bolus was administered through the existing epidural infusion.

Ondansetron 4 mg IV every 8 hours was administered to prevent postoperative nausea and vomiting. Ramsay Sedation Scale was used to assess sedation up to 24 hours postoperatively, and a score of more than five was considered deep sedation. Patients were supplemented with oxygen, and the need for ventilatory assistance, if any, was assessed.

Statistical analysis

Categorical variables were presented as frequencies and percentages. Continuous variables were checked for normality using the Shapiro–Wilk test. Those following a normal distribution were expressed as mean ± standard deviation, while non-normally distributed variables were reported as median with interquartile range. For comparisons, the independent t-test was used for normally distributed quantitative data, and the Mann–Whitney U test was applied to non-normal quantitative variables. Categorical variables were compared using the Chi-square test, with Fisher's exact test used in situations where expected frequencies in any cell were less than five. All collected data were coded and entered into Microsoft Excel, and statistical analysis was carried out using SPSS software (version 25.0, IBM Corp., Chicago, USA). A p-value of less than 0.05 was taken as statistically significant.

Results

A total of 42 patients were recruited for the study and randomly allocated into two groups. The mean ± SD age in Group T and Group E was 46.05 ± 4.01 and 47.10 ± 4.15 years, respectively (p = 0.41). Mean BMI values were 26.86 ± 1.96 kg/m² and 27.62 ± 3.81 kg/m², respectively (p = 0.422). The mean surgery duration in Group T and Group E was 3.31 ± 0.40 and 3.45 ± 0.63 hours, respectively (p = 0.388). ASA grades distribution was comparable (Grade I: 38.10% vs 42.86%; Grade II: 61.90% vs 57.14%; p = 0.753). [Table 1]

Intraoperative hemodynamic parameters showed no significant inter-group differences [Table 2]. The mean heart rate was 84.48 ± 5.65 bpm in Group T and 82.76 ± 6.40 bpm in Group E (p = 0.363). Mean SpO_2 was 98.43 ± 0.81% vs 98.67 ± 0.97% (p = 0.392). Mean systolic blood pressure measured 133.05 ± 12.99 mmHg in Group T compared to 134.00 ± 11.44 mmHg in Group E (p = 0.802), while mean diastolic pressure was 82.86 ± 8.45 mmHg versus 83.05 ± 7.47 mmHg (p = 0.939).

Post-operative heart rate remained broadly similar at 0, 2, 4, 18 and 24 hours (p > 0.05); however, at 6 hours (86.19 ± 6.14 vs 82.33 ± 5.42 bpm; p = 0.037), 8 hours (86.57 ± 6.61 vs 82.29 ± 5.57 bpm; p = 0.029) and 12 hours (86.38 ± 6.69 vs 82.43 ± 5.42 bpm; p = 0.042) Group T recorded significantly higher rates than Group E [Figure 2]. Post-operative mean arterial pressure remained comparable at all measured intervals [Figure 3].

Pain assessment by VAS scores was similar at 0, 2, 4, 18 and 24 hours (p > 0.05). In contrast, at 6 h [3 (2–3) vs 3 (3–4), p = 0.019], 8 h [2 (2–3) vs 3 (3–4), p < 0.0001] and 12 h [2 (2–2) vs 3 (3–3), p < 0.0001], Group E exhibited significantly lower scores compared to Group T [Figure 4]. Sedation (Ramsay) and motor block (Bromage) scores were similar between the groups at any time point (both median scores consistently 2 and 1 respectively; p > 0.05).

Rescue analgesic requirements were comparable between the groups: no additional analgesia was needed in 57.14% of Group T versus 80.95% of Group E (p = 0.28). The fraction requiring Tramadol alone (14.29% vs 9.52%; p = 1), Tramadol + Diclofenac (14.29% vs 9.52%; p = 1), and Tramadol + Diclofenac + Epidural bolus (14.29% vs 0%; p = 0.232) did not differ significantly. Epidural drug consumption was significantly higher in Group T (123.67 ± 4.41 mL) than in Group E (113.81 ± 3.63 mL; p < 0.0001). The rate of adverse events were comparable across groups: no events in 57.14% of Group T versus 80.95% of Group E (p = 0.286); nausea occurred in 28.57% vs 14.29%; and vomiting in 14.29% vs 4.76%, respectively. Patient satisfaction was significantly higher in Group E, with 76.19% rating "good" and 14.29% "excellent", compared to 28.57% "good", 0% "excellent" and 71.43% "average" in Group T (p < 0.0001) [Table 3].

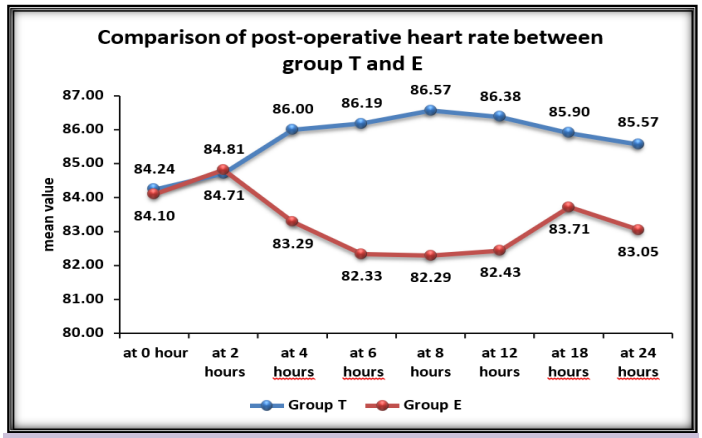

Figure 2: Comparison of trends of post-operative heart rate at different time intervals between group T and E.

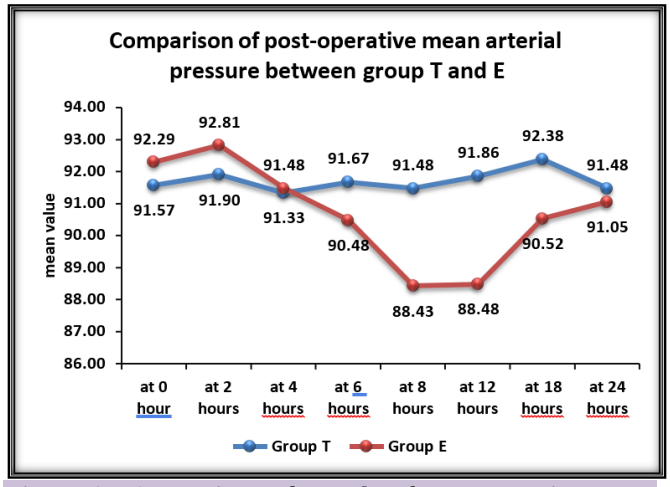

Figure 3: Comparison of trends of post-operative mean arterial pressure at different time intervals between group T and E.

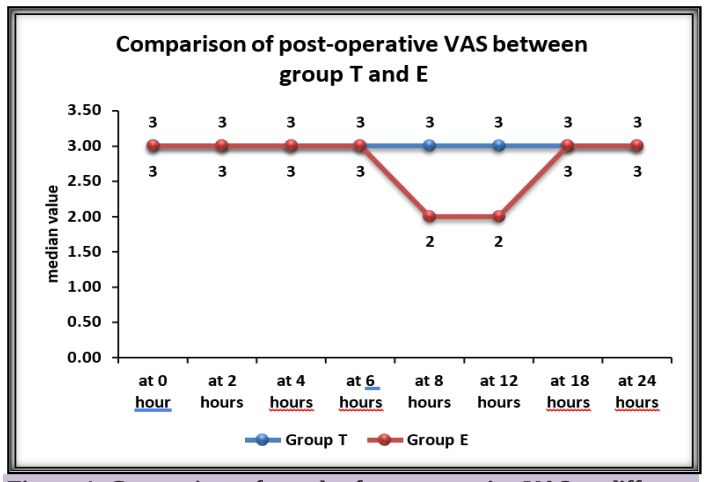

Figure 4: Comparison of trends of post-operative VAS at different time intervals between group T and E.

Table 1: Comparison of demographic characteristics between group T and E.

Parameters	Group T(n=21)	Group E(n=21)	P value
Age(years)	46.05 ± 4.01(38-53)	47.1 ± 4.15(41-56)	0.41‡
ASA grade 1	8 (38.10%)	9 (42.86%)	0.753†
ASA grade 2	13 (61.90%)	12 (57.14%)	
Body mass index (kg/m²)	26.86 ± 1.96(24-30)	27.62 ± 3.81(20-35)	0.422‡
Duration of surgery (hours)	3.31 ± 0.4(2.5-4)	3.45 ± 0.63(2.5-4.5)	0.388‡

‡ **Independent t test,** † **Chi square test**

Table 2: Comparison of intra-operative vitals between group T and E.

Intra-operative vitals	Group T(n=21)	Group E(n=21)	P value
Heart rate	84.48 ± 5.65(74-92)	82.76 ± 6.4(68-90)	0.363‡
SpO_2	98.43 ± 0.81(97-100)	98.67 ± 0.97(97-100)	0.392‡
SBP	133.05 ± 12.99(110-160)	134 ± 11.44(118-154)	0.802‡
DBP	82.86 ± 8.45(60-92)	83.05 ± 7.47(66-94)	0.939‡

‡ **Independent t test; SBP: Systolic blood pressure; DBP: Diastolic blood pressure**

Table 3: Comparison of patient satisfaction score between group T and E.

Patient satisfaction score	Group T(n=21)	Group E(n=21)	P value
Average	15 (71.43%)	2 (9.52%)	<.0001*
Good	6 (28.57%)	16 (76.19%)	
Excellent	0 (0%)	3 (14.29%)	
Total	21 (100%)	21 (100%)	

* **Fisher's exact test**

Discussion

This study is one of the landmark studies that compared transdermal and continuous epidural infusion for managing postoperative pain in patients undergoing total abdominal hysterectomy. The participants were randomly allocated into two groups. Both groups were comparable at baseline with respect to demographic and clinical parameters, including age, ASA grade, BMI, duration of surgeries were comparable, which ensured that any differences in the outcomes could purely be ascribed to the differential intervention.

We found that on comparing transdermal and continuous epidural infusion, there was no significant differences in hemodynamic status of the patient in the postoperative stage. As for the pain relief, Group T had significantly higher postoperative VAS scores at 6 hours, 8 hours and 12 hours, while at later time points difference was not statistically significant with median postoperative VAS score of 3 at all the time points.

On the contrary, Rallabhandi et al,[3] found that the VAS scores were not comparable, suggesting that the analgesic effects of fentanyl were effective when administered by transdermal fentanyl patch, as pain intensity scores were significantly lower in the transdermal route (3.80±0.12 vs. 4.67±1.18, $p<0.05$) when compared to IV fentanyl. However, their study population consisted of patients who underwent major abdominal surgical procedures.

The reason for this may be that the present study focused specifically on patients undergoing total abdominal hysterectomy, which is performed only in women. It may be

possible that females have different pain thresholds and sensitivities than males, and moreover during pregnancy, pain thresholds may vary.

Moreover, our findings matched with Nidhi et al,[6] study, who showed a significant reduction in postoperative pain scores at the 6th, 8th, and 12th hours in the epidural fentanyl group in comparison with the fentanyl patch group. The reason can also be inadequate therapeutic levels of fentanyl in some patients with the fentanyl patch, likely resulting from interindividual variability in transdermal fentanyl pharmacokinetics.[7,8]

It must be mentioned here that Fentanyl patches are typically applied before surgery at varying time intervals, including immediately before surgery or at 30 minutes, 1, 2, and 8 hours after the operation, with the onset of analgesia noted at approximately 1.2 hours. After application, a fentanyl depot forms in the upper layers of the skin, requiring several hours before clinical effects are observed. This delay may be related to changes in skin perfusion, which are influenced by temperature fluctuations, circulating blood volume, and cardiac output—all of which are likely to vary during the perioperative period. The comparable pain scores in the later stages may be because the effect of a single fentanyl patch generally lasts for about 72 hours.[3]

The higher pain scores in Group T were also reflected in the epidural drug consumption, which was significantly higher in Group T than Group E (123.67 ± 4.41 vs. 113.81 ± 3.63, P<.0001). However, the Ramsay sedation score and Bromage scale was statistically comparable. Group T had higher time to rescue analgesia, however, the values failed to cross the boundaries of significance. Likewise, Rallabhandi et al,[3] found that there was a significantly higher mean time interval for the first rescue analgesia in the transdermal fentanyl group than IV group (345.50±33.34 vs. 58.10±12.88, P<0.05).

In terms of safety, adverse events like nausea and vomiting were seen in 9 cases in Group T against 4 cases in Group E. Group T had lower overall patient satisfaction score than Group E (28.57% vs. 76.19%, P<.0001) indicating that Group T was not superior to Group E, and Transdermal fentanyl use may not be superior over continuous epidural infusion. Rather, continuous epidural infusion of fentanyl provides excellent and consistent analgesia, effectively overcoming the short duration of action observed with bolus administration. Epidural fentanyl produced reliable postoperative pain relief, with minimal side effects.[9] Consequently, continuous infusion can remain the preferred method in the postoperative period. When compared with transdermal delivery, epidural administration demonstrates superior analgesic efficacy, better dose control, and fewer non-respiratory side effects, underscoring its advantage as the preferred route for postoperative analgesia in TAH.

In addition to clinical efficacy, cost and feasibility are important considerations, particularly in resource-limited settings. Continuous epidural fentanyl infusion was found to be relatively economical as well, with a single ampoule of fentanyl (100 µg in 2 mL) costing approximately ₹45, allowing flexible dose titration at a low cost. In contrast, a transdermal fentanyl patch delivering 25 µg/hour costs approximately ₹650, representing a substantially higher upfront expense. Although transdermal fentanyl offers ease of application and avoids invasive catheter placement, its higher cost may limit widespread use in low-resource settings. Thus, from a cost- effectiveness and feasibility perspective, epidural fentanyl may be a more economical option, while transdermal fentanyl may be better suited for selected patients where technical expertise or epidural facilities are unavailable.

Limitations

This study has certain limitations that should be acknowledged. Being conducted at a single institution with a relatively small sample size, the generalizability of the findings may be limited. In addition, owing to the nature of the interventions, blinding of the patients and investigators was not feasible, which may have introduced observer or performance bias.

The study included only female patients undergoing TAH, thereby limiting extrapolation of the results to other surgical procedures or male patients. Variability in pain perception, skin permeability, ambient temperature, and individual physiological factors may have influenced the absorption of transdermal fentanyl. Furthermore, plasma fentanyl concentrations were not measured, precluding assessment of pharmacokinetic variability between the two modalities.

Conclusion

Continuous epidural fentanyl demonstrated superior analgesic efficacy, better pain control during the intermediate postoperative period, and higher patient satisfaction compared to transdermal fentanyl. Both showed consistent safety and hemodynamic stability, making them reliable options for postoperative pain management; however, transdermal fentanyl did not demonstrate superior overall efficacy compared to continuous epidural infusion in patients undergoing TAH.

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Conflicts of interest

There are no conflicts of interest.

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