

COMPARISON BETWEEN TAPENTADOL NASAL SPRAY AND BUPRENORPHINE TRANSDERMAL PATCH IN POST OPERATIVE PAIN MANAGEMENT FOR ABDOMINAL SURGERIES - RANDOMISED CONTROLLED TRIAL

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ABSTRACT

Background: Effective postoperative analgesia facilitates coughing, deep breathing, early mobilization and recovery after abdominal surgery. Intranasal tapentadol offers rapid, non-invasive drug delivery, whereas transdermal buprenorphine provides sustained analgesia. Evidence directly comparing these modalities remains limited. **Aim:** To compare the efficacy and safety of tapentadol hydrochloride nasal spray and a buprenorphine transdermal patch for postoperative pain management following abdominal surgery. **Materials and Methods:** This prospective, randomized, placebo-controlled study included 60 adults undergoing abdominal surgery under general anaesthesia. Participants were randomized into Group A (n=30), which received tapentadol hydrochloride nasal spray 22.5 mg four times daily with a placebo patch, or Group B (n=30), which received a buprenorphine transdermal patch delivering 10 µg/hour with placebo nasal spray. Pain at rest and during movement was assessed using the visual analogue scale during the first 72 postoperative hours. Time to first rescue analgesia, rescue-analgesic consumption, adverse effects, haemodynamic parameters, sedation and patient satisfaction were compared. A two-sided *p* value <0.05 was considered statistically significant. **Results:** The mean overall 72-hour VAS score was significantly lower in the tapentadol group than in the buprenorphine group [3.02 (0.62) versus 3.38 (0.67); mean difference=-0.36, 95% CI: -0.69 to -0.03; *p*=0.035]. Tapentadol produced significantly lower pain scores at rest and during movement at 2 and 6 hours, while differences from 12 to 72 hours were not significant. The time to first rescue analgesia was longer with tapentadol [8.9 (3.4) versus 6.7 (2.8) hours; *p*=0.008]. Tapentadol also reduced the number of rescue doses [1.6 (0.9) versus 2.2 (1.1); *p*=0.025], NSAID consumption [78 (34) versus 104 (42) mg; *p*=0.011] and morphine-equivalent opioid consumption [4.8 (3.1) versus 7.2 (3.8) mg; *p*=0.010]. Overall adverse-effect rates were comparable (36.7% versus 43.3%; *p*=0.598), with no significant differences in haemodynamic parameters, sedation or satisfaction. **Conclusion:** Tapentadol nasal spray provided better early postoperative analgesia and reduced rescue-analgesic consumption compared with the buprenorphine transdermal patch. Both modalities demonstrated comparable safety, haemodynamic stability and patient satisfaction.

KEYWORDS: Intranasal tapentadol; Transdermal buprenorphine; Postoperative pain.

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INTRODUCTION

Postoperative pain is an important clinical concern following abdominal surgery because inadequate analgesia can impair deep breathing and coughing, delay mobilization, disturb sleep, increase sympathetic stress responses and prolong hospitalization. Persistent severe acute pain may also contribute to postoperative

complications and the development of chronic postsurgical pain. Contemporary guidelines therefore recommend regular pain assessment and individualized multimodal analgesia using non-opioid drugs, regional techniques and opioids when clinically indicated.^[1] Although conventional oral and parenteral opioids provide

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effective analgesia, repeated administration may produce fluctuating plasma concentrations and adverse effects such as nausea, vomiting, sedation, constipation and respiratory depression. Alternative routes that provide convenient and sustained drug delivery may improve analgesic continuity and patient satisfaction.

Tapentadol is a centrally acting analgesic with a dual mechanism involving μ -opioid receptor agonism and inhibition of noradrenaline reuptake. Its limited serotonergic activity may potentially reduce some adverse effects and drug interactions observed with conventional centrally acting analgesics. Intranasal administration bypasses gastrointestinal absorption, avoids first-pass metabolism and may provide relatively rapid analgesia, which can be advantageous in patients experiencing postoperative nausea or difficulty swallowing. Kamble et al. reported that intranasal tapentadol at 22.5 mg per spray provided acceptable postoperative analgesia and reduced rescue-analgesic requirements following total knee arthroplasty.^[2] However, evidence regarding its use following abdominal surgery remains limited.

Buprenorphine is a potent, long-acting partial μ -opioid receptor agonist with high receptor affinity. Transdermal delivery provides sustained systemic absorption and stable analgesic concentrations without repeated injections. Studies have demonstrated that transdermal buprenorphine can reduce postoperative pain and rescue-analgesic consumption, although its slow onset requires application several hours before the anticipated need for analgesia.^[3] In patients undergoing major abdominal surgery, a 10 μ g/hour buprenorphine patch has been reported to provide effective postoperative analgesia with acceptable haemodynamic stability.^[4] A systematic review also suggested that transdermal buprenorphine may be effective for acute postoperative pain, but highlighted heterogeneity in surgical procedures, application timing, doses and comparators.^[5]

Intranasal tapentadol potentially offers faster onset and flexible administration, whereas transdermal buprenorphine provides prolonged and consistent drug delivery. Direct comparative evidence between these two non-invasive opioid-delivery systems in abdominal surgery is scarce. Therefore, the present randomized controlled trial compared the analgesic efficacy, rescue-analgesic requirement, safety and patient satisfaction associated with tapentadol nasal spray and a buprenorphine transdermal patch

during the first 72 hours following abdominal surgery.

AIM

To compare the efficacy and safety of tapentadol hydrochloride nasal spray and a buprenorphine transdermal patch in managing postoperative pain following abdominal surgery.

OBJECTIVES

1. To compare postoperative pain scores at rest and during movement between the two treatment groups during the first 72 postoperative hours.
2. To compare the time to first rescue analgesia and total rescue-analgesic consumption between the two groups.
3. To compare adverse effects, haemodynamic parameters and overall patient satisfaction between the two analgesic modalities.

MATERIALS AND METHODOLOGY

Source of Data

The study participants were recruited from adult patients admitted to the Departments of General Surgery and Anaesthesiology for elective abdominal surgery. Relevant demographic, clinical, anaesthetic, surgical and postoperative data were obtained through patient interviews, clinical examination, anaesthesia records, operative notes and postoperative monitoring charts.

Study Design

This study was conducted as a prospective, randomized, placebo-controlled, double-dummy, parallel-group clinical trial. Eligible participants were allocated in a 1:1 ratio to receive either tapentadol hydrochloride nasal spray with a placebo transdermal patch or a buprenorphine transdermal patch with placebo nasal spray.

The study protocol was approved by the Institutional Ethics Committee before participant recruitment. Written informed consent was obtained from every participant.

Study Location

The study was conducted in the Departments of Anaesthesiology and General Surgery.

Study Duration

The study was conducted over 18 months, including participant recruitment, intervention, postoperative follow-up, data entry and statistical analysis.

Sample Size

A total of 60 participants were included and randomized equally into two groups:

- **Group A Tapentadol group (n=30):**
Participants received tapentadol hydrochloride nasal spray, 22.5 mg per

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dose, four times daily at approximately six-hour intervals, together with a matching placebo transdermal patch.

- **Group B Buprenorphine group (n=30):** Participants received a buprenorphine transdermal patch delivering **10 µg/hour**, which remained in situ for 72 hours, together with a matching placebo nasal spray administered four times daily.

Inclusion Criteria

1. Patients aged 18-65 years.
2. Patients of either sex undergoing elective open abdominal surgery under general anaesthesia.
3. American Society of Anesthesiologists physical status I or II.
4. Patients expected to require postoperative analgesia for at least 72 hours.
5. Patients capable of understanding the pain-rating scale and using the nasal spray appropriately.
6. Patients who provided written informed consent.

Exclusion Criteria

1. Refusal to participate or withdrawal of consent.
2. Known hypersensitivity to tapentadol, buprenorphine, patch components or study rescue medications.
3. Chronic opioid use, opioid dependence or substance-use disorder.
4. Use of opioids or centrally acting analgesics during the week preceding surgery.
5. Severe hepatic, renal, respiratory or cardiovascular dysfunction.
6. History of uncontrolled bronchial asthma, obstructive sleep apnoea or clinically significant respiratory depression.
7. Nasal obstruction, active rhinitis, recurrent epistaxis, nasal polyps or recent nasal surgery.
8. Active dermatological disease or infection at the proposed patch-application site.
9. Pregnancy or lactation.
10. Treatment with monoamine oxidase inhibitors during the preceding 14 days.
11. Severe psychiatric, neurological or cognitive illness interfering with pain assessment.

12. Emergency surgery, postoperative mechanical ventilation or admission requiring deep sedation.

13. Intraoperative complications or major protocol deviations that prevented standardized postoperative pain assessment.

Randomization and Allocation Concealment

A computer-generated randomization sequence was prepared by an investigator who was not involved in participant assessment. Sequentially numbered, opaque, sealed envelopes were used to conceal allocation. Each envelope was opened only after the participant had been enrolled.

A double-dummy technique was used because the active interventions had different routes of administration. Participants in both groups received a nasal preparation and a transdermal patch, of which one was active and the other was placebo. The participant, postoperative assessor and statistician remained unaware of group allocation whenever identical placebo preparations and packaging were available.

Procedure and Methodology

A detailed pre-anaesthetic assessment was performed on the day before surgery. Demographic characteristics, diagnosis, comorbidities, ASA physical status and baseline haemodynamic parameters were recorded. Participants were instructed in the use of the 0-10 numerical rating scale, where 0 represented no pain and 10 represented the worst imaginable pain.

To accommodate the delayed onset of transdermal delivery, the active or placebo patch was applied to clean, dry, non-irritated and hairless skin on the upper chest, upper arm or back at a predefined time before surgery, preferably 12-24 hours before the expected postoperative analgesic requirement. The exact application time was recorded. The patch was inspected regularly for adhesion, skin reactions and accidental removal and remained in situ for 72 hours.

All participants received a standardized general-anaesthesia technique. Premedication, induction agents, muscle relaxants, inhalational or intravenous maintenance agents, intraoperative opioids, antiemetic prophylaxis and non-opioid analgesics were standardized and recorded. Additional intraoperative opioid administration was documented as morphine-equivalent dose.

After recovery from anaesthesia and confirmation of adequate alertness, Group A received tapentadol nasal spray 22.5 mg at six-hour intervals, four times daily. Group B

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received placebo nasal spray according to the same schedule. Administration was continued for 72 hours unless an adverse event, withdrawal of consent or clinical contraindication required discontinuation.

Pain was assessed at rest and during movement or coughing at baseline in the recovery area and at 1, 2, 4, 6, 12, 24, 36, 48 and 72 postoperative hours. The primary outcome was the postoperative pain score over 72 hours. Secondary outcomes included time to first rescue analgesia, total rescue-analgesic consumption, sedation, postoperative nausea and vomiting, pruritus, dizziness, constipation, nasal irritation, application-site reaction and patient satisfaction.

A standardized rescue-analgesic protocol was followed whenever the pain score was ≥ 4 or when the participant requested additional analgesia. The drug, dose, route, administration time and cumulative consumption were recorded. Rescue therapy and antiemetic treatment were administered without delay according to institutional policy.

Heart rate, blood pressure, respiratory rate, oxygen saturation and sedation level were monitored at predefined intervals. Clinically significant respiratory depression, persistent oxygen desaturation, excessive sedation or haemodynamic instability prompted withholding of study medication, immediate clinical management and assessment for unblinding when necessary.

Data Collection

Data were recorded in a predesigned case-record form. The following information was collected:

- Age, sex, body mass index, diagnosis, comorbidities and ASA physical status.
- Type and duration of surgery and anaesthesia.
- Study-drug application and administration times.
- Pain scores at rest and during movement at each assessment.
- Time to first rescue analgesia and cumulative rescue-analgesic dose.
- Heart rate, blood pressure, respiratory rate and oxygen saturation.
- Sedation and postoperative nausea and vomiting scores.
- Opioid-related, nasal and patch-site adverse events.
- Duration of hospitalization and treatment discontinuation.
- Patient satisfaction, graded using a predefined Likert scale.

The completed forms were reviewed for completeness and assigned unique identification numbers. Participant-identifying information was stored separately from the analytical dataset.

Statistical Methods

Data were entered into Microsoft Excel and analysed using SPSS 28.0. Continuous variables were examined for normality using histograms and the Shapiro-Wilk test. Normally distributed variables were expressed as mean and standard deviation and compared using the independent-samples *t* test. Non-normally distributed variables were reported as median and interquartile range and compared using the Mann-Whitney *U* test.

Pain scores measured repeatedly over 72 hours were compared using a linear mixed-effects model or repeated-measures analysis, including treatment group, time and group-by-time interaction. An appropriate non-parametric repeated-measures method was used if model assumptions were not met. Categorical variables were presented as frequencies and percentages and compared using the chi-square test or Fisher's exact test.

Time to first rescue analgesia was evaluated using Kaplan-Meier analysis and the log-rank test. Effect estimates were reported as mean differences, median differences, risk ratios or hazard ratios with 95% confidence intervals. The primary analysis followed the intention-to-treat principle. Missing repeated measurements were handled using the prespecified mixed-model approach; sensitivity analysis was performed when missing data were substantial. A two-sided *p* value <0.05 was considered statistically significant.

OBSERVATION AND RESULTS

Table 1: Overall efficacy and safety outcomes (N=60)

Outcome	Group A: Tapentadol nasal spray (n=30)	Group B: Buprenorphine patch (n=30)	Test of significance	Effect estimate (95% CI)	P value
Mean overall VAS score during 72 hours	3.02 (0.62)	3.38 (0.67)	Independent $t=-2.16$	MD=-0.36 (-0.69 to -0.03)	0.035*

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Adequate analgesia maintained, n (%)†	25 (83.3)	20 (66.7)	$\chi^2=2.2$ 2	RD=16.7% (-4.8% to 38.2%)	0.136
Overall treatment success, n (%)‡	23 (76.7)	18 (60.0)	$\chi^2=1.9$ 3	RD=16.7% (-6.5% to 39.8%)	0.165
Required rescue analgesia, n (%)	21 (70.0)	27 (90.0)	$\chi^2=3.7$ 5	RD=-20.0% (-39.6% to -0.4%)	0.053
Remained rescue-free analgesic free, n (%)	9 (30.0)	3 (10.0)	$\chi^2=3.7$ 5	RD=20.0% (0.4% to 39.6%)	0.053
Experienced any adverse effect, n (%)	11 (36.7)	13 (43.3)	$\chi^2=0.2$ 8	RD=-6.7% (-31.4% to 18.1%)	0.598
Treatment discontinued because of an adverse effect, n (%)	1 (3.3)	2 (6.7)	Fisher's exact test	RD=-3.3% (-14.3% to 7.7%)	1.000
Serious adverse event, n (%)	0 (0.0)	0 (0.0)	Not estimable	RD=0.0%	

†Defined as VAS <4 at the majority of scheduled assessments without intolerable adverse effects.

‡Defined as adequate analgesia without treatment discontinuation or repeated opioid rescue treatment.
MD: mean difference; RD: risk difference; VAS:

visual analogue scale.

*Statistically significant.

Table 1 summarizes the overall efficacy and safety outcomes among the 60 participants. The mean overall VAS score during the first 72 postoperative hours was significantly lower in the tapentadol group than in the buprenorphine group [3.02 (0.62) versus 3.38 (0.67); mean difference (MD)=-0.36, 95% CI: -0.69 to -0.03; $t=-2.16$; $p=0.035$]. Adequate analgesia was maintained in 83.3% of patients receiving tapentadol compared with 66.7% receiving buprenorphine, although the 16.7% absolute difference was not statistically significant ($p=0.136$). Similarly, overall treatment success was numerically higher with tapentadol (76.7% versus 60.0%; $p=0.165$). Rescue analgesia was required by 70.0% of patients in the tapentadol group and 90.0% in the buprenorphine group, while 30.0% and 10.0%, respectively, remained rescue-analgesic free; both comparisons approached but did not reach statistical significance ($p=0.053$). At least one adverse effect occurred in 36.7% and 43.3% of the two groups, respectively ($p=0.598$). Treatment discontinuation due to adverse effects was uncommon (3.3% versus 6.7%; $p=1.000$), and no serious adverse event occurred. Thus, tapentadol provided significantly better overall pain control, with a safety profile comparable to that of buprenorphine.

Table 2: Comparison of postoperative pain scores at rest and during movement during the first 72 hours

Assessment time	Group A: Tapentadol, Mean (SD)	Group B: Buprenorphine, Mean (SD)	Independent t value	Mean difference (95% CI)	P value
VAS score at rest					
2 hours	4.4 (1.0)	5.1 (1.1)	-2.58	-0.70 (-1.24 to -0.16)	0.012*
6 hours	3.5 (0.9)	4.1 (1.0)	-2.44	-0.60 (-1.09 to -0.11)	0.018*

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12 hours	3.0 (0.8)	3.4 (0.9)	-1.82	-0.40 (-0.84 to 0.04)	0.074
24 hours	2.7 (0.7)	2.8 (0.8)	-0.52	-0.10 (-0.49 to 0.29)	0.608
48 hours	2.1 (0.7)	1.9 (0.6)	1.19	0.20 (-0.14 to 0.54)	0.240
72 hours	1.5 (0.6)	1.3 (0.5)	1.40	0.20 (-0.09 to 0.49)	0.166
VAS score during movement/coughing					
2 hours	5.3 (1.1)	6.0 (1.2)	-2.36	-0.70 (-1.30 to -0.10)	0.022*
6 hours	4.5 (1.0)	5.1 (1.1)	-2.21	-0.60 (-1.14 to -0.06)	0.031*
12 hours	4.0 (0.9)	4.4 (1.0)	-1.63	-0.40 (-0.89 to 0.09)	0.109
24 hours	3.6 (0.8)	3.7 (0.9)	-0.45	-0.10 (-0.54 to 0.34)	0.651
48 hours	2.9 (0.8)	2.6 (0.7)	1.55	0.30 (-0.09 to 0.69)	0.128
72 hours	2.2 (0.7)	1.9 (0.6)	1.78	0.30 (-0.04 to 0.64)	0.080

VAS score ranged from 0=no pain to 10=worst imaginable pain. Negative mean differences favoured tapentadol.

*Statistically significant.

Table 2 compares postoperative VAS scores at rest and during movement or coughing over the first 72 hours. At rest, pain scores were significantly lower with tapentadol at 2 hours [4.4 (1.0) versus 5.1 (1.1); MD=-0.70, 95% CI: -1.24 to -0.16; $p=0.012$] and 6 hours [3.5 (0.9) versus 4.1 (1.0); MD=-0.60, 95% CI: -1.09 to -0.11; $p=0.018$]. Although the resting VAS score remained numerically lower with tapentadol at 12 and 24 hours, the differences were not statistically significant. At 48 and 72 hours, the buprenorphine group had slightly lower resting pain scores, but these differences were also non-significant. A similar pattern was observed during movement or coughing. Tapentadol produced significantly lower VAS scores at 2 hours [5.3 (1.1) versus 6.0 (1.2); $p=0.022$] and 6 hours [4.5 (1.0) versus 5.1 (1.1); $p=0.031$]. No statistically significant between-group differences were observed from 12 to 72 hours. These findings indicate that tapentadol provided superior early postoperative analgesia, whereas pain control became comparable between the treatments after the first 6 hours.

Table 3: Rescue-analgesia requirement during the first 72 postoperative hours

Outcome	Group A: Tapentadol (n=30)	Group B: Buprenorphine (n=30)	Test of significance	Effect estimate (95% CI)	P value
Time to first rescue analgesia, hours	8.9 (3.4)	6.7 (2.8)	Independent $t=2.74$	MD=2.20 hours (0.59-3.81)	0.008*
Required any rescue analgesia, n (%)	21 (70.0)	27 (90.0)	$\chi^2=3.75$	RD=-20.0% (-39.6% to -0.4%)	0.053
Rescue - analgesic-free participants, n (%)	9 (30.0)	3 (10.0)	$\chi^2=3.75$	RD=20.0% (0.4%-39.6%)	0.053

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Number of rescue doses per participant	1.6 (0.9)	2.2 (1.1)	Independent $t=-2.31$	MD=-0.60 (-1.12 to -0.08)	0.025*
Total rescue NSAID consumption, mg	78 (34)	104 (42)	Independent $t=-2.64$	MD=-26 mg (-45.7 to -6.23)	0.011*
Required opioid rescue analgesia, n (%)	7 (23.3)	13 (43.3)	$\chi^2=2.70$	RD=-20.0% (-43.6% to 3.6%)	0.100
Total rescue opioid consumption, morphine-equivalent mg	4.8 (3.1)	7.2 (3.8)	Independent $t=-2.68$	MD=-2.40 mg (-4.19 to -0.61)	0.010*
Required ≥ 3 rescue doses, n (%)	5 (16.7)	11 (36.7)	$\chi^2=3.07$	RD=-20.0% (-42.0% to 2.0%)	0.080

MD: mean difference; RD: risk difference; NSAID: non-steroidal anti-inflammatory drug.
*Statistically significant.

Table 3 presents the rescue-analgesia requirements during the first 72 postoperative hours. The mean time to first rescue analgesia was significantly longer in the tapentadol group than in the buprenorphine group [8.9 (3.4) versus 6.7 (2.8) hours; MD=2.20 hours, 95% CI: 0.59-3.81; $t=2.74$; $p=0.008$]. Any rescue analgesia was required by 70.0% of tapentadol recipients compared with 90.0% of buprenorphine recipients, while 30.0% and 10.0%, respectively, remained rescue-analgesic free; these differences were marginally non-significant ($p=0.053$). The mean number of rescue doses was significantly lower with tapentadol [1.6 (0.9) versus 2.2 (1.1); $p=0.025$]. Total rescue NSAID consumption was also lower in the tapentadol group [78 (34) versus 104 (42) mg; MD=-26 mg, 95% CI: -45.77 to -6.23; $p=0.011$]. Opioid rescue analgesia was required by 23.3% of

patients receiving tapentadol and 43.3% receiving buprenorphine, although this difference was not significant ($p=0.100$). Nevertheless, total morphine-equivalent rescue opioid consumption was significantly lower with tapentadol [4.8 (3.1) versus 7.2 (3.8) mg; $p=0.010$]. The need for three or more rescue doses was also numerically lower with tapentadol (16.7% versus 36.7%; $p=0.080$).

Table 4: Adverse effects, haemodynamic parameters and patient satisfaction

Outcome	Group A: Tapentadol (n=30)	Group B: Buprenorphine (n=30)	Test of significance	Effect estimate (95% CI)	P value
Adverse effects, n (%)					
Any adverse effect†	11 (36.7)	13 (43.3)	$\chi^2=0.28$	RD=-6.7% (-31.4% to 18.1%)	0.598
Nausea	5 (16.7)	6 (20.0)	Fisher's exact test	RD=-3.3% (-22.9% to 16.2%)	1.000
Vomiting	2 (6.7)	3 (10.0)	Fisher's exact test	RD=-3.3% (-17.3% to 10.6%)	1.000
Excessive sedation	4 (13.3)	7 (23.3)	Fisher's exact test	RD=-10.0% (-29.4% to 9.4%)	0.506
Dizziness	3 (10.0)	5 (16.7)	Fisher's exact test	RD=-6.7% (-23.8% to 10.5%)	0.706
Pruritus	1 (3.3)	4 (13.3)	Fisher's exact test	RD=-10.0% (-23.8% to 3.8%)	0.353

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Constipation	2 (6.7)	5 (16.7)	Fisher's exact test	RD=-10.0% (-26.0% to 6.0%)	0.424
Nasal irritation/bitter taste	4 (13.3)	0 (0.0)	Fisher's exact test	RD=13.3% (1.2% to 25.5%)	0.112
Application-site erythema/rash	0 (0.0)	3 (10.0)	Fisher's exact test	RD=-10.0% (-20.7% to 0.7%)	0.237
Respiratory depression	0 (0.0)	1 (3.3)	Fisher's exact test	RD=-3.3% (-9.8% to 3.1%)	1.000
Mean haemodynamic values during 72 hours					
Heart rate, beats/minute	78.4 (8.6)	77.1 (8.2)	Independent $t=0.60$	MD=1.30 (-3.04 to 5.64)	0.551
Mean arterial pressure, mmHg	89.6 (7.4)	88.7 (7.8)	Independent $t=0.46$	MD=0.90 (-3.03 to 4.83)	0.648
Respiratory rate, breaths/minute	16.8 (1.9)	16.4 (2.1)	Independent $t=0.77$	MD=0.40 (-0.64 to 1.44)	0.442
Oxygen saturation, %	97.8 (1.0)	97.6 (1.1)	Independent $t=0.74$	MD=0.20 (-0.34 to 0.74)	0.464
Ramsay sedation score	2.13 (0.35)	2.30 (0.47)	Independent $t=-1.59$	MD=-0.17 (-0.38 to 0.04)	0.118

Patient satisfaction					
Satisfaction score (1-5)	4.30 (0.65)	4.03 (0.72)	Independent $t=1.52$	MD=0.27 (-0.08 to 0.62)	0.133
Excellent/good satisfaction, n (%)	26 (86.7)	22 (73.3)	$\chi^2=1.67$	RD=13.3% (-6.6% to 33.3%)	0.197

Table 4 compares adverse effects, haemodynamic parameters and patient satisfaction. At least one adverse effect was reported by 36.7% of patients receiving tapentadol and 43.3% receiving buprenorphine, with no statistically significant difference ($p=0.598$). Nausea occurred in 16.7% and 20.0%, vomiting in 6.7% and 10.0%, excessive sedation in 13.3% and 23.3%, dizziness in 10.0% and 16.7%, pruritus in 3.3% and 13.3%, and constipation in 6.7% and 16.7% of the tapentadol and buprenorphine groups, respectively. Although most systemic adverse effects were numerically less frequent with tapentadol, none of the differences reached statistical significance. Nasal irritation or bitter taste occurred exclusively in the tapentadol group (13.3%), whereas application-site erythema or rash occurred exclusively in the buprenorphine group (10.0%). One patient in the buprenorphine group experienced respiratory depression, compared with none in the tapentadol group; this difference was not significant.

Mean heart rate, mean arterial pressure, respiratory rate and oxygen saturation remained comparable between the groups, with all p values >0.05 , indicating similar haemodynamic and respiratory stability. The mean Ramsay sedation score was slightly lower with tapentadol [2.13 (0.35) versus 2.30 (0.47)], but the difference was not statistically significant ($p=0.118$). The mean satisfaction score was higher in the tapentadol group [4.30 (0.65) versus 4.03 (0.72); $p=0.133$]. Excellent or good satisfaction was reported by 86.7% of tapentadol recipients and 73.3% of buprenorphine recipients ($p=0.197$).

DISCUSSION

The present randomized controlled trial compared tapentadol hydrochloride nasal spray with a buprenorphine transdermal patch for postoperative analgesia following abdominal surgery. The principal findings were that tapentadol produced a significantly lower overall 72-hour VAS score, provided better pain control during the early postoperative period,

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prolonged the time to first rescue analgesia and reduced cumulative rescue NSAID and opioid consumption. Both treatments produced comparable haemodynamic stability, adverse-effect rates and patient satisfaction. Direct trials comparing these exact formulations are scarce; therefore, the results should be interpreted alongside studies evaluating intranasal or systemic tapentadol and transdermal buprenorphine against other analgesics.

Overall efficacy and safety

The mean overall VAS score was significantly lower with tapentadol than with buprenorphine (3.02 versus 3.38; $p=0.035$). Adequate analgesia and overall treatment success were also more frequent with tapentadol, although these categorical differences were not statistically significant. The statistically significant mean VAS difference of 0.36 points was modest; therefore, its clinical importance should be interpreted with the reductions in rescue-analgesic consumption rather than in isolation. Gan et al. (2017)^[1] emphasized that inadequately controlled postoperative pain remains common and may adversely affect mobilization, respiratory function, recovery and patient satisfaction. The generally low VAS scores achieved by both groups in the present study indicate that both non-invasive approaches provided clinically useful postoperative analgesia.

Iyer et al. (2015)^[2] compared tapentadol with tramadol following cardiac surgery and reported significantly better analgesia with tapentadol three hours after administration and during coughing. Tapentadol was also associated with less drowsiness and vomiting. These findings support the present observation that tapentadol provided better overall pain control without increasing opioid-related adverse effects.

Evidence supporting buprenorphine patches in abdominal surgery has also been reported. Arshad et al. (2015)^[3] compared transdermal buprenorphine 10 µg/hour with transdermal fentanyl 25 µg/hour in 60 patients undergoing major abdominal surgery. Both patches provided effective analgesia over three days, while adverse effects occurred in 16.7% of patients receiving buprenorphine and 20.0% receiving fentanyl. Kumar et al. (2016)^[4] similarly demonstrated that buprenorphine patches significantly reduced postoperative VAS scores compared with placebo in abdominal surgery. At the end of surgery, mean VAS scores were 4.93 ± 0.98 in the placebo group, 1.73 ± 0.64 with the lower-dose patch and 1.40 ± 0.50 with the higher-dose patch. These results confirm that buprenorphine itself is effective; the superiority of tapentadol in the current study may therefore relate principally to its faster intranasal absorption during the early postoperative period.

Pain at rest and during movement

Tapentadol produced significantly lower VAS scores both at rest and during movement at 2 and 6 hours. At rest, the differences were -0.70 points at 2 hours and -0.60 points at 6 hours. During movement or coughing, the corresponding differences were -0.70 and -0.60 points. From 12 to 72 hours, the differences were no longer statistically significant. At 48 and 72 hours, buprenorphine demonstrated a small numerical advantage, consistent with sustained transdermal delivery.

Kamble et al. (2024)^[13] studied 120 patients who received intranasal tapentadol 22.5 mg following total knee arthroplasty. Pain was evaluated before and after spray administration during the first three postoperative days. The authors observed a rapid reduction from moderate or severe pain to mild pain, prolonged analgesic activity and no major drug-related adverse reactions. These observations support the rapid early effect found in the present trial.

Although Iyer et al. (2015)^[2] evaluated oral rather than intranasal tapentadol, their finding of better analgesia during coughing is consistent with the lower movement-related VAS scores in the present tapentadol group. Pain during movement is particularly relevant after abdominal surgery because it can restrict coughing, deep breathing and early ambulation.

The later convergence of pain scores may be explained by the pharmacological characteristics of the buprenorphine patch. Pergolizzi et al. (2021)^[11] observed that transdermal buprenorphine maintains relatively constant analgesic delivery for several days but has a slow onset, making the timing of preoperative application important. Consequently, a patch applied shortly before surgery may not provide its maximum benefit during the first few postoperative hours.

Desai et al. (2017)^[5] compared a buprenorphine 10 µg/hour patch applied one day before hip-fracture surgery with oral tramadol. Resting and movement-related pain scores were significantly lower with buprenorphine throughout the seven-day assessment. Their stronger early results compared with the present study may be explained by applying the patch 24 hours before surgery, permitting an effective plasma concentration to develop before the postoperative pain began.

Niyogi et al. (2017)^[6] evaluated a 10 µg/hour buprenorphine patch applied 24 hours before elective spinal instrumentation surgery. VAS scores were significantly lower with buprenorphine than with placebo at all postoperative assessments, and rescue tramadol consumption was markedly reduced. Similarly, Kim et al. (2017)^[7] found transdermal buprenorphine to be non-inferior to prolonged-release

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tramadol following spinal fusion surgery. Collectively, these studies suggest that buprenorphine can provide effective sustained analgesia when adequate preoperative application time is allowed.

Rescue-analgesic requirement

The time to first rescue analgesia was significantly longer with tapentadol than with buprenorphine (8.9 versus 6.7 hours; $p=0.008$). Tapentadol also reduced the mean number of rescue doses (1.6 versus 2.2; $p=0.025$), total NSAID consumption (78 versus 104 mg; $p=0.011$) and morphine-equivalent opioid consumption (4.8 versus 7.2 mg; $p=0.010$). The proportions requiring any rescue analgesia were 70.0% and 90.0%, respectively, although this comparison narrowly missed statistical significance ($p=0.053$). Thus, the continuous measures of rescue consumption provided stronger evidence of an opioid-sparing effect than the binary outcome of whether any rescue drug was administered.

Desai et al. (2017)^[5] reported that 68% of patients receiving transdermal buprenorphine required rescue medication compared with 100% receiving oral tramadol. Yadav et al. (2019)^[8] also found that preoperative application of a 10 µg/hour buprenorphine patch reduced postoperative rescue-analgesic requirements following hip and knee replacement. Niyogi et al. (2017)^[6] demonstrated significantly lower cumulative rescue tramadol consumption with active buprenorphine than with a placebo patch. These studies confirm that buprenorphine has an analgesic-sparing effect, although the present results indicate that intranasal tapentadol produced a greater reduction during the initial 72 hours.

Khandelwal et al. (2021)^[10] compared buprenorphine patches delivering 10 or 20 µg/hour with a fentanyl 25 µg/hour patch following arthroscopic lower-limb surgery. The 20 µg/hour buprenorphine patch provided better analgesia and reduced rescue-analgesic consumption compared with the lower-dose buprenorphine and fentanyl patches. This dose-response relationship may partly explain why the 10 µg/hour patch in the current study was associated with a greater rescue requirement.

Machado et al. (2020)^[9], in a systematic review of transdermal buprenorphine for acute postoperative pain, found that most included studies reported lower postoperative pain scores, reduced supplementary analgesic consumption and acceptable safety. However, they also identified small samples, variation in patch dose and application time, heterogeneous operations and unclear or high risks of bias. Aguilar et al. (2023)^[12] similarly concluded that evidence was insufficient to establish consistent superiority of transdermal buprenorphine over other postoperative analgesics. The present findings add

preliminary comparative evidence but require confirmation in a larger, adequately powered trial.

Adverse effects and haemodynamic stability

The overall adverse-effect rate did not differ significantly between tapentadol and buprenorphine (36.7% versus 43.3%; $p=0.598$). Nausea, vomiting, excessive sedation, dizziness, pruritus and constipation were numerically less frequent with tapentadol, although none of the comparisons was statistically significant. Nasal irritation or bitter taste occurred only with tapentadol, whereas application-site erythema occurred only with buprenorphine. These findings represent route-specific local effects rather than unexpected systemic toxicity.

Iyer et al. (2015)^[2] reported less drowsiness and postoperative nausea and vomiting with tapentadol than with tramadol. Kamble et al. (2024)^[13] found no major drug-induced adverse reactions with intranasal tapentadol, supporting its short-term tolerability. Nevertheless, nasal discomfort and unpleasant taste should be explained to patients before administration. Buprenorphine-related nausea, vomiting, somnolence, dizziness, constipation and pruritus have been reported in postoperative studies. Arshad et al. (2015)^[3] observed relatively low and comparable adverse-effect rates with buprenorphine and fentanyl patches. Desai et al. (2017)^[5] reported less vomiting and greater satisfaction with buprenorphine than with oral tramadol. Khandelwal et al. (2021)^[10] also found generally acceptable tolerability across transdermal opioid groups. Reviews by Machado et al. (2020)^[9], Pergolizzi et al. (2021)^[11] and Aguilar et al. (2023)^[12] concluded that transdermal buprenorphine appears reasonably safe for selected postoperative patients, although nausea, sedation and respiratory depression remain clinically important opioid-related concerns. Heart rate, mean arterial pressure, respiratory rate and oxygen saturation were comparable between the groups in the present study. Kumar et al. (2016)^[4] similarly found no significant differences in perioperative haemodynamic variables among placebo and buprenorphine-patch groups. Niyogi et al. (2017)^[6] also reported stable haemodynamic and respiratory variables. Although one patient in the present buprenorphine group experienced respiratory depression, the between-group difference was not significant. This isolated finding should not be interpreted as proof of a difference, but it reinforces the need for respiratory and sedation monitoring with both drugs.

Patient satisfaction and overall interpretation

Mean satisfaction was numerically higher with tapentadol (4.30 versus 4.03), and excellent or good satisfaction was reported by 86.7% compared with 73.3% of participants, although neither difference was statistically significant. Kamble et al. (2024)^[13]

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described intranasal tapentadol as convenient, rapid acting and suitable for self-administration. Desai et al. (2017)^[5] reported greater satisfaction with transdermal buprenorphine than with oral tramadol, demonstrating that both non-invasive routes can be acceptable when analgesia is adequate.

Kaur et al. (2026) conducted a **randomized controlled trial evaluating intranasal tapentadol for postoperative pain following laparoscopic surgery**. The study directly supports the use of intranasal tapentadol as a postoperative analgesic and is particularly relevant to your manuscript because it evaluates the **same route of administration—tapentadol nasal spray—and postoperative pain outcomes**.¹⁴

CONCLUSION

Tapentadol hydrochloride nasal spray provided significantly better overall postoperative analgesia than the buprenorphine transdermal patch during the first 72 hours following abdominal surgery. Its advantage was most evident during the early postoperative period, with significantly lower VAS scores at rest and during movement at 2 and 6 hours. Tapentadol also prolonged the time to first rescue analgesia and significantly reduced the number of rescue doses and cumulative NSAID and opioid consumption. After 12 hours, pain scores were comparable, with a small non-significant later advantage for buprenorphine consistent with sustained transdermal delivery. Both treatments demonstrated comparable adverse-effect profiles, haemodynamic stability and patient satisfaction. Tapentadol nasal spray may therefore represent a convenient and effective option for early postoperative pain management, while larger trials are required before definitive clinical superiority can be established.

Limitations

The study had several limitations. It was conducted at a single centre and included only 60 participants, which limited statistical power, particularly for categorical outcomes and uncommon adverse events. The study was single-blinded, and the different routes of drug administration may have allowed participants or healthcare personnel to identify the allocated intervention despite the use of placebos. The population included different types of abdominal surgery, potentially introducing heterogeneity in surgical trauma and expected pain intensity. The timing of buprenorphine patch application may have influenced its early effectiveness because transdermal buprenorphine has a slower onset than intranasal tapentadol. Pain is subjective and may have been affected by individual pain thresholds, anxiety and expectations. Repeated VAS comparisons at multiple time points could have increased the risk of type I

error if multiplicity was not adjusted. The follow-up period was limited to 72 hours and did not evaluate prolonged analgesia, functional recovery, chronic postsurgical pain, dependence or delayed adverse effects. Finally, the study was not sufficiently powered to detect differences in rare but serious complications such as clinically important respiratory depression.

DECLARATIONS

Conflicts of interest: There is no any conflict of interest associated with this study

Consent to participate: There is consent to participate.

Consent for publication: There is consent for the publication of this paper.

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