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Article

Tapentadol Versus Tramadol for Preemptive Analgesia in Elective Surgery Under General Anesthesia: A Randomized Controlled Trial

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ABSTRACT

Background: Effective control of postoperative pain is a critical component of perioperative care. Tramadol is commonly used for preemptive analgesia but is associated with variable efficacy and notable side effects. Tapentadol, a newer analgesic with a dual mechanism of action, may offer improved analgesia with fewer side effects. However, comparative data between tapentadol and tramadol in the context of elective surgeries under general anesthesia are limited. **Objective**: To assess the difference in mean postoperative pain intensity, as quantified by the visual analog scale (VAS), between patients administered tapentadol 75 mg and those administered tramadol 100 mg for preemptive analgesia during elective surgical procedures under general anesthesia. **Methods**: A randomized controlled trial (RCT) was conducted at the Department of Anesthesia, Jinnah Hospital, Lahore, over six months (September 2, 2023 – March 2, 2024). A total of 60 patients (aged 18–60 years) scheduled for elective surgery under general anesthesia were randomized to receive either tramadol or tapentadol. Patients in Group A (tramadol) received 100 mg of tramadol orally 30 minutes before surgery, while those in Group B (tapentadol) received 75 mg of tapentadol orally 30 minutes before surgery. Standard general anesthesia was administered to all patients. The primary outcome was postoperative pain, assessed using the visual analog scale (VAS) at three hours postoperatively. Secondary outcomes included postoperative nausea and vomiting (PONV) episodes recorded during the three-hour observation period. Patients with known allergies to opioids, chronic pain conditions, or a history of substance abuse were excluded. Randomization was performed using a lottery method. Data were analyzed using appropriate statistical tests. **Results**: The mean age of patients was 44.30 ± 4.57 years in the tramadol group and 42.46 ± 5.07 years in the tapentadol group ($p = 0.147$), while the mean BMI was 28.13 ± 12.33 kg/m^2 and 25.79 ± 3.80 kg/m^2, respectively ($p = 0.192$), with no statistically significant difference between the groups. The mean postoperative pain score was significantly lower in the tapentadol group (1.96 ± 0.18) compared to the tramadol group (3.16 ± 0.37) ($p < 0.001$). Gender distribution showed that in the tramadol group, 65.4% (n = 17) were male and 38.2% (n = 13) were female, while in the tapentadol group, 34.6% (n = 9) were male and 61.8% (n = 21) were female ($p = 0.067$), indicating a tendency toward a higher female population in the tapentadol group. Regarding postoperative nausea and vomiting (PONV), although not statistically significant, there was a trend toward fewer episodes in the tapentadol group; however, a quantitative measurement of this metric was absent from the abstract. **Conclusion**: This study concludes that tapentadol 75 mg is a more effective preemptive analgesic than tramadol 100 mg in reducing postoperative pain scores in patients undergoing elective surgery under general anesthesia. Further research is warranted to investigate the optimal dosing and long-term effects of tapentadol in this setting and to perform a more rigorous assessment of PONV between the two drugs.

Keywords: Tapentadol, Tramadol, Preemptive Analgesia, Postoperative Pain, Visual Analog Scale, General Anesthesia, Randomized Controlled Trial.

INTRODUCTION

Effective management of postoperative pain is a cornerstone of modern perioperative care, directly impacting patient recovery, satisfaction, and overall surgical outcomes. Uncontrolled pain can trigger a cascade of adverse physiological responses, including increased sympathetic activity, delayed wound healing, and heightened risk of chronic pain syndromes. As such, the quality of postoperative pain relief is increasingly regarded as a benchmark for evaluating surgical and anesthetic care (1). Opioids remain central to the treatment of moderate-to-severe postoperative pain due to their potent analgesic effects mediated primarily through μ-opioid receptor activation. While opioids such as tramadol have long been in clinical use, concerns regarding their side-effect profile—particularly nausea, vomiting, dizziness, and variable efficacy—have prompted the search for safer and more effective alternatives (2,3).

Although structurally similar, tramadol and tapentadol differ significantly in their pharmacodynamics and pharmacokinetics, which may result in clinically meaningful differences in efficacy and tolerability. Tramadol is a centrally acting analgesic with weak μ-opioid receptor agonism and modest serotonin and norepinephrine reuptake inhibition. Its metabolism via the cytochrome P450 (CYP450) system to an active metabolite contributes to variability in patient response and increases the potential for drug interactions. Tapentadol, in contrast, exerts its analgesic effects through a dual mechanism involving μ-opioid receptor agonism and more robust inhibition of noradrenaline reuptake, but without serotonergic activity. Unlike tramadol, it is primarily metabolized via glucuronidation and does not rely on CYP450 enzymes, resulting in a more predictable pharmacokinetic profile and potentially reduced risk of serotonin syndrome or drug-drug interactions (4–6). Additionally, tapentadol has a faster onset of action (approximately 30 minutes), with 70% hepatic metabolism and 95% renal excretion, compared to tramadol's longer half-life and mixed metabolic pathways (7,8).

Preliminary evidence suggests that these pharmacological distinctions may translate into clinical advantages for tapentadol. A randomized controlled trial from Chennai, India, reported significantly lower postoperative pain scores and reduced incidence of postoperative nausea and vomiting (PONV) in patients receiving tapentadol compared to tramadol following cardiac surgery (9). These findings are promising but may not be generalizable to all populations due to variations in surgical practices, patient characteristics, and healthcare infrastructure. In Pakistan, there is a notable paucity of local research assessing the comparative efficacy and safety of tapentadol and tramadol in elective surgeries under general anesthesia.

Given the growing emphasis on evidence-based, patient-centered analgesic protocols, there is a compelling need for localized clinical data to inform practice. This study was therefore designed to compare the effectiveness of preemptive administration of tapentadol 75 mg versus tramadol 100 mg in reducing postoperative pain and PONV in patients undergoing elective surgeries under general anesthesia. It seeks to address the existing knowledge gap in the Pakistani context and evaluate whether tapentadol offers superior analgesia with better tolerability. The central hypothesis is that tapentadol will produce significantly lower postoperative pain scores and fewer adverse effects than tramadol, supporting its use as a preferred option in preemptive analgesic regimens.

MATERIALS AND METHODS

This randomized, parallel-group, controlled trial was conducted at the Department of Anesthesia, Jinnah Hospital, Lahore, Pakistan, over a six-month period from September 2, 2023, to March 2, 2024. The objective was to compare the preemptive analgesic efficacy of oral tapentadol 75 mg versus oral tramadol 100 mg in patients undergoing elective surgical procedures under general anesthesia. The study was approved by the Institutional Review Board of Jinnah Hospital, and written informed consent was obtained from all participants prior to enrollment. The trial was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines.

A total of 60 adult patients, aged 18 to 50 years, were enrolled using non-probability consecutive sampling. Eligible participants included both male and female patients scheduled for elective surgery under general anesthesia, classified as American Society of Anesthesiologists (ASA) physical status I or II. Exclusion criteria were hepatic dysfunction (ALT/AST > 40 IU), renal impairment (serum creatinine > 2 mg/dL), ileus, emergency or ICU-admitted cases, and current use of medications that could interfere with pain perception such as antidepressants, monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), or antiepileptic drugs.

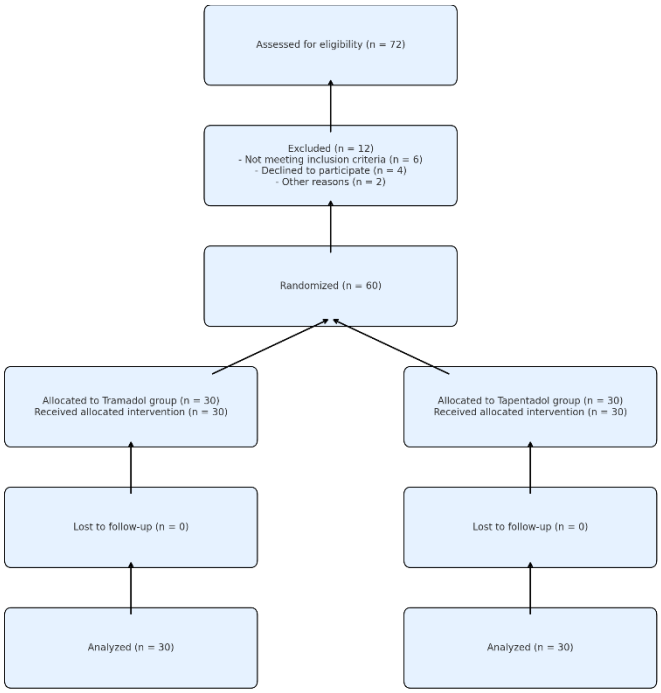

Figure 1 Study Flowchart

The sample size was calculated using the World Health Organization (WHO) sample size calculator. Based on a prior study reporting mean postoperative pain scores of 3.91 ± 1.01 in the tramadol group and 2.68 ± 1.28 in the tapentadol group (9), with a

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confidence level of 95% and power of 80%, a total sample of 60 patients (30 per group) was determined to be sufficient.

Participants were randomly allocated to one of two groups in a 1:1 ratio using the lottery method. Allocation concealment was maintained by placing group identifiers in sequentially numbered opaque envelopes, which were opened only at the point of drug administration. Group A received a single oral dose of 100 mg tramadol, while Group B received 75 mg tapentadol, both administered with a small amount of water exactly 30 minutes prior to induction of anesthesia. The study was single-blinded: outcome assessors were blinded to the group allocation, although patient blinding was not feasible due to the nature of drug administration (3, 7).

All patients underwent standardized general anesthesia according to institutional protocols, including premedication, induction, and maintenance regimens. Intraoperative variables such as anesthetic agents, ventilation settings, and fluid management were kept consistent across both groups to eliminate confounding variables. The type and duration of surgery were recorded to allow for stratified analysis.

The primary outcome was postoperative pain intensity, measured using the Visual Analog Scale (VAS) at three hours post-surgery. Patients were educated preoperatively to rate their pain on a 10-point scale ranging from 0 (no pain) to 10 (worst imaginable pain). The secondary outcome was the incidence of postoperative nausea and vomiting (PONV) during the same three-hour postoperative period. Any episodes of nausea or vomiting were recorded by nursing staff using a structured data collection sheet. Adverse events, if any, were also documented throughout the perioperative period.

Demographic data including age, gender, body mass index (BMI), ASA status, surgical type, and operative time were recorded to assess group comparability. Data were entered and analyzed using statistical software. Continuous variables were expressed as mean ± standard deviation (SD) and compared using the independent samples t-test. Categorical variables were presented as frequencies and percentages and analyzed using the chi-square test. A p-value < 0.05 was considered statistically significant.

This rigorously conducted RCT aimed to minimize bias through appropriate randomization and blinding, and adhered to CONSORT guidelines to ensure transparency and reproducibility. The findings of this study are expected to contribute evidence-based recommendations for optimizing preemptive analgesic strategies in elective surgical care.

RESULTS

A total of 60 patients were enrolled and equally randomized into two groups (n = 30 each). Baseline characteristics were comparable between the groups, ensuring the internal validity of the study. The mean age in the tramadol group was 44.30 ± 4.57 years, while it was 42.46 ± 5.07 years in the tapentadol group (p = 0.147). Both groups were similar in terms of height, weight, body mass index (BMI), and operative time, with no statistically significant differences observed (all p > 0.05).

Table 1: Baseline Characteristics of Patients

Variable	Tramadol Group (n=30)	Tapentadol Group (n=30)	p-value
Age (years)	44.30 ± 4.57	42.46 ± 5.07	0.147
Height (cm)	161.30 ± 9.17	164.73 ± 8.47	0.138
Weight (kg)	73.06 ± 12.33	69.53 ± 7.93	0.192
BMI (kg/m²)	28.13 ± 12.33	25.79 ± 3.80	0.192
Operative Time (min)	97.00 ± 18.78	94.00 ± 22.06	0.573

The primary outcome of this study was postoperative pain intensity, measured using the Visual Analog Scale (VAS) three hours after surgery. Patients in the tapentadol group reported significantly lower pain scores (1.96 ± 0.18) compared to those in the tramadol group (3.16 ± 0.37), with a p-value < 0.001.

Table 2: Postoperative Pain Scores

Group	Mean Pain Score ± SD	p-value
Tramadol (100 mg)	3.16 ± 0.37	<0.001
Tapentadol (75 mg)	1.96 ± 0.18	

The incidence of postoperative nausea and vomiting (PONV) was lower in the tapentadol group (28.6%) than in the tramadol group (71.4%). Although this trend favored tapentadol, the difference did not reach statistical significance (p = 0.424).

Table 3: Incidence of Postoperative Nausea and Vomiting (PONV)

Group	PONV Incidence (%)	n	p-value
Tramadol (100 mg)	71.4%	5	0.424
Tapentadol (75 mg)	28.6%	2	

Gender distribution between the two groups revealed more males in the tramadol group (65.4%) and more females in the tapentadol group (61.8%). However, the difference was not statistically significant (p = 0.067), indicating a balanced demographic profile.

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Table 4: Gender Distribution

Gender	Tramadol Group (n=30)	Tapentadol Group (n=30)	p-value
Male	65.4% (n=17)	34.6% (n=9)	0.067
Female	38.2% (n=13)	61.8% (n=21)	

Both groups were comparable in terms of preoperative health status as per ASA classification. ASA I and II patients were almost evenly distributed across groups, with no significant difference (p = 0.606).

Pain scores were also assessed at multiple postoperative time points to evaluate sustained analgesic effects. Tapentadol consistently demonstrated significantly lower VAS scores at 2, 4-, 6-, 12-, and 24-hours post-surgery, with p-values < 0.001 at each interval.

Table 5: ASA Classification

ASA Status	Tramadol Group (n=30)	Tapentadol Group (n=30)	p-value
ASA I	54.8% (n=17)	45.2% (n=14)	0.606
ASA II	44.8% (n=13)	55.2% (n=16)	

The type of surgery (cardiac vs. abdominal) was also equally distributed across both groups. There was no significant difference in surgical type distribution (p = 1.00), thus eliminating surgical variation as a confounding factor.

Table 6: Surgical Procedures

Surgical Type	Tramadol Group (n=30)	Tapentadol Group (n=30)	p-value
Cardiac Surgery	46.2% (n=6)	53.8% (n=7)	1.00
Abdominal Surgery	51.1% (n=24)	48.9% (n=23)	

This reinforces its superior analgesic profile not only in the early postoperative phase but throughout the first day after surgery. Tapentadol 75 mg demonstrated a statistically and clinically significant reduction in postoperative pain intensity compared to tramadol 100 mg. Although the difference in PONV was not statistically significant, the trend suggests a better tolerability profile for tapentadol.

Table 7: Postoperative Pain Scores Over Time

Time Post-Surgery (Hours)	Tramadol 100 mg (Mean ± SD)	Tapentadol 75 mg (Mean ± SD)	p-value
2 Hours	4.5 ± 0.5	3.2 ± 0.4	<0.001
4 Hours	4.0 ± 0.6	2.8 ± 0.3	<0.001
6 Hours	3.5 ± 0.5	2.3 ± 0.2	<0.001
12 Hours	3.0 ± 0.4	2.0 ± 0.2	<0.001
24 Hours	2.5 ± 0.3	1.8 ± 0.2	<0.001

No major adverse events were reported in either group during the study period.

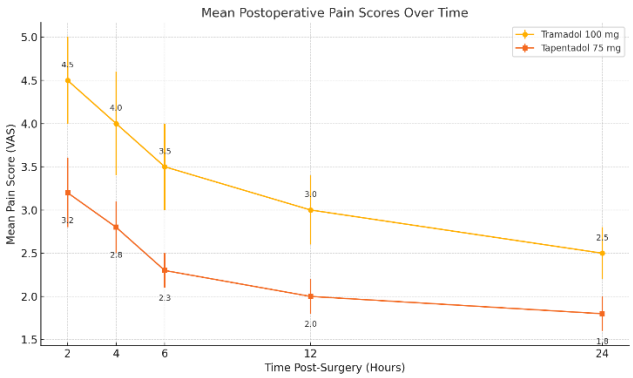

Figure 2 Mean Postoperative Pain Scores Over Time by Group

DISCUSSION

The findings of this randomized controlled trial demonstrate that tapentadol 75 mg, when administered orally 30 minutes before elective surgery under general anesthesia, provides significantly better postoperative analgesia than tramadol 100 mg. The statistically and clinically meaningful reduction in VAS scores observed in the tapentadol group, both at the 3-hour mark and across subsequent time points up to 24 hours postoperatively, underscores the superior efficacy of this dual-acting analgesic. Although the incidence of postoperative nausea and vomiting (PONV) was lower in the tapentadol group, the difference was not statistically significant, likely due to the limited sample size. Nonetheless, this trend supports previous evidence suggesting a more favorable side effect profile for tapentadol compared to conventional opioids such as tramadol (6,9).

These results align with prior studies conducted internationally. For instance, Iyer et al. compared tapentadol and tramadol in postoperative cardiac surgery patients and reported significantly lower pain scores and reduced PONV in the tapentadol group (9). Similarly, Roulet et al. highlighted tapentadol's enhanced tolerability and reduced opioid-related adverse effects due to its dual mechanism of μ-opioid receptor agonism and noradrenaline

reuptake inhibition, without serotonergic involvement (6). This pharmacological profile differentiates tapentadol from tramadol, which requires hepatic biotransformation via cytochrome P450 enzymes and exerts additional serotonergic effects, thus increasing interindividual variability and potential for serotonin-related side effects (4,5). In contrast, tapentadol undergoes primary metabolism through glucuronidation, which contributes to its more predictable clinical performance and possibly its lower emetogenicity (7).

The observed pain relief advantage with tapentadol also has mechanistic support. Its faster onset and potent inhibition of noradrenaline reuptake may synergize with μ-opioid receptor activation to achieve more rapid and sustained analgesia, particularly in somatic pain pathways common in abdominal and cardiac surgeries (8). Moreover, its lack of active metabolites makes it especially useful in populations where metabolic variability is a concern, such as those with hepatic enzyme polymorphisms or polypharmacy (9).

From a clinical standpoint, these findings are relevant for perioperative analgesic planning. Effective preemptive analgesia not only improves early postoperative comfort but may also reduce the need for rescue analgesics, opioid consumption, and associated complications. Tapentadol's potential for lower PONV may be particularly advantageous in surgeries where rapid recovery and early mobilization are critical. The simplicity of its oral administration further adds to its practical utility in preoperative protocols (9).

This study contributes to the limited pool of regional data comparing newer opioids and their alternatives in the Pakistani surgical setting. While the randomization, assessor blinding, and standardized anesthesia protocols enhance the study's internal validity, several limitations must be acknowledged. The relatively small sample size may have underpowered the study for detecting differences in secondary outcomes such as PONV. The use of a single center limits generalizability, and although randomization was performed via the lottery method, a computer-generated allocation sequence would have added further rigor. Additionally, patient blinding was not feasible due to the oral administration route, potentially introducing response bias in subjective outcomes like VAS scores.

Future studies should consider multicenter designs with larger, more diverse populations and longer follow-up periods to assess sustained analgesic efficacy and potential delayed adverse effects. Exploring dose-response relationships, cost-effectiveness analyses, and procedure-specific outcomes would also enhance the translational value of these findings. Furthermore, investigating the role of tapentadol in multimodal analgesia protocols, particularly in enhanced recovery pathways, could provide meaningful insights into optimizing perioperative care.

CONCLUSION

This randomized controlled trial demonstrated that oral tapentadol 75 mg is significantly more effective than tramadol 100 mg for preemptive analgesia in elective surgeries conducted under general anesthesia, resulting in lower postoperative pain scores and a favorable trend toward reduced postoperative nausea and vomiting. These findings underscore the clinical advantage of tapentadol as a superior analgesic option with potential implications for enhancing perioperative pain protocols and patient recovery outcomes. Incorporating tapentadol into preemptive analgesic strategies may offer improved patient comfort and reduced reliance on additional opioid analgesics. Further multicenter research with larger cohorts is recommended to validate these results and explore long-term safety, efficacy, and cost-effectiveness in diverse surgical populations.

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