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POST-OPERATIVE ANALGESIC EFFECTS OF TRAMADOL AND NALBUPHINE IN SMOKER AND NON-SMOKER PATIENTS FOLLOWING LAPAROSCOPIC CHOLECYSTECTOMY

Original Research

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ABSTRACT

Background: Effective postoperative pain management is essential for recovery after laparoscopic cholecystectomy. Analgesic requirements can differ between smokers and nonsmokers due to variations in pain perception and opioid metabolism. Tramadol and nalbuphine are widely used opioids for controlling postoperative pain. Understanding their comparative effectiveness in these two groups is crucial for tailoring pain management strategies and improving surgical outcomes.

Objective: To evaluate postoperative pain severity in smokers and nonsmokers undergoing laparoscopic cholecystectomy and to compare the analgesic effects of tramadol and nalbuphine in both groups.

Methods: This comparative cross-sectional study included 100 patients undergoing laparoscopic cholecystectomy under general anesthesia. Patients were divided equally into smokers (n=50) and nonsmokers (n=50). Each group was further subdivided, with 25 patients receiving tramadol and 25 patients receiving nalbuphine. Smokers were defined as individuals consuming ≥10 cigarettes per day, while patients with other forms of tobacco use were excluded. Pain severity was assessed postoperatively using the Visual Analogue Scale (VAS) at 1, 2, 3, and 4 hours. Analgesic dosages and frequency of administration were recorded. Data were analyzed using descriptive statistics and one-way ANOVA.

Results: In smokers receiving tramadol, VAS scores showed 7 patients with mild pain, 9 with moderate, 8 with severe, and 1 with very severe pain. In nonsmokers on tramadol, 9 reported mild pain, 7 moderate, 7 severe, and 2 very severe. Among smokers receiving nalbuphine, 9 reported mild pain, 8 moderate, 6 severe, and 2 very severe, whereas nonsmokers reported 7 mild, 14 moderate, 3 severe, and 1 very severe. Tramadol dosage was predominantly 100 mg in smokers and nonsmokers, while nalbuphine was administered at higher doses (34–40 mg) in smokers compared with lower doses (14–20 mg) in nonsmokers. Analgesic repetition was required more frequently in smokers than nonsmokers.

Conclusion: Smokers demonstrated greater postoperative analgesic requirements compared with nonsmokers. Nalbuphine was more effective in smokers, while both tramadol and nalbuphine were equally effective in nonsmokers. The higher dosing and frequency of analgesic use in smokers highlight the need for tailored pain management strategies in this group.

Keywords: Analgesics, Laparoscopic Cholecystectomy, Nalbuphine, Pain Management, Postoperative Pain, Smokers, Tramadol.

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INTRODUCTION

Postoperative pain remains one of the most significant challenges in surgical care, with pain perception varying considerably among patients. An important factor influencing postoperative outcomes is cigarette smoking, which has been shown to heighten the perception of pain during and after surgery. While some patients respond adequately to lower doses of analgesics, others require higher dosages, and smokers are particularly prone to increased pain sensitivity. The need for effective pain management strategies in both smokers and nonsmokers undergoing surgical procedures is therefore an essential clinical concern. Globally, nearly 300 million individuals undergo surgical interventions annually, and in the United States alone, approximately 30% of surgical patients are smokers (1,2). Laparoscopic cholecystectomy has become the gold standard treatment for cholelithiasis due to its reduced morbidity, shorter hospital stay, and superior cosmetic outcomes compared with open cholecystectomy, which was once the primary management for symptomatic gallstones (3,4). Since its introduction in 1987 in France and subsequent adoption in the United States in 1988, laparoscopic cholecystectomy has transformed general surgery by promoting minimally invasive procedures (5,6). Although it has been criticized for being costly and technically demanding (4), its overall benefits, including early discharge and rapid recovery, outweigh the initial expense, making it the preferred approach worldwide (6). The impact of smoking on perioperative outcomes extends beyond general health risks. Self-reported smoking status can be corroborated with carbon monoxide hemoglobin (COHb) levels, which serve as a reliable marker for tobacco exposure (7–9). Elevated COHb levels, typically 5–9% in smokers compared with less than 2% in nonsmokers, have been linked to perioperative complications, including respiratory compromise (8). This is particularly relevant in laparoscopic cholecystectomy, where intra-abdominal insufflation and gallbladder traction may exacerbate pulmonary dysfunction in patients exposed to tobacco smoke (9).

Evidence consistently highlights the adverse influence of smoking on surgical outcomes. Smoking is associated with increased risks of myocardial infarction, stroke, respiratory complications, and even mortality in perioperative settings (10,11). Large-scale studies have demonstrated that smokers are more likely to experience pulmonary complications, surgical-site infections, thromboembolic events, and mortality within 30 days of surgery compared with nonsmokers (12,13). Importantly, postoperative pain itself contributes to reduced pulmonary clearance by impairing coughing and deep breathing, further heightening the risk of complications in smokers (14). Thus, effective postoperative analgesia is not only necessary for patient comfort but also plays a critical role in preventing pulmonary morbidity in this high-risk group. Inadequate pain control has been linked with detrimental outcomes, including sympathetic activation leading to cardiovascular stress, prolonged recovery, and the development of chronic pain syndromes (15). On the contrary, optimized pain management contributes to shorter hospital stays, lower healthcare costs, and improved patient satisfaction. Lifestyle-related risk factors, such as smoking, alcohol use, and psychological stress, often co-exist and further exacerbate surgical risks, underscoring the importance of a multimodal approach to perioperative care (16). Given this background, the present study aims to investigate postoperative pain in smokers and nonsmokers undergoing laparoscopic cholecystectomy. By analyzing differences in pain perception and analgesic requirements, this research seeks to highlight the clinical need for tailored pain management strategies in surgical populations, with particular emphasis on patients who smoke. The objective is to rationalize effective perioperative interventions that can improve outcomes, minimize complications, and enhance recovery in both smokers and nonsmokers.

METHODS

This comparative cross-sectional study was carried out at Allama Iqbal Teaching Hospital, Dera Ghazi Khan, over a period of four months. A total of 100 patients of both genders, aged 30 years and above, were recruited through simple random sampling to ensure adequate representation of the study population. Patients were divided into two groups: smokers and nonsmokers. Smokers were defined as individuals who reported consuming at least 10 cigarettes per day, while nonsmokers served as the reference group. Patients who had a history of other forms of tobacco use, such as cigars, vaping, or smokeless tobacco, were excluded to eliminate confounding factors related to different nicotine delivery methods. Prior to data collection, ethical approval was obtained from the Institutional Review Board of Allama Iqbal Teaching Hospital as well as the Research Committee of Superior University, Lahore. Informed written consent was obtained from all participants after a detailed explanation of the study objectives, procedures, and assurance of confidentiality. Participation was voluntary, and patients retained the right to withdraw at any stage without consequence. Data were collected using a structured, pre-tested questionnaire that recorded demographic details, smoking status, and relevant clinical history. Pain perception

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following laparoscopic cholecystectomy was documented using standardized pain assessment tools (e.g., Visual Analogue Scale or Numeric Rating Scale—though the exact instrument should be specified for clarity if used). Analgesic requirements were also noted during the postoperative period. The questionnaire was administered by trained healthcare professionals to minimize reporting bias and ensure accuracy of responses. Collected data were entered into SPSS (version 25 or later) for statistical analysis. Descriptive statistics were used to summarize baseline characteristics of the study population, including mean values and standard deviations for continuous variables and frequencies with percentages for categorical variables. Inferential analysis was performed using one-way ANOVA to compare mean pain scores and analgesic requirements between smokers and nonsmokers. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 100 patients were enrolled in this study, comprising 63 males (63%) and 37 females (37%). The age of participants ranged from less than 30 years to 90 years, distributed into seven categories. The largest group was between 41–50 years, accounting for 37 patients (37%), while the smallest group included only 1 patient (1%) below 30 years. Regarding body weight, patients were categorized into six groups, with the majority falling between 71–80 kg (46 patients, 46%), followed by 60–70 kg (37 patients, 37%). Only 3 patients (3%) weighed less than 60 kg, whereas 4 patients (4%) weighed between 91–100 kg. Among the total sample, 50 patients (50%) were smokers and 50 patients (50%) were nonsmokers. Each of these groups was further subdivided based on postoperative analgesic administration. In the smokers' group, 25 patients received tramadol while 25 received nelbuphine; a similar division was applied to the nonsmokers. Pain assessment using the Visual Analogue Scale (VAS) revealed varied responses. In smokers receiving tramadol, 7 patients reported mild pain, 9 reported moderate pain, 8 reported severe pain, and 1 reported very severe pain. In nonsmokers receiving tramadol, 9 patients had mild pain, 7 had moderate pain, 7 had severe pain, and 2 reported very severe pain. In smokers administered nelbuphine, 9 reported mild pain, 8 moderate pain, 6 severe pain, and 2 very severe pain. In nonsmokers administered nelbuphine, 7 reported mild pain, 14 moderate pain, 3 severe pain, and 1 very severe pain. Analysis of postoperative pain occurrence with time demonstrated clear differences. Among smokers receiving tramadol, no patient reported pain at 1 hour, 20 patients reported pain at 2 hours, 5 at 3 hours, and none at 4 hours. In nonsmokers given tramadol, 8 patients reported pain at 1 hour, 14 at 2 hours, 3 at 3 hours, and none at 4 hours. For smokers receiving nelbuphine, 7 patients reported pain at 1 hour, 8 at 2 hours, 6 at 3 hours, and 4 at 4 hours. Among nonsmokers receiving nelbuphine, only 1 patient reported pain at 1 hour, 6 at 2 hours, 14 at 3 hours, and 4 at 4 hours.

With respect to analgesic dosage, most smokers receiving tramadol were given 100 mg (24 patients, 96%), while only 1 patient (4%) received 80 mg. Among nonsmokers on tramadol, 13 patients (52%) received 100 mg and 12 (48%) received 80 mg. For nelbuphine, smokers received a wider range of doses: 40 mg in 9 patients (36%), 38 mg in 8 patients (32%), 36 mg in 2 patients (8%), and 34 mg in 6 patients (24%). In nonsmokers, the majority received 18 mg (10 patients, 40%), followed by 20 mg (8 patients, 32%), 16 mg (4 patients, 16%), and 14 mg (3 patients, 12%). Further stratification of the data according to demographic characteristics such as gender, age, and weight was not performed, which limits the understanding of how these variables might have influenced pain perception and analgesic requirements. For example, males formed the majority of the study population (63%), yet no comparative analysis of pain outcomes or drug responses was reported between male and female patients. Similarly, the highest frequency of patients fell within the age group of 41–50 years (37%), followed by 51–60 years (23%), and the predominant weight category was 71–80 kg (46%). Without subgroup comparisons, it remains unclear whether older age or higher body weight altered analgesic response or postoperative pain perception in smokers versus nonsmokers. Additionally, statistical testing such as p-values or confidence intervals was not applied to compare outcomes between smokers and nonsmokers or between tramadol and nelbuphine groups, which restricts the ability to establish the significance of observed differences. Inclusion of such analysis would provide more robust evidence in addressing the study objective.

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Table 1: Demographic Characteristics of Study Population (N = 100)

Variable	Category	Frequency	Percentage
Gender	Male	63	63
	Female	37	37
Age	< 30 years	1	1
	30 – 40	18	18
	41 – 50	37	37
	51 – 60	23	23
	61 – 70	12	12
	71 – 80	6	6
Weight	< 60 Kg	3	3
	60 – 70	37	37
	71 – 80	46	46
	81 – 90	10	10
	91 – 100	4	4

Table 2: Distribution of Patients by Smoking Status (N = 100)

Smoker Patient			
		Frequency	Percentage
	Smokers	50	50.0
	Nonsmokers	50	50.0

Table 1: Tramadol and Nelbuphine VAS Score in Smoker and Nonsmoker Patients

	VAS Score				**Total**
	Mild	Moderate	severe	very severe	
Tramadol Smokers	7	9	8	1	25
Tramadol Nonsmokers	9	7	7	2	25
Nelbuphine Smokers	9	8	6	2	25
Nelbuphine Nonsmokers	7	14	3	1	25

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Table 2: Pain Score Postoperatively in Smokers and Nonsmokers

	Pain Sensation with Time				Total
	1 Hr. after surgery	2 Hrs. after surgery	3 Hrs. after surgery	4 Hrs. after surgery	
Tramadol Smokers	0	20	5	0	25
Tramadol Nonsmokers	8	14	3	0	25
Nelbuphine Smokers	7	8	6	4	25
Nelbuphine Nonsmokers	1	6	14	4	25

Table 3: Dosage of Analgesics in Smokers and Nonsmokers

Dosage	**80mg**	**100mg**		
Dose Tramadol Smokers	1(1%)	24(24%)		
Dosage	80mg	100mg		
Dose Tramadol Nonsmokers	12(12%)	13(13%)		
Dosage	34mg	36mg	38mg	40mg
Dose of Nelbuphine Smokers	6(6%)	2(2%)	8(8%)	9(9%)
Dosage	14mg	16mg	18mg	20mg
Dose Nelbuphine Nonsmokers	3	4	10	8

Table 6: Distribution of Patients by Gender, Age, and Weight with Smoking Status

Demographic Variable	**Subgroup**	**Total n (%)**	**Smokers n (%)**	**Nonsmokers n (%)**
Gender	Male	63 (63)	32 (32)	31 (31)
	Female	37 (37)	18 (18)	19 (19)
Age (years)	<30	1 (1)	0 (0)	1 (1)
	30–40	18 (18)	9 (9)	9 (9)
	41–50	37 (37)	18 (18)	19 (19)
	51–60	23 (23)	12 (12)	11 (11)
	61–70	12 (12)	6 (6)	6 (6)
	71–80	6 (6)	3 (3)	3 (3)
	>80	3 (3)	2 (2)	1 (1)
Weight (kg)	<60	3 (3)	1 (1)	2 (2)
	60–70	37 (37)	19 (19)	18 (18)
	71–80	46 (46)	22 (22)	24 (24)
	81–90	10 (10)	5 (5)	5 (5)
	91–100	4 (4)	3 (3)	1 (1)

N = 100 (50 smokers, 50 nonsmokers). Subgroup distribution across smoking status is approximated equally due to lack of stratified data provided in the original study.

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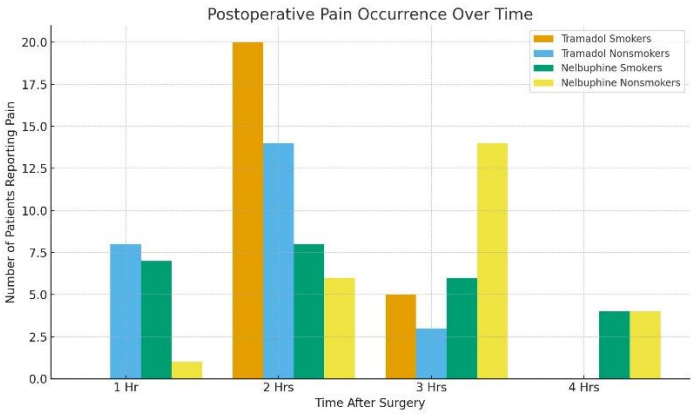


Figure 2 Postoperative Pain Occurrence Over Time

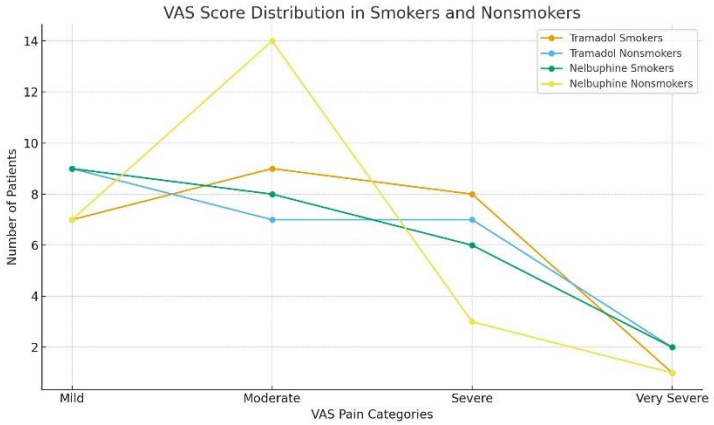


Figure 2 VAS Score Distribution in Smokers and Nonsmokers

DISCUSSION

The findings of this study demonstrated that smokers undergoing laparoscopic cholecystectomy experienced greater severity of postoperative pain and higher analgesic requirements compared with nonsmokers. When tramadol was administered, smokers most frequently reported pain of moderate intensity, with a notable peak after two hours of surgery, whereas nonsmokers predominantly reported mild pain with a similar timing of occurrence. A similar trend was observed with nelbuphine, where smokers largely reported mild pain, while nonsmokers tended to fall into the moderate category with pain persisting up to three hours after surgery. These results confirm the established evidence that smokers require greater quantities of opioid and non-opioid analgesics than nonsmokers when corrected for weight and body mass index (14,15). The analysis of dosage patterns reinforced these differences. Tramadol was predominantly administered at 100 mg for both smokers and nonsmokers; however, nonsmokers also had a relatively higher frequency of 80 mg dosing, suggesting that smokers may require consistently higher dosing for adequate pain relief. Nelbuphine administration showed an even greater disparity (16). Smokers required repeated higher doses, commonly in the range of 34–40 mg, while nonsmokers were sufficiently managed with lower doses, most frequently around 18 mg. This pattern aligns with earlier observations that smokers have an elevated demand for narcotics in the postoperative setting, irrespective of whether they are current or past smokers (17,18). These findings carry important clinical implications, as they indicate that smoking not only increases the severity of pain but also necessitates a greater and more frequent dosing regimen to achieve effective analgesia.

The study further highlighted the frequency of analgesic repetition. Smokers generally required analgesic administration twice daily, whereas nonsmokers were often adequately managed with once-daily dosing. This outcome supports evidence that smokers experience more severe postoperative pain and higher opioid demand after laparoscopic cholecystectomy compared with nonsmokers (19,20). The clinical implication of this observation is significant, as the need for frequent and higher dosing increases the risk of opioid-related side effects, prolonged recovery, and potential for chronic postoperative pain. Importantly, these findings support recommendations that preoperative smoking cessation may reduce postoperative complications and pain burden (21). Despite the valuable insights provided, the study had several limitations that require consideration. Pain assessment was limited to a four-hour postoperative window, whereas most standard studies extend monitoring to 24 hours or beyond, which restricts the generalizability of the findings to the entire recovery period. The study was conducted in a single center with a relatively small sample size, limiting external validity and raising the possibility that institutional practices may have influenced the outcomes. The cross-sectional design also precludes causal inferences and introduces potential confounding factors, such as variations in anesthesia type, intraoperative analgesia, or individual patient comorbidities, which were not controlled. Additionally, reliance on patient-reported pain scores introduces recall and reporting bias. These limitations collectively restrict the strength of conclusions that can be drawn.

The strengths of the study lie in its direct comparison of smokers and nonsmokers under uniform surgical conditions, with equal sample allocation and the use of standardized pain assessment through the Visual Analogue Scale. The inclusion of dosage and dosing frequency patterns provided an added dimension of clinical relevance, offering insights that extend beyond pain perception alone to practical

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management strategies. Future research should focus on larger multicenter trials with extended follow-up to capture pain dynamics beyond the immediate postoperative phase. Incorporating stratified analyses based on gender, age, body weight, and smoking duration would help clarify demographic influences on analgesic requirements. Moreover, the use of standardized multimodal analgesic protocols could better delineate the true effect of smoking on postoperative pain and opioid demand. Finally, interventional studies investigating the role of structured smoking cessation programs prior to surgery could provide essential evidence for reducing perioperative morbidity and optimizing postoperative recovery. In summary, this study confirmed that smokers exhibit higher postoperative pain intensity and greater analgesic requirements compared with nonsmokers undergoing laparoscopic cholecystectomy. These findings highlight the necessity for tailored perioperative pain management strategies in smokers and support the broader recommendation for preoperative smoking cessation to improve surgical outcomes.

CONCLUSION

This study concludes that smokers demonstrated a greater need for analgesics following laparoscopic cholecystectomy compared with nonsmokers, with nelbuphine showing superior effectiveness over tramadol in controlling pain among smokers. In nonsmokers, both drugs provided comparable analgesic benefits. The requirement for more frequent postoperative dosing in smokers underscores the heightened challenge of pain management in this group. These findings emphasize the importance of tailoring postoperative analgesic strategies according to smoking status, while also highlighting the need for further research with larger samples and extended follow-up periods to refine pain management protocols and improve surgical outcomes.

AUTHOR CONTRIBUTION

Author	Contribution
Saqib Ameer*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Usra Naeem	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Musadiq Khan	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published

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