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ORIGINAL ARTICLE

Comparison of Intravenous Tramadol and Morphine in attenuation of Hemodynamic Stress Response in Patients Undergoing Laparoscopic Cholecystectomy

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ABSTRACT

Objective: The primary objective of this study is to compare the efficacy of intravenous Tramadol and intravenous Morphine in attenuating the hemodynamic stress response during laryngoscopy and endotracheal intubation in patients undergoing laparoscopic cholecystectomy.

Place and duration:

Methodology: This Randomized controlled Trial study was conducted at Sahiwal Teaching Hospital, Sahiwal, from March 2023 to August 2023. In this research, 80 participants slated for laparoscopic cholecystectomy and aged between 20 and 50 years, with American Society of Anesthesiologists (ASA) Grade I or Grade II, were randomly assigned to two groups—Group-T (Tramadol) and Group-M (Morphine)—using a lottery method, each comprising 40 patients.

Results: It was seen that SBP, DBP, MAP and heart rate Morphine group was lower than Tramadol Group. The mean recovery time of Tramadol and Morphine Groups was 46.29±8.65 minutes and 30.47±5.22 minutes, respectively. nausea & vomiting was noted as 14 (42.5%) and 6 (15.05), in Tramadol and Morphine Groups, respectively (p<0.001). It was seen that morphine was effective in 37 (92.5%) patients whereas tramadol was effective in 27 (67.5%) patients. Therefore, morphine was more effective than tramadol (p<0.001).

Conclusion: Intravenous Morphine is more effective than intravenous Tramadol in attenuating the hemodynamic stress response to laryngoscopy and endotracheal intubation during laparoscopic cholecystectomy.

Keywords: Cholecystectomy, Hemodynamic stress response, Intravenous morphine, Tracheal intubation, Tramadol.

INTRODUCTION

Laryngoscopy and endotracheal intubation are essential procedures in general anesthesia but are associated with significant hemodynamic stress responses[1]. These responses, including transient hypertension and tachycardia, result from sympathetic stimulation and can lead to complications, particularly in patients with cardiovascular comorbidities[2]. Various pharmacological agents have been investigated to attenuate these hemodynamic perturbations, with opioids being among the most commonly used[3].

Tramadol and morphine are both opioid analgesics with distinct pharmacodynamic properties. Tramadol, a centrally acting analgesic, exerts its effect via weak μ-opioid receptor agonism and inhibition of serotonin and norepinephrine reuptake, which contributes to its analgesic and sympatholytic properties[4,5]. In contrast, morphine, a potent μ-opioid receptor agonist, provides more profound analgesia and sedation, potentially leading to greater hemodynamic stability. However, the comparative effectiveness of these two opioids in modulating hemodynamic responses during laryngoscopy and intubation remains a subject of debate[6].

Laparoscopic cholecystectomy, a commonly performed minimally invasive procedure, necessitates precise hemodynamic control due to pneumoperitoneum-induced cardiovascular changes[7]. The choice of opioid for mitigating the hemodynamic stress response during induction and intubation is important for optimizing patient safety and perioperative outcomes[8].

Multiple clinical trials have compared the effects of tramadol and morphine on hemodynamic responses during laryngoscopy and intubation. Some studies have reported that morphine, due to its potent opioid activity, is more effective in blunting the sympathetic response, while others suggest that tramadol achieves similar hemodynamic stability with fewer adverse effects. A randomized controlled trial by Elnabtity et al[9] found that tramadol provided effective hemodynamic control with a lower incidence of postoperative nausea and vomiting compared to morphine. Similarly, research by Singh et al[10] highlighted tramadol's efficacy in maintaining stable heart rate and blood pressure while minimizing opioid-related complications.

Existing studies evaluating the effects of intravenous tramadol and morphine on hemodynamic parameters are limited and heterogeneous, with variations in study design, patient populations, and dose regimens. Furthermore, most available literature primarily focuses on their analgesic efficacy rather than their direct role in attenuating hemodynamic fluctuations during laryngoscopy and intubation. Specifically, data on laparoscopic cholecystectomy patients, who experience additional hemodynamic perturbations due to pneumoperitoneum, are sparse.

This study aims to fill this gap by providing comparative data on the efficacy of intravenous tramadol versus morphine in blunting the hemodynamic stress response in patients undergoing laparoscopic cholecystectomy. By addressing this knowledge deficit, the study will contribute to optimizing perioperative anesthetic management and improving patient safety, particularly in populations at risk of hemodynamic instability.

METHODOLOGY

The Randomized Controlled Trial conducted at the Department of Anesthesia, Sahiwal Teaching Hospital, Sahiwal, from March 2023 to August 2023, and received approval from the Hospital Ethical Committee under IRB number ERC5233/2022. The sample size was determined using the WHO sample size calculator, with 99% confidence level and 80% power of study, considering the effectiveness of Morphine in attenuating the hemodynamic stress response at 88.14% and Tramadol at 71.08% [12].n = $(Z_{\alpha/2}+Z_{\beta})^2$ * $(p_1(1-p_1)+p_2(1-p_2))$ / $(p_1-p_2)^2$, formula was used for sample size calculation.

The study included patients of both genders, aged 20-50 years, who were scheduled for laparoscopic cholecystectomy and had American Society of Anesthesiologists (ASA) Grade I or Grade II classification and Mallampati score 1 and 2.Patients with allergies to Morphine or Tramadol, preexisting hypertension,

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ischemic heart disease, arrhythmia, pregnancy confirmed by ultrasound, or those unable to be intubated within one minute during anesthesia induction were excluded from the study.

The preanesthesia assessment was conducted in accordance with hospital guidelines, encompassing a thorough evaluation of clinical, laboratory, and radiological findings for patients scheduled for the procedure. Subsequently, using Helanski method patients were allocated into two groups, namely Group-T (Tramadol) and Group-M (Morphine), with 40 patients assigned to each group.

On the day of surgery, patients were transferred to the operation theatre, where baseline vitals and demographics were documented. Following the hospital protocol, each patient underwent noninvasive monitoring, including pulse oximetry, electrocardiography, noninvasive blood pressure cuff, and a temperature probe. The assigned group for premedication consisted of nalbuphine 0.1mg/kg, Inj dexamethasone 0.1mg/kg, and either Injection Tramadol 2mg/kg or Injection Morphine 0.1mg/kg. Induction of anesthesia was done by using intravenous Propofol at 2mg/kg. Ventilation adequacy was confirmed before administering Atracurium at 0.5mg/kg for muscle relaxation, followed by ventilation with 100% O2 for the next 3 minutes. Subsequently, Direct Laryngoscopy was performed using an appropriately sized Macintosh blade Laryngoscope.

The trachea was successfully intubated using a 7-8 size endotracheal tube, and the placement was confirmed through end-tidal CO2 measurement and auscultation of breath sounds. Anesthesia was maintained with Isoflurane at 1.5-2 minimum alveolar concentration, supplemented by additional shorts of Atracurium at 0.1 mg/kg. Hemodynamic parameters were recorded before and after intubation, as well as at three and five minutes post-intubation. During recovery, a 1.5 mg/kg intravenous Lignocaine plan was administered, and reversal was achieved using Neostigmine at 2.5 mg combined with Glycopyrrolate at 0.5 mg.

Primary outcome of study was hemodynamic stress response to laryngeoscopy and intubation. Secondary outcomes were nausea, vomiting and recovery time. Efficacy was considered "Yes" if the patient's systolic blood pressure and heart rate remained within 20% of their baseline values between 1 and 10 minutes after endotracheal intubation. If either value varied by more than 20% above or below the baseline during this period, efficacy was labeled as "No."

The data analysis involved utilizing Statistical Package for the Social Sciences (SPSS) version 23, wherein frequencies and percentages were computed for qualitative variables such as gender, ASA score, and efficacy. Meanwhile, quantitative variables like age and weight were analyzed using mean and standard deviation calculations. A student t-test was applied to compare numerical means like BMI, SBP, DBP, Heart rate, and recovery time between the groups. Chi-square test was applied to compare categorical variable like, gender, ASA status, Nausea Vomiting and efficacy between the groups, considering a significance level of $p \leq 0.05$.

RESULTS

Eighty patients were included in this study and distributed in two equal groups as Group (T) Tramadol 40 (50.0%) and Group (M) Morphine 40 (50.0%). There were 33 (82.5%) patients had ASA I in Group (T) and 26 (65.0%) patients in Group (M), Whereas there were 7 (17.5%) patients had ASA II in Group (T) and 14 (35.0%) in Group (M), (p=0.075). In this study baseline SBP in Tramadol group was 128.23±1.42 mm/Hg and in Morphine group 128.30±1.26 mm/Hg, DBP in Tramadol group was 80.33±2.22 mm/Hg and in morphine group 80.20±1.78 mm/Hg. Mean heart rate in Tramadol group was 85.25±4.13 mm/Hg and in morphine group 85.70±4.30 mm/Hg. (Table. I).

Comparison of SBP, DBP, MAP and heart rate in both the study groups was shown in table. II. It was seen that SBP, DBP, MAP and heart rate Morphine group was lower than Tramadol Group. The mean recovery time of Tramadol and Morphine Groups was 46.29±8.65 minutes and 30.47±5.22 minutes, respectively. This difference was statistically significant, (p<0.001). nausea & vomiting was noted as 14 (42.5%) and 6 (15.05), in Tramadol and Morphine Groups, respectively. (p<0.001). (Figure. I). It was seen that morphine was effective in 37 (92.5%) patients whereas tramadol was effective in 27 (67.5%) patients. Therefore, morphine was more effective than tramadol. (p<0.001).(Table. II).

Table 1: Association of ASA with both the study groups

Variable	Group		p-value
	Tramadol (T)	Morphine (M)	
Age (years)	46.50±3.38	47.10±3.48	0.436
Gender			
Male	31 (77.5)	29 (72.5)	0.606
Female	9 (22.5)	11 (27.5)	
BMI (kg/m^2)	25.52±2.08	26.10±2.51	0.414
SBP (mm/Hg)	128.23±1.42	128.30±1.26	0.804
DBP (mm/Hg)	80.33±2.22	80.20±1.78	0.782
MAP (mm/Hg)	95.07±3.68	95.78±4.19	0.430
Heart rate (beats/min)	85.25±4.13	85.70±4.30	0.635
ASA			
I	33 (82.5)	26 (65.0)	0.075
II	7 (17.5)	14 (35.0)	
Total	40 (100.0)	40 (100.0)	

Table 2: Comparison of SBP, DBP, MAP and heart rate with both the study groups

Variable	Group		p-value
	Tramadol (T)	Morphine (M)	
SBP (mm/Hg)			
Induction	109.14±6.41	108.32±4.21	0.658
L-1	122.34±6.84	125.63±4.85	0.036
1	123.54±4.85	123.54±6.31	0.841
2	120.54±3.52	119.21±3.21	0.635
3	118.62±3.84	115.62±4.69	0.034
4	116.32±4.52	114.52±4.62	0.041
5	115.87±4.74	113.62±3.84	0.035
7	114.65±4.51	111.41±5.52	0.012
10	113.52±8.62	110.32±9.54	0.002
DBP (mm/Hg)			
Induction	65.32±4.62	64.52±3.62	0.541
L-1	76.58±6.32	77.62±3.12	0.041
1	75.62±7.32	74.62±4.62	0.321
2	73.64±8.65	71.25±3.65	0.051
3	74.65±4.62	73.21±41.8	0.062
4	73.62±4.21	69.52±6.74	0.010
5	72.35±5.62	74.32±4.87	0.003
7	71.52±7.69	68.96±1.24	0.004
10	69.63±4.95	65.62±4.69	0.005
MAP (mm/Hg)			
Induction	81.52±4.78	82.62±4.62	0.418
L-1	92.62±4.62	90.35±6.22	0.621
1	90.32±4.62	90.35±4.62	0.698
2	89.32±4.68	86.64±6.98	0.541
3	88.52±6.58	85.62±6.32	0.035
4	87.65±9.54	84.69±7.69	0.032
5	85.52±3.22	82.65±4.98	0.014
7	86.65±7.54	81.62±6.78	0.011
10	84.62±4.69	82.62±4.98	0.041
Heart rate (mm/Hg)			
Induction	67.69±6.54	65.32±4.74	0.321
L-1	80.65±6.99	80.65±4.62	0.814
1	78.62±4.52	77.65±4.75	0.358
2	77.62±4.62	79.54±4.62	0.685
3	77.54±6.85	76.52±5.62	0.147
4	76.52±6.98	74.62±3.65	0.268
5	74.62±5.88	73.65±9.55	0.471
7	75.62±4.56	74.63±5.48	0.658
10	74.62±4.66	72.62±3.35	0.021
Mean recovery time (minutes)			
Mean±S.D	46.29±8.65	30.47±5.22	<0.000
Mean±standard deviation			

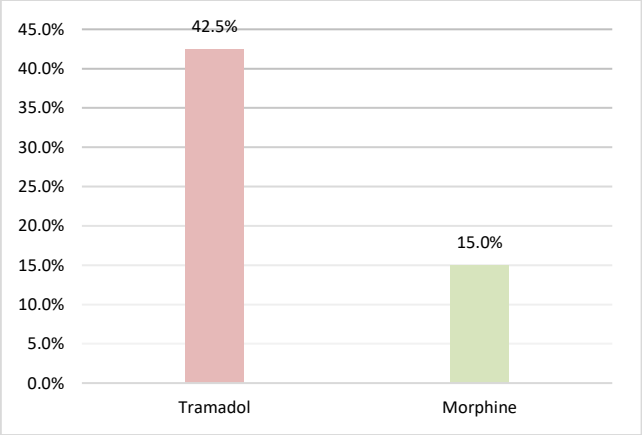

Figure 1: Presence of nausea and vomiting in both the study groups

Table 3: Association of drug efficacy with both the study groups

Efficacy	Group		Total	p-value
	Tramadol (T)	Morphine (M)		
Yes	27 (67.5)	37 (92.5)	64 (80.0)	<0.001
No	13 (32.5)	3 (7.5)	160 (20.0)	
Total	40 (100.0)	40 (100.0)	80 (100.0)	
N (%)				

DISCUSSION

In our study, we found that intravenous Morphine demonstrated a superior effectiveness 92.5% compared to Tramadol 67.5% in attenuating the stress response to laryngoscopy and endotracheal intubation, indicating a more pronounced modulation of the neuroendocrine response. A mixed opioid agonist-antagonist like Nalbuphine, attenuates hemodynamic stress during tracheal intubation by reducing tachycardia and hypertension. Its kappa agonism provides analgesia with minimal respiratory depression, while mu antagonism lowers the risk of excessive sedation or euphoria. It is a valuable adjunct in anesthesia, requiring dose adjustments to avoid interactions and maintain stability[13].

A study by Hoda et al[14] compared the effects of intravenous morphine and tramadol on these responses. The findings indicated that morphine was more effective than tramadol in attenuating the hemodynamic changes associated with these procedures. Specifically, patients receiving morphine exhibited a maximum heart rate increase of 11.86% from baseline, compared to 28.92% in the tramadol group. Additionally, the maximum decrease in systolic blood pressure was 18% in the morphine group, whereas the tramadol group experienced a 10.48% decrease. These results suggest that morphine provides better stabilization of hemodynamic parameters during laryngoscopy and intubation. Additionally, in another study comparing lignocaine and local nitroglycerine spray for mitigating heart rate and blood pressure changes following laryngoscopy and endotracheal intubation, the findings indicated a superior efficacy of nitroglycerine over lignocaine spray[15].

In a study Niyogiet al[16] comparing melatonin, a methoxytryptamine agonist with an anxiolytic effect commonly used in sleep disorders, and clonidine, an alpha blocker known for its central sympatholytic effect, both drugs were found to effectively reduce catecholamine release following laryngoscopy and endotracheal intubation; however, the findings suggested a somewhat subordinate role for melatonin in this regard.

The administration of a low dose (0.75 micrograms per kg) of an alpha 2 receptor agonist, as an adjunct to general anesthesia, has demonstrated remarkable efficacy in reducing the need for analgesia and mitigating episodes of hypertension and tachycardia following laryngoscopy. This recent advancement highlights its potential as a valuable therapeutic approach for minimizing stress-induced tachycardia and hypertension subsequent to airway manipulation[17].

In a study conducted by Khan et al[13], it was concluded that intravenous Morphine demonstrated greater efficacy in attenuating the hemodynamic stress response to laryngoscopy and endotracheal intubation during laparoscopic cholecystectomy compared to intravenous Tramadol. The results indicated that intravenous Tramadol was effective in 48 out of 68 patients 70.5%, whereas intravenous Morphine exhibited effectiveness in 60 patients 88.24%.

Arora et al[18] conducted a study comparing the hemodynamic stability of Tramadol and morphine, revealing that the mean maximum increase in systolic blood pressure (SBP) was 8.06% in the Tramadol group, while the decrease was 18% and 10.48% in the morphine and Tramadol groups, respectively. Similarly, the maximum increase and decrease in diastolic blood pressure (DBP) and mean arterial pressure (MAP) followed a consistent pattern, with blood pressure increases remaining below 15% of the baseline values.

In studies conducted by Coetzee et al[19] and Pang et al[20], the authors proposed that pre-treatment with Tramadol results in dose-dependent cerebral activation on EEG, indicating that Tramadol may not guarantee a deeper level of anesthesia and may not effectively attenuate the hemodynamic response.Recent advances in the field of anesthesia include novel airway adjuncts such as the King video laryngoscope and GlideScope, which have been studied for their effectiveness in attenuating the stress response associated with laryngoscopy and intubation, demonstrating positive outcomes in hemodynamic alterations[21,22].

The observed results align with the pharmacological profiles of morphine and tramadol. Morphine, a potent μ-opioid receptor agonist, provides strong analgesia and hemodynamic stress attenuation but may cause side effects like respiratory depression and histamine release, contributing to instability. Tramadol, a weak μ-opioid agonist with dual norepinephrine and serotonin reuptake inhibition, offers broader action with fewer side effects, making it effective for mild to moderate stress responses[23].

Combining these agents could harness morphine's potency and tramadol's stabilizing effects, reducing morphine doses and minimizing adverse effects. This synergy could improve efficacy and safety during laryngoscopy and intubation. Future studies should explore optimal dosing, timing, and administration of this combination to maximize clinical benefits[24].

CONCLUSION

The study findings indicate that intravenous Morphine is more effective than intravenous Tramadol in attenuating the hemodynamic stress response to laryngoscopy and endotracheal intubation during laparoscopic cholecystectomy, suggesting that routine use of intravenous Morphine is recommended for achieving superior hemodynamic outcomes in all patients undergoing such procedures.

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