

Taylor & Francis

OPEN ACCESS OPEN ACCESS

# Efficacy of esmolol versus magnesium sulphate on quality of recovery in patients undergoing laparoscopic cholecystectomy: Randomized controlled study

Hassan Saeed ElHoshy in and Ahmed Galal El-Din Yacout

Anaesthesia and Surgical Intensive Care Department, Alexandria University, Alexandria, Egypt

#### ABSTRACT

**Background:** Ambulatory procedures have a universal objective of rapid, efficient and secure recovery and release. Preliminary advances utilizing intraoperative esmolol infusion have registered a postoperative opioid saving outcomes. In the current study, we compared intraoperative esmolol versus magnesium sulphate infusions on postoperative recovery profile and stay in the postanaesthesia care unit (PACU).

**Patients and methods:** Sixty patients, of both sexes, of ASA I or II planned for ambulatory laparoscopic cholecystectomy under general anaesthesia were engaged into two groups. Esmolol group was given loading dose (1 mg/kg) over a period of 10 minutes followed by (30 µg/kg/min) all through the surgery, whereas magnesium sulphate (MgSo<sub>4</sub>) group was given loading dose (40 mg/kg) over 10 minutes then maintenance dose (15 mg/kg/h) till end of surgery. General anaesthesia and postoperative analgesia were standardized for all patients. Variables denoting immediate recovery from anaesthesia, pain score and time for first call to analgesia were recorded. White-Song score  $\geq$  12 were employed as a tool to review the rapidity of recovery.

**Results:** Compared to MgSo<sub>4</sub> group, the esmolol group exhibited statistically significant shorter times for sponteaous eye opening, tongue extension, extubation and patients' capability to recall their names. Incidence of vomiting as well as the total amount of ondansetron consumed in the PACU were evidently less among the esmolol group, whereas pain scores and the time of recall for first rescue analgesia did not vary significantly among the two studied groups. Members of the esmolol group displayed significant higher White -Song score at all times of measurements except at 120 minutes compared to those of MgSo<sub>4</sub> group.

**Conclusions:** Perioperative esmolol infusion is accompanied by superior and fast-tracked recovery profile compared to MgSo<sub>4</sub> infusion.

# 1. Introduction

Advancements in perioperative implementations, sedation, and invasive performances have rendered laparoscopic cholecystectomy feasible to be executed upon an outpatient back ground and so huge decline in expanses together with ideal degrees of patients' satisfaction [1]. Ambulatory surgeries institute a unique test facing anesthesiologist. A weighing scale should be established between adequate level of anaesthesia along with its potential adverse events (like delirium, postoperative pain, nausea and vomiting) and the requirements for quick, smooth recovery that ensure securely discharge of patients [2,3].

Traditional handling of these events with opioids or ordinary inhalational and intravenous anaesthetics may not address desirable quality for safe postoperative recovery profile and perhaps preclude patient's satisfaction [4]. Moreover, the emphasis on using opioid- in balanced multimodal anaesthesia- as a prime treatment for the intense pain following pneumoperitoneum may add to the burden. Indeed cardiorespiratory depression, somnolence and prolonged recovery might follow [5].

For instant, with raising number of laparoscopic procedures and the necessity of early patient liberation, the scope of postoperative recovery had evolved from quick return of consciousness with no agony, to involve numerous aspects like regain of patients' physical and psychological capabilities, thus attaining successful early phase recovery [5,6].

Esmolol, a highly cardio selective  $\beta_1$  –adrenoceptor blocker, possessing an ultra-short duration of action and rapid metabolism to inactive metabolites via plasma esterase [7]. It dampens hemodynamic interactions to deleterious stimuli thus mitigating the injuries perioperative stress response [8]. Currently, Esmolol utilization is not acknowledged for opioid sparing

CONTACT Hassan Saeed ElHoshy Alexandria University, Alexandria, Egypt

#### **ARTICLE HISTORY**

Received 18 May 2023 Revised 15 July 2023 Accepted 20 July 2023

#### **KEYWORDS**

Esmolol; magnesium sulphate; quality of recovery; laparoscopic cholecystectomy

 $<sup>\</sup>ensuremath{\mathbb C}$  2023 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0/), which permits

unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The terms on which this article has been published allow the posting of the Accepted Manuscript in a repository by the author(s) or with their consent.

properties and heart protection only but its role as an anaesthesia adjunct is similarly well explored [8,9].

Also, Magnesium sulphate (MgSO<sub>4</sub>) a main noncompetitive N-methyl- D-aspartate (NMDA) receptor blocker having indirect antinociceptive outcomes throughout hindering calcium ions from entering cells thus blunting a cascade of various modifications to the central nervous system involving central sensitization, hyperalgesia and pain wind-up which affect the extent and severity of postoperative pain [10]. Several advances had verified its saving impacts on anaesthetic requirements, postoperative hyperalgesia and perioperative unpleasant experiences like shivering, nausea and vomiting [10,11].

The rationale of the current study is to assess the efficacy of intraoperative Esmolol versus MgSo<sub>4</sub> infusions on the postoperative recovery profile in patients planned for ambulatory laparoscopic cholecystectomy.

## 2. Aim of the study

The primary end point were variables denoting instant postoperative recovery like times crucial for spontaneous eye opening, tongue extension, extubation and patients' ability to recall names. Secondary outcomes included evaluation of the quality of the recovery profile using the White – song score, postoperative pain assessment, time of recall for first rescue analgesia, total amount of postoperative fentanyl consumption and overall dose of rescue antiemetics.

## 3. Patients and methods

This comparative, prospective, randomized single blinded study was accomplished between October 2022 and May 2023 at Alexandria university hospitals. Trial registry on Clinical Trials.gov (Identifier: NCT05850832) and (IRB-NO: 00012098 - FWA-NO: 00018699). Following attaining Ethical committee agreement and patients' written consent- after broad explanation of the entire procedure- 60 patients aged 20-65 years of both sexes of American society of Anesthesiologists (ASA) physical status I – II planned for ambulatory laparoscopic cholecystectomy under general anaesthesia were engaged.

Exclusion criteria: patients on chronic use or known allergic to study drugs, body mass index >35 kg.m–2, significant organ dysfunction, cardiac dysrhythmias, neuromuscular diseases, liver or renal disease, known asthma and reactive airway diseases.

Preoperatively all participants were carefully evaluated via complete history taking, comprehensive physical examination and routine laboratory investigations. Also, all participants were instructed carefully on how to utilize the verbal rating scale (VRS).

Randomization was achieved prior to the study by means of randomization table prepared by computer

software to assign the number of cases among the studied groups. Subjects were randomly allocated with aid of closed envelopes technique into two equal groups (n = 30 each):

- Group (E): (Esmolol group) received loading dose 1 mg/kg slowly i.v- over a period of 10 minutesfollowed by maintenance dose of 30 μg/kg/min all through the surgery.
- Group (M): (Magnesium sulphate group) received loading dose 40 mg/kg slowly i.v- over a period of 10 minutes- and then maintenance infusion at a rate 15 mg/kg/h till end of surgery.

Due to variation in formulation of both the loading and maintenance doses of both the study medications, double blinding was not feasible in the current study. Accordingly -via standardizing the infusion regimensfor every single case, a hundred-ml syringe planned for loading infusion and a twenty-ml syringe planned for maintenance infusion were sent to the operating anaesthesiologist containing either Esmolol (Esmolol hydrochloride; Baxter Health Corp., USA) or MgSo4 (Egyptian international pharmaceutical indust., EYGPT).

Loading dose was started soon after induction, whereas maintenance infusion was continued till end of surgery. At any time, infusions were removed immediately and discard if the patient developed an overt adverse reaction and managed appropriately.

No premedication was offered. In the operating room, an i.v cannula was placed and secured before induction of anaesthesia and then standard monitoring (including pulse oximetry, ECG, non- invasive blood pressure and end tidal carbon dioxide) was applied to every subject (Datex ohmeda S/5).

Anaesthesia was induced with (1 µg/kg) fentanyl and (1.5-2) mg/kg propofol till cessation of verbal contact. Cisatracurium (0.15 mg/kg) was utilized for neuromuscular relaxation and endotracheal intubation (tube size: 8-8.5 mm for males, 7-7.5 mm for female patients). Soon after induction, in both groups IV dexamethasone (8 mg) was given and (1 g) paracetamol IV was infused over 15 mins. Maintenance of anaesthesia was achieved by sevoflurane 1-2% with 50% oxygen in air. Increments of IV fentanyl (0.5 µg/kg) were given for analgesia whenever systolic blood pressure or heart rate exceeded its baseline value by more than twenty percent, also increments of cisatracurium (0.03 mg/kg) were utilized to maintain neuromuscular blockade guided by a nerve stimulator. Patients were mechanically ventilated to maintain ETCO<sub>2</sub> between (33–35 mmHg) and an oxygen saturation of 98%. The port sites were infiltrated by the surgical team with 5 ml of 0.25% bupivacaine with epinephrine 1:200,000. Pneumoperitoneum with carbon dioxide was achieved, maintaining the intraabdominal pressure at (12 mm Hg) all over the surgery. After intraperitoneal CO<sub>2</sub> insufflation- in order to attain better accesses to the gall bladder- positioning in 30 degrees anti-Trendelenburg position along with rotation to the left side was attained for every patient. At any instance, episodes of bradycardia were recognized if patients experienced heart rate < 50 b/m. The infusion was temporarily stopped till resuming acceptable heart rate and if no response i.v. (0.5 mg) atropine blouse was injected. Also, the infusion was held if the patients developed any significant adverse effect and managed accordingly. IV warmed normal saline (0.9%) NaCL was infused throughout surgery at a rate of (6 ml/kg/hr). After completion of surgery, the supine position was resumed and the remaining intraperitoneal Co<sub>2</sub> was expelled by gentle abdominal compression slowly. Once more the surgical incisions were enriched by (5 ml) 0.25% bupivacaine with epinephrine 1:200,000. Esmolol and Mgso<sub>4</sub> infusions were stopped and discarded at end of the procedure which was marked at the end of skin closure and wound coverage. Discontinuation of Anaesthesia was done, followed by administration of 100% oxygen. Neostigmine (0.04–0.08 mg/kg) and atropine (0.02 mg/kg) were injected slowly intravenously to antagonize residual neuromuscular paralysis after oropharyngeal secretions were suctioned, and then extubation of the patients fully awake were done after ensuring adequate spontaneous ventilation with return of the defensive airway reflexes and full muscle strength. Times passed from cessation of anaesthesia till spontaneous eyes opening, extubation, tongue extension, and patients' capability to recall names were recorded. Duration of surgery (time elapsed from start of skin incision to end of procedure and wound coverage) and duration of anaesthesia (time elapsed from induction until the patients were well oriented to time, place and personnel or providing an appropriate cognitive response and ready to be shifted from operating table to the PACU) were also recorded.

In the postanesthesia care unit (PACU) monitoring of heart rate, arterial blood pressure, respiration, and temperature was done via recovery nurses blind to the study design to avoid bias. Also, postoperative data collectors were unaware to the group allocation and had no interaction with the recovery nurses. Postoperative pain assessment was achieved by aid of pain numerical rating scale (NRS) on immediate arrival to PACU and every 30 mins for the first 2 hours afterwards. Pain NRS is 0-10 scale, 0 denotes pain free state, whereas 10 refers to maximum imagined pain. Fentanyl (25 µg) IV was used when NRS exceeded 4. Times to first rescue analgesia and total amount of postoperative fentanyl consumed were recorded. IV ondansetron (4 mg) as a rescue antiemetic was given for vomiting and/or persistent nausea lasting more than 5 min which was repeated as required with maximum three times within an interval of three hours. Total dose of ondansetron consumed was noted. Any incidence of adverse effects like hypotension, bradycardia, headache or dizziness were recorded and managed accordingly.

The White-song scoring system [12], a more up to date quick track scoring framework incorporating fundamental fast track variables like physical steadiness, vitals and consciousness level, had been proposed to evaluate the recovery profile. Furthermore it involved assessment of adverse events like postoperative pain and vomiting, which were unfortunately missed by the modified Aldrete score. It was evaluated on immediate arrival to PACU and every 30 mins for the first 2 hours postoperatively. The time elapsed to attain a score of  $\geq$ 12 was employed as a tool to review the rapidity of recovery. A minimum score (12/14) + NRS < 4 should be established prior to patient safe fast-tracked to the step down unit. Home discharge was ordered after attaining the standardized institutionally defined criteria used for all outpatient surgery; alert, awake, stable hemodynamics, with oxygen saturation > 95% on room air, minimal pain (VRS <4 on ambulation), absence of nausea and vomiting, ability to tolerate oral fluids and to urinate, and walk unassisted.

## 4. Statistical analysis

Estimation of sample size was grounded on White *et al.'s* [13] review; it very well may be speculated that recovery periods would be declined near 45–50% along with esmolol administration intraoperatively. Taking into account standard deviations among their review reference study, 28 subjects per single group was estimated satisfactory to provide 80% power together with 5% importance level. Accordingly, 30 subjects were entailed per single research group.

After data extraction and revision, they were statistically analyzed by means of SPSS software package version 20 (Armonk; NY: IBM Cop.). Quantitative (numerical) variables were denoted as: mean  $\pm$  standard deviation (SD). Whereas, qualitative (categorical) data were verified utilizing case number and % (Fisherexact X<sub>2</sub> test was applied whenever possible). Unpaired (*t*-) test along with analysis of variance (ANOVA) was utilized for unpaired numerical data. A (*P*) Value of  $\leq$  0.05 was judged as significant level. Moreover,  $\leq$  0.01 was counted extremely significant.

#### 5. Results

67 patients listed as possible participants. Of these, seven were declined to continue as their surgery was turned to laparotomy. The remaining 60 eligible patients were distributed equally into two groups throughout the study with no drop out (Figure 1).

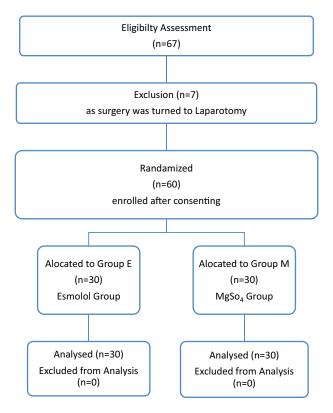


Figure 1. Study flow chart.

Both groups showed comparable demographic characteristics (Table 1). Variables interpreting immediate recovery like times elapsed till spontaneous eye opening, patients' extubation, tongue extension, and capability to recall names were shorter significantly in the esmolol group compared to the MgSO4 group (p = 0.006, p = 0.026 and p = 0.025 respectively) (Table 2).

Postoperative pain assessment using pain numerical rating scale revealed no statistically significant variation among both comparative groups (Figure 2). Furthermore, members of the esmolol group displayed significant higher White -Song score at all times of measurements except at 120 minutes compared to

Та	b	e	1.	Demograp	hic	varia	b	les.
----	---	---	----	----------	-----	-------	---	------

those of MgSO<sub>4</sub> group (p = 0.003, p = 0.034, p = 0.035, p = 0.010) respectively (Table 3).

Moreover, there was no statistically evident significant difference noted among the two studied groups either in the amount of intraoperative or postoperative fentanyl consumed (p = 0.186, p = 0.346) respectively (Table 4).

Also, there was no significant variation in the time of recall for first rescue analgesia among the two studied groups (p = 0.431) (Table 4).

Compared to MgSo<sub>4</sub> group, number of patients with vomiting episodes together with the total amount of ondansetron consumed in the PACU were significantly lower among the esmolol group (p = 0.039, p = 0.012) respectively (Table 4).

#### 6. Discussion

The results of the present randomized, comparative study revealed that esmolol administrated intraoperatively enriched all aspects of rapid postoperative recovery profile, for instance former eye opening, tongue extension, tracheal extubation, and patient's capacity to specify his name. Postoperatively, patients treated with esmolol experienced comparable level of postoperative analgesia, with fast- tracked overall recovery period and significant low incidence of nausea and vomiting compared to those treated with magnesium sulphate.

Ordinarily, laparoscopic cholecystectomy is accompanied with temporarily acute haemodynamics perturbations typically during insertion of trocars and pneumoperitoneum establishment. Moreover the adverse events following CO<sub>2</sub> insufflation, together with intravascular volume shift that progress after the Trendelenburg position, furthermore load the burden [1,2]. This necessitates an adequate -pain free- level of anaesthesia. Simultaneously protected, satisfied and fast discharge from PACU persists a significant

	Group E	Group M	P- value
Age (years)	43.4 ± 1.1	46.07 ± 9.61	.145
Sex (Male/Female)	16/14	13/17	.438
Weight (kg)	69.2 ± 11.86	72.57 ± 11.83	.142
ASA (I/II)	14/16	12/18	.602
Duration of surgery (min)	89.13 ± 14.48	85.93 ± 16.68	.219
Duration of anaesthesia (min)	106.03 ± 14.96	102.7 ± 16.76	.214

Values are presented as mean  $\pm$  SD, numbers and percentage.

\*p is significant if  $\leq 0.05$ . ASA : American society of Anesthesiologists.

Table 2. Changes	in v	ariables	of	immediate	recovery	profile	in	studied	group	S.

Recovery profile variables	Group E	Group M	P- value
Time needed for eye opening (min)	$6.43 \pm 1.58$	7.53 ± 1.63	.006*
Extubation time (min)	$8.4 \pm 1.74$	$10 \pm 1.71$	.000*
Time needed for tongue protrusion (min)	$1.8 \pm 2.17$	11.87 ± 1.93	.026*
Time needed to be able to mention his/her name (min)	12.77 ± 2.25	13.83 ± 1.77	.025*

Values are presented as mean  $\pm$  SD.

\*p is significant if  $\leq 0.05$ .

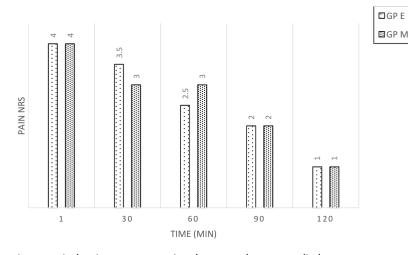




 Table 3. Changes in White-Song score among the two studied groups.

White-Song score	Group E	Group M	P- value	
1 min	12 (11–12)	11 (10–12)	.003*	
30 min	13 (12–13)	12 (11–13)	.034*	
60 min	14 (12–14)	13 (12–14)	.035*	
90 min	14 (13–14)	13 (13–14)	.010*	
120 min	14 (13–14)	14 (13–14)	.086	

Values are presented as median (interquartile range).

\**p* is significant if  $\leq 0.05$ .

Table 4. Analysis of perioperative variables among the two studied groups.

, , , , , , , , , , , , , , , , , , , ,	<b>J</b> 1		
Perioperative variables	Group E	Group M	P- value
Total dose of intraoperative fentanyl (µg)	4.17 ± 14.23	43.33 ± 12.47	.186
Total dose of postoperative fentanyl (µg)	15.83 ± 24.57	18.33 ± 23.21	.346
Time of first call for rescue analgesic (min)	19.9 ± 3.52	19.73 ± 3.74	.431
Number of patients receiving fentanyl in PACU	10 (33.3%)	14 (46.6%)	.292
Number of patients with vomiting and/or persistent nausea	7 (23.33%)	12 (43.33%)	.039*
Total dose of ondansetron (mg)	1.47 ± 2.83	$3.60 \pm 4.05$	.012*
Number of patients having bradycardia	5 (16.66%)	3 (10%)	.448

Values are presented as mean  $\pm$  SD or percentage.

\*p is significant if ≤0.05.

objective postoperatively. In order to attain this goal, numerous attempts have been postulated to enhance the speed and excellence of comprehensive postoperative recovery profile, and promptly manage variables that preclude rapid patients' release [2–5]. Indeed, postoperative analgesia along with steady hemodynamics are in the heart of this recovery paradigm [4–6]. Consequently, infusion of intraoperative esmolol versus magnesium sulphate was used in this study to verify their impacts on quality of postoperative recovery profile.

In the present study, concerning factors assessing immediate recovery from anaesthesia (like eye opening, tongue extension, tracheal extubation, and patient's capacity to specify his name) esmolol members exhibited faster early recovery profile characteristics compared to MgSo<sub>4</sub> members. This may be promptly linked to the sedative properties MgSO<sub>4</sub> possess, along with valuable pain control.

In accordance with our results, Altan *et al.* [14] evaluated effects of clonidine and  $MgSO_4$  on

haemodynamics, propofol consumption, and postoperative recovery. They reported that magnesium sulphate caused delayed recovery, whereas clonidine caused bradycardia and hypotension. One study reported that there was a depressant effect on the CNS of animals treated with MgSo<sub>4</sub> and even there was a sleep-like state [15]. In addition to, the NMDA receptors blocker effect of MgSo<sub>4</sub> on the CNS, reduced catecholamine release and inhibited peripheral sensitization with a resultant attenuation of surgical stress response were claimed in another research with the sedative state accompanying MgSo<sub>4</sub> infusion [16].

Moreover, Apan and colleagues [17] in their investigation on whether MgSO<sub>4</sub> infusion was efficient on emergence phenomenon and discomfort in paediatric adenoidectomy  $\pm$  tonsillectomy, emphaziesed that there was a delay in the recovery characteristics of children treated with MgSo<sub>4</sub>.

Esmolol -as an anaesthesia adjuvant- has been found to facilitate the postoperative recovery profile via various synergistic cofactors including effective postoperative analgesia together with intraoperative anaesthetic and opioid sparing effects and inhibition of opioid-provoked hyperalgesia [18].

In line with our results, Qiao and colleagues [19] assessed the effects of esmolol on BIS index, and whether it can reduce anaesthetic dose and decrease emergence time on 60 patients planned for dilation and curettage surgery. They reported decrease anaesthesia emergence time with favorable recovery profile within the esmolol group.

Also, in accordance with our study, Celebi *et al* [20]. inspected the consequences of intraoperative esmolol versus remifentanil i.v infusions on postoperative analgesia and their effect on anaesthesia depth. The esmolol group consumed significantly less analgesia with subsequent improvement of the recovery parameters compared to the other group. Even more, Hwang *et al* [21]. proved the efficacy of esmolol in enhancing the postoperative recovery by diminishing postoperative pain severity.

In contrast to our results the study carried by De Oliveira and colleagues [22] on 58 subjects planned for outpatient hysteroscopic surgery. They were randomized to receive i.v. bolus esmolol (0.5 mg/kg) followed by maintenance infusion at a rate of (5–15  $\mu$ g/kg/min) versus the same amount of 0.9% Nacl. They reported no overt beneficial impact of esmolol administration on patients' related pattern of recovery.

In the current study, pain numerical rating scale displayed statistically no significant variation within the two comparative groups at all times of measurements. Furthermore, there was no significant variation noted among the two studied groups whether in the total amount of fentanyl consumed (intraoperative and postoperative) or in the time of first recall for rescue analgesia postoperatively.

The influence of MgSO<sub>4</sub> on the quality of postoperative analgesia had been well ascertained [23]. Despite the fact that MgSO<sub>4</sub> exerts no direct antinociceptive impacts, it restrains calcium entry into cells (likened as physiological antagonist) via blocking NMDA receptors bringing about analgesia, which is mainly attributed to inhibition of the central sensitization that result from tissue insult and responsible for pain hypersensitivity [24].

Additionally, MgSO<sub>4</sub> may not only alter postoperative pain control, but correspondingly has been successfully utilized to decrease the amount of opioid consumption [23,24]. In support with our results, Jarahzadeh *et al.* [25] illustrated in their double blinded clinical trial that i.v infusion of MgSO<sub>4</sub> in a dose (50 mg/ kg) has led to effective postoperative analgesia and reduced morphine demand in patients planned for total abdominal hysterectomy. A research of liver transplantation emphasized that co-administration of i.v MgSo4 could save mechanical ventilation and reduced tramadol requirement [26].

Similarly, the impacts of esmolol on postoperative pain control were obvious. The mechanism by which it exerts its antinociceptive and anaesthetic sparing effects is still obscure and may be attributed to numerous theories [27]. Hypothetically, esmolol can promptly block injurious sensory response at various levels along the pathway. Blocking the abundant beta adrenergic receptors within the reticular activating system exerts the central effects. Along with it, a peripheral antiinflammatory related effect has been also postulated [28]. Correspondingly, several studies point to possible stimulation of the hippocampal beta adrenoceptor which might participate in nociceptive perception. Blockage of such adrenoceptor should blunt nociception with a resultant attenuation of pain perception [29]. One interesting explanation refers to its effect on cardiac output and subsequent reduction in hepatic blood flow affecting the dissemination of pharmacokinetics and clearance of concurrent propofol or inhalational anaesthetics [30]. Lastly, relatively weak experimental evidence refers to possible inherent antinociceptive property of esmolol [31].

In agreement with the current results, White et al. [13] reported in their research that usage of Intraoperative esmolol has promptly control postoperative pain and led to longer opportunity for rescue analgesic requirements, thereby it could be a proper substitute to remifentanil throughout desflurane inhalational anaesthesia among fast-tracked female scheduled for laparoscopic surgeries. Also, Collard et al. [32] in their comparative randomized study on 90 patients underwent ambulatory laparoscopic cholecystectomy reported that usage of intraoperative esmolol - in absences of opioids use- promoted to obvious reduction in perioperative consumption of fentanyl along with enhancement of earlier PACU discharge. Moreover, Chia et al. [33] injected (3 µg/kg) fentanyl then esmolol slowly infusion in females planned for total abdominal hysterectomy. The overall amount of morphine demanded was considerably decreased.

On the contrary, Coloma *et al.* [34] assessed the usage of esmolol infusion as a substitute for remifentanil in outpatient gynecological laparoscopic surgeries and showed significantly larger use of hydrocodone in esmolol group postoperatively, but similarly to our study, they reported lower incidences of nausea.

In the present study, members of esmolol group showed least incidence of nausea and vomiting as they consumed the least amount of rescue antiemetic ondansetron in the PACU. Despite the fact that there was no agreement concerning one assumption, the utilization of beta adrenoceptor blockers preoperatively diminishes the requirements for opioids with its subsequent adverse events like nausea and vomiting [8,34]. An alternative mechanism related the occurrence of PONV to acute perioperative cardiovascular perturbations and so esmolol usage can alleviate such hemodynamic fluctuations and preclude PONV [35].

In coincidence with our results, Lee *et al* [36]. during their research on 60 female scheduled for laparoscopic appendectomy using  $(5-10 \ \mu g/kg/min)$ esmolol plus remifentanil infusions (group E) versus same volume of normal saline (group C), concluded that esmolol administration had led to overt reduction in PONV incidence which accelerates faster discharge.

In against to our findings, Kurita *et al.* [37] referred to the high hydrophilic nature of esmolol with subsequent low permeability via blood brain barrier, thus it is unapparent whether esmolol possess that impact or not.

In the current study, the esmolol group members displayed significant higher White -Song score at all times of measurements except at 120 minutes. This is not surprising as the White-Song frame work takes in account effective pain control, consciousness level, emetic symptoms, vitals and physical steadiness which are all in favor of the esmolol group.

In support of our results, Bajracharya and colleagues [38] evaluated the outcomes of esmolol administration intraoperatively versus lidocaine injection on perioperative analgesia in patients scheduled for laparoscopic cholecystectomy, then concluded that patients received esmolol were less sedated and with enhanced recovery profile.

Similarly, Sultan [39] after evaluating the advantages of esmolol on postoperative recovery pattern and hospital discharge in subjects underwent gynecologic laparoscopic surgery, concluded that recovery performance went excellent and facilitated earlier home discharge.

On the contrary, the study conducted by Das *et al* [40]. on 60 patients underwent Functional endoscopic sinus surgery, where dexmedetomidine group received (1  $\mu$ g/kg/hr) loading then (0.5  $\mu$ g/kg/hr) maintance infusion whereas esmolol group received (1 mg/kg). They reported evident superior recovery profile and surgeon/s satisfaction in dexmedetomidine group comparable to the esmolol group.

There are some particular limitations related to the design of the current study. Ensure the same anaesthetic depth along the two groups via bispectral index (BIS) monitor was not achieved. Also, regular monitoring of serum magnesium level was not done and double blinding was not feasible. We evaluated patients belonging to ASA physical status I, II to ensure safety among this setting.

## 7. Conclusion

Using intraoperative esmolol infusion as an anaesthetic adjuvant is accompanied with a superior recovery profile.

### **Disclosure statement**

No potential conflict of interest was reported by the author(s).

# ORCID

Hassan Saeed ElHoshy (b) http://orcid.org/0000-0002-0924-2431

### References

- Richardson WS, Fuhrman GS, Burch E, et al. Outpatient laparoscopic cholecystectomy: outcomes of 847 planned procedures. Surg Endosc. 2001 Feb;15 (2):193–195. doi: 10.1007/s004640000301
- [2] Lau H, Brooks DC. Contemporary outcomes of ambulatory laparoscopic cholecystectomy in a major teaching hospital. World J Surg. 2002 Sep;26(9):1117–1121. doi: 10.1007/s00268-002-6264-1
- [3] Kehlet H. Postoperative opioid sparing to hasten recovery: what are the issues? J Am Soc Anesthesiologists. 2005 Jun 1;102(6):1083–1085.
- [4] Karlsen AP, Pedersen C, Laigaard J, et al. Opioid consumption as a core outcome domain in postoperative pain management. Pain. 2022 Jun 1;163(6):e786–7.
- [5] Ma H, Tang J, White PF, et al. Perioperative rofecoxib improves early recovery after outpatient herniorrhaphy. Anesthesia & Analgesia. 2004 Apr 1;98 (4):970–975.
- [6] Murphy GS, Szokol JW, Greenberg SB, et al. Preoperative dexamethasone enhances quality of recovery after laparoscopic cholecystectomy: effect on in-hospital and post discharge recovery outcomes. J Am Soc Anesthesiologists. 2011 Apr 1;114(4):882–890.
- [7] Fu L, Yu B, Li Z, et al. The therapeutic potential of ultrashort-acting  $\beta$ -receptor antagonists in perioperative analgesic: Evidence from preclinical and clinical studies. Front Pharmacol. 2022;13:4159. doi:10.3389/ fphar.2022.914710
- [8] Ozturk T, Kaya H, Aran G, et al. Postoperative beneficial effects of esmolol in treated hypertensive patients undergoing laparoscopic cholecystectomy. Br J Anaesth. 2008 Feb 1;100(2):211–214.
- [9] Gelineau AM, King MR, Ladha KS, et al. Intraoperative esmolol as an adjunct for perioperative opioid and postoperative pain reduction: a systematic review, meta-analysis, and meta-regression. Anesthesia & Analgesia. 2018 Mar 1;126(3):1035–1049.
- [10] Hansen KB, Yi F, Perszyk RE, et al. Structure, function, and allosteric modulation of NMDA receptors. J General Physiol. 2018 Aug 6;150(8):1081–1105.
- [11] Soave PM, Conti G, Costa R, et al. Magnesium and anaesthesia. Curr Drug Targets. 2009 Aug 1;10 (8):734–743.
- [12] White PF, Song D. New criteria for fast-tracking after outpatient anesthesia: a comparison with the modified Aldrete's scoring system. Anesthesia & Analgesia. 1999 May 1;88(5):1069–1072.
- [13] White PF, Wang B, Tang J, et al. The effect of intraoperative use of esmolol and nicardipine on recovery after ambulatory surgery. Anesthesia & Analgesia. 2003 Dec 1;97(6):1633–1638.
- [14] Altan A, Turgut N, Yıldız F, et al. Effects of magnesium sulphate and clonidine on propofol consumption,

haemodynamics and postoperative recovery. Br J Anaesth. 2005 Apr 1;94(4):438–441.

- [15] Thompson SW, Moscicki JC, DiFazio CA. The anesthetic contribution of magnesium sulfate and ritodrine hydrochloride in rats. Anesthesia & Analgesia. 1988 Jan 1;67(1):31–34.
- [16] den Berg AA V, Savva D, Honjol NM. Attenuation of the haemodynamic responses to noxious stimuli in patients undergoing cataract surgery. A comparison of magnesium sulphate, esmolol, lignocaine, nitroglycerine and placebo given iv with induction of anaesthesia. Eur J Anaesthesiol. 1997 Mar;14 (2):134–147. doi: 10.1046/j.1365-2346.1997.00069.x
- [17] Apan A, Aykaç E, Kazkayasi M, et al. Magnesium sulphate infusion is not effective on discomfort or emergence phenomenon in paediatric adenoidectomy/ tonsillectomy. Int J Pediatr Otorhinolaryngol. 2010 Dec 1;74(12):1367–1371.
- [18] Watts R, Thiruvenkatarajan V, Calvert M, et al. The effect of perioperative esmolol on early postoperative pain: a systematic review and meta-analysis. J Anaesthesiol Clin Pharmacol. 2017 Jan;33(1):28.
- [19] Qiao Q, Gu XJ, Xu J, et al. Effect of intravenous esmolol on BIS index and anesthesia emergence during sedation anesthesia for ambulatory surgery. Zhonghua Yi Xue Za Zhi. 2010 Jun 1;90(23):1631–1634.
- [20] Celebi N, Cizmeci EA, Canbay O. Intraoperative esmolol infusion reduces postoperative analgesic consumption and anaesthetic use during septorhinoplasty: a randomized trial. Rev Bras Anestesiol. 2014 Sep;64 (5):343–349. doi: 10.1016/j.bjane.2013.10.015
- [21] Hwang WJ, Moon YE, Cho SJ, et al. The effect of a continuous infusion of low-dose esmolol on the requirement for remifentanil during laparoscopic gynecologic surgery. J Clin Anesth. 2013 Feb 1;25 (1):36–41.
- [22] De Oliveira GS Jr, Kendall MC, McCarthy RJ. Esmolol does not improve quality of postsurgical recovery after ambulatory hysteroscopy: A prospective, randomized, double-blinded, placebo-controlled, clinical trial. Medicine. 2018 Oct;97(41):e12647. doi: 10.1097/MD. 000000000012647
- [23] Hansen KB, Yi F, Perszyk RE, et al. NMDA receptors in the central nervous system. NMDA receptors: Methods and protocols. Pro Triheteromeric N-Methyld-Aspartate. 2017;1–80.
- [24] Latremoliere A, Woolf CJ. Central sensitization: a generator of pain hypersensitivity by central neural plasticity. J Pain. 2009 Sep 1;10(9):895–926.
- [25] Jarahzadeh MH, Harati ST, Babaeizadeh H, et al. The effect of intravenous magnesium sulfate infusion on reduction of pain after abdominal hysterectomy under general anesthesia: a double-blind, randomized clinical trial. Electron Physician. 2016 Jul;8(7):2602. doi: 10. 19082/2602
- [26] Gucyetmez BÜ, Atalan HK, Aslan S, et al. Effects of intraoperative magnesium sulfate administration on postoperative tramadol requirement in liver transplantation: A prospective, double-blind study. Transplant Proc. 2016 Oct 1;48(8):2742–2746.
- [27] Ünal YU, Özsoylar Ö, Sarıgüney D, et al. The efficacy of esmolol to blunt the haemodynamic response to

endotracheal extubation in lumbar disc surgery. Res J Med Sci. 2008;2(2).

- [28] Kadoi Y, Saito S. Possible indications of beta-blockers in the perioperative period other than prevention of cardiac ischemia. J Anesth. 2010 Feb;24(1):81–95. doi: 10.1007/s00540-009-0865-x
- [29] Tanahashi S, Iida H, Dohi S, et al. Comparative effects of ultra-short-acting β1-blockers on voltage-gated tetrodotoxin-resistant Na+ channels in rat sensory neurons. Eur J Anaesthesiol. 2009 Mar 1;26(3):196–200.
- [30] Takeda S, Masuda R, Kanazawa T, et al. Esmolol attenuates hepatic blood flow responses during sodium nitroprusside-induced hypotension in dogs. Can J Anaesth. 2004 Apr 1;51(4):348.
- [31] Oda Y, Nishikawa K, Hase I, et al. The short-acting β1-adrenoceptor antagonists esmolol and landiolol suppress the bispectral index response to tracheal intubation during sevoflurane anesthesia. Anesthesia & Analgesia. 2005 Mar 1;100(3):733–737.
- [32] Collard V, Mistraletti G, Taqi A, et al. Intraoperative esmolol infusion in the absence of opioids spares postoperative fentanyl in patients undergoing ambulatory laparoscopic cholecystectomy. Anesthesia & Analgesia. 2007 Nov 1;105(5):1255–1262.
- [33] Chia YY, Chan MH, Ko NH, et al. Role of β-blockade in anaesthesia and postoperative pain management after hysterectomy. Br J Anaesth. 2004 Dec 1;93(6):799–805.
- [34] Coloma M, Chiu JW, White PF, et al. The use of esmolol as an alternative to remifentanil during desflurane anesthesia for fast-track outpatient gynecologic laparoscopic surgery. Anesthesia & Analgesia. 2001 Feb 1;92(2):352–357.
- [35] Thiruvenkatarajan V, Watts R, Calvert M, et al. The effect of esmolol compared to opioids on postoperative nausea and vomiting, postanesthesia care unit discharge time, and analgesia in noncardiac surgery: a meta-analysis. J Anaesthesiol Clin Pharmacol. 2017 Apr;33(2):172.
- [36] Lee SJ, Lee JN. The effect of perioperative esmolol infusion on the postoperative nausea, vomiting and pain after laparoscopic appendectomy. Korean J Anesthesiol. 2010 Sep 1;59(3):179–184.
- [37] Kurita T, Takata K, Morita K, et al. Lipophilic βadrenoceptor antagonist propranolol increases the hypnotic and anti-nociceptive effects of isoflurane in a swine model. Br J Anaesth. 2008 Jun 1;100 (6):841–845.
- [38] Bajracharya JL, Subedi A, Pokharel K, et al. The effect of intraoperative lidocaine versus esmolol infusion on postoperative analgesia in laparoscopic cholecystectomy: a randomized clinical trial. BMC Anesthesiol. 2019 Dec;19(1):1–9. doi: 10.1186/s12871-019-0874-8
- [39] Sultan SS. Effects of esmolol infusion on recovery profile and discharge from postanesthesia care unit after ambulatory gynecologic laparoscopic surgeries. Ain-Shams J Anaesth. 2015 Oct 1;8(4):555.
- [40] Das A, Chhaule S, Bhattacharya S, et al. Controlled hypotension in day care functional endoscopic sinus surgery: A comparison between esmolol and dexmedetomidine: A prospective, double-blind, and randomized study. Saudi J Anaesth. 2016 Jul;10(3):276. doi: 10.4103/1658-354X.174919