SCIENTIFIC ARTICLE

Effects of lidocaine and esmolol infusions on hemodynamic changes, analgesic requirement, and recovery in laparoscopic cholecystectomy operations

Serpil Dagdelen Dogan, Faik Emre Ustun, Elif Bengi Sener, Ersin Koksal*, Yasemin Burcu Ustun, Cengiz Kaya, Fatih Ozkan

Ondokuz Mayıs University, Medicine Faculty, Anesthesiology Department, Samsun, Turkey

Abstract

Objective: We compared the effects of lidocaine and esmolol infusions on intraoperative hemodynamic changes, intraoperative and postoperative analgesic requirements, and recovery in laparoscopic cholecystectomy surgery.

Methods: The first group ($n = 30$) received IV lidocaine infusions at a rate of 1.5 mg/kg/min and the second group ($n = 30$) received IV esmolol infusions at a rate of 1 mg/kg/min. Hemodynamic changes, intraoperative and postoperative analgesic requirements, and recovery characteristics were evaluated.

Results: In the lidocaine group, systolic arterial blood pressures values were lower after the induction of anesthesia and at 20 min following surgical incision ($p < 0.05$). Awakening time was shorter in the esmolol group ($p < 0.001$); Ramsay Sedation Scale scores at 10 min after extubation were lower in the esmolol group ($p < 0.05$). The modified Aldrete scores at all measurement time points during the recovery period were relatively lower in the lidocaine group ($p < 0.05$). The time to attain a modified Aldrete score of ≥ 9 points was prolonged in the lidocaine group ($p < 0.01$). Postoperative resting and dynamic VAS scores were higher in the lidocaine group at 10 and 20 min after extubation ($p < 0.05$, $p < 0.01$, respectively). Analgesic supplements were less frequently required in the lidocaine group ($p < 0.01$).

Conclusion: In laparoscopic cholecystectomies, lidocaine infusion had superiorities over esmolol infusions regarding the suppression of responses to tracheal extubation and postoperative need for additional analgesic agents in the long run, while esmolol was more advantageous with respect to rapid recovery from anesthesia, attenuation of early postoperative pain, and modified Aldrete recovery (MAR) scores and time to reach MAR score of 9 points.

* Corresponding author.
  E-mail: ersin.koksal@omu.edu.tr (E. Koksal).

PALAVRAS-CHAVE

Lidocaína;
Esmolol;
Recuperação;
Colecistectomia
laparoscópica

Efeitos das infusões de lidocaína e esmolol sobre as alterações hemodinâmicas, necessidade de analgésicos e recuperação após colecistectomia laparoscópica

Resumo

Objetivo: Comparamos os efeitos de infusões de lidocaína e esmolol sobre as alterações hemodinâmicas no período intraoperatório, a necessidade de analgésicos intra- e pós-operatoriamente e a recuperação após colecistectomia laparoscópica.

Métodos: O primeiro grupo (n = 30) recebeu infusões IV de lidocaína a uma taxa de 1,5 mg/kg/min e o segundo grupo (n = 30) recebeu infusões IV de esmolol a uma taxa de 1 mg kg/min. Alterações hemodinâmicas, necessidade de analgésicos no intra- e pós-operatório e características da recuperação foram avaliadas.

Resultados: No grupo lidocaína, os valores da pressão arterial sistólica foram menores após a indução da anestesia e 20 minutos após a incisão cirúrgica ($p < 0,05$). O tempo até o despertar foi menor no grupo esmolol ($p < 0,001$), os escores na escala de Sedação de Ramsay 10 minutos após a extubação foram menores no grupo esmolol ($p < 0,05$). Os escores de Aldrete modificados em todos os tempos mensurados durante o período de recuperação foram relativamente baixos no grupo lidocaína ($p < 0,05$). O tempo necessário para atingir um escore de Aldrete ≥ 9 pontos foi prolongado no grupo lidocaína ($p < 0,01$). Os escores Eva em repouso e em movimento no pós-operatório foram maiores no grupo lidocaína nos minutos 10 e 20 após a extubação ($p < 0,05$, $p < 0,01$, respectivamente). Analgésicos suplementares foram necessários com menos frequência no grupo lidocaína ($p < 0,01$).

Conclusão: Em colecistectomia laparoscópica, a infusão de lidocaína foi superior às infusões de esmolol quanto a suprimir as respostas à extubação traqueal e necessidade de analgésicos adicionais no pós-operatório, enquanto esmolol foi mais vantajoso quanto à rápida recuperação da anestesia, à atenuação da dor no pós-operatório imediato e aos escores de recuperação de Aldrete modificado (RAM) e o tempo até atingir o escore RAM de 9 pontos.

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Introduction

During the perioperative period, as a hemodynamic response to laryngoscopy, intubation, and surgical excision, complications including tachycardia, hypertension, myocardial ischemia, arrhythmia, myocardial infarction, and cerebral hemorrhages can be seen. To prevent development of these unwanted effects, various measures such as increasing the depth of anesthesia and the administration of topical anesthesia, IV lidocaine, vasodilators, alfa$_2$ agonists, beta-adrenergic blockers, opioids, and precurarizaton procedures have been implemented.[1–4]

In the control of unfavorable hemodynamic changes developed secondary to intubation, lidocaine can be administered intravenously before the induction of anesthesia and several studies have demonstrated its preventive effects on postoperative pain.[5–7]

Esmolol is effective in the suppression of adrenergic responses against laryngoscopic procedures, intubation, and many other perioperative stimulations.[8,9] Furthermore, some studies have indicated that beta adrenergic receptor blockers decrease the need for anesthetics and postoperative analgesic consumption.[10–12] Even though pain scores are lower in laparoscopic colecystectomy relative to conventional open chlecystectomy, multimodal analgesic regimens should be performed, including preoperative treatment.[13]

Though many studies have compared the effects of both drugs on hemodynamic responses, comparative studies related to their effects on recovery and analgesia are lacking. In our study, we have aimed to compare the effects of lidocaine and esmolol infusions on intraoperative hemodynamic changes, intra- and postoperative analgesic requirements, and recovery.

Materials and methods

This double-blind study was performed on 60 ASA I-II patients aged 18–65 years scheduled for laparoscopic cholecystectomy after obtaining informed consent from of the patients. Patients with allergies to local anesthetics and opioids, morbid obesity, or advanced respiratory, renal, hematological, hepatic or cardiovascular diseases; chronic use of opiate, beta adrenergic receptor antagonists, or alcohol; and drug addicts, pregnant women, and mentally retarded cases were excluded from the study. For premedication, patients were given 40 mg famotidine and 10 mg diazepam orally. The patients underwent electrocardiographic (EKG) examinations, pulse oxymetric measurements of peripheral oxygen saturation (SpO$_2$), and noninvasive monitoring of arterial pressure. The patients were randomized into 2 groups using the sealed envelope method.

The first group (group L) received an IV lidocaine infusion slowly at a rate of 1.5 mg/kg/min for a total dose of

2 mg/kg/h 3 min before the induction of anesthesia. The second group (group E) was given IV esmolol infusion slowly at a rate of 1 mg/kg/min for a total dose of 15 μg/kg/min 3 min before induction of anesthesia. Lidocaine and esmolol infusions were terminated immediately after extubation.

Heart rates (BPM); systolic (SBP), diastolic (DBP), and mean (MABP) arterial blood pressures; and the SpO_2 of the patients were measured, and adverse effects such as bradycardia, hypotension, and arrhythmias were recorded preoperatively (t1), after induction (t2), after the intubation at 1 (t3) and 5 (t4) min and, during the surgical incision (t5), after the surgical incision at 5 (t6), 10 (t7), 15 (t8), 20 (t9), 30 (t10), 40 (t11), 50 (t12), and 60 (t13) min, before extubation (t14), and after the extubation at 1 (t15) and 5 (t16) min. During induction, 2–2.5 mg/kg iv propofol, 1 μg/kg iv fentanyl, and 0.1 mg/kg iv vecuronium for muscular relaxation were used. For the maintenance of anesthesia, a mixture of 65% N_2O and 35% O_2, desflurane, and IV vecuronium at a dose of 0.01 mg/kg for muscular relaxation were administered at 30 min intervals. Twenty minutes before the estimated end time of the operation, 75 mg IM diclofenac sodium and 10 mg IV metochlopramide were administered. Dosages of all anesthetic agents were tapered 50% at the start of skin suturing and discontinued at the last skin suture. The effects of muscular relaxants were reversed using 0.04 mg/kg neostigmine and 0.02 mg/kg atropine. The time interval between the discontinuation of anesthetic agents and the spontaneous eye opening of the patients was recorded as the ''awakening time.''

The patients were brought into the post-anesthesia care unit (PACU) after extubation, and fentanyl was delivered using a patient-controlled analgesia device (PCAD). The PCAD was adjusted to deliver an initial bolus dose of 3 cm³ (15 μg) fentanyl (5 μg/cm³) with a lockout time of 20 min and a 1-h limit of 45 μg. A loading dose was not administered. SBP, DBP, MABP, SS, Ramsay Sedation Score, and resting and dynamic VAS scores were recorded at 10 (t17), 20 (t18), 30 (t19), and 40 (t20) min of their PACU stay. The first demand for an analgesic, total requirement for anesthesia, modified Aldrete scores at 10, 20, 30, and 40 min, and the time to achieve a MAS of ≥9 points were recorded. The patients were transferred to a service when they had attained a modified Aldrete score of ≥9 points. Heart rates (HRs); systolic (SBPs), diastolic (DBPs), and mean arterial (MABPs) blood pressures; respiratory rates; Ramsay sedation scores (RSS); maximal resting and dynamic VAS scores; number of demands for PCA; amount of analgesics administered; and adverse effects, including nausea, vomiting, pruritus, and constipation, among others were recorded at 2 (t21), 6 (t22), 12 (t23), and 24 (t24) h of hospital stay in the service. Resting VAS scores of ≥4 points at any time during the postoperative period, despite patient-controlled analgesia, necessitated 75 mg diclofenac sodium IM administered at 12 h intervals, which was recorded as an additional need for analgesia. The nausea and vomiting scores of the patients were as follows: 0 = absence of nausea, 1 = mild nausea, 2 = moderate nausea and vomiting, 3 = frequent vomiting and 4 = severe vomiting. Metochlopramide (10 mg IV) was administered when the nausea and vomiting score was ≥2 points.

Statistical analysis

The statistical analysis of the data obtained was performed using the SPSS for Windows 16.0 statistical package program. The data were expressed as arithmetic means ± SD (standard deviation), numbers, and percentages. Normality tests for the distribution of data were performed. For intergroup comparisons, the *chi*-square and Mann–Whitney *U* tests were used. The Friedman test was employed in intragroup comparisons. For parameters showing intergroup differences, the Wilcoxon *t*-test with Bonferroni correction was used. Values with $p < 0.05$ were accepted as statistically significant.

Results

Intergroup difference was not detected for demographic characteristics, age, gender, body weight, or height ($p > 0.05$).

Heart rates (bpm) measured at any time did not differ between the groups ($p > 0.05$). Bradycardia developed in the lidocaine ($n = 1$) and esmolol ($n = 2$) groups and responded to the administration of 0.5 g atropine.

In intergroup comparisons, systolic blood pressures (mmHg) measured following the induction of anesthesia (t2) and 20 min (t9) after surgical incision were found to be significantly lower in the esmolol group (respectively, $p = 0.041$; $p = 0.045$) (Fig. 1). In the lidocaine group, hypertension developed in two patients, and was treated with iv 100 μg nitroglycerine.

The mean arterial blood pressure (mmHg) in the esmolol group measured after the induction of anesthesia (t2) was lower relative to the lidocaine group ($p = 0.006$) (Fig. 2).

In all of the measurement periods, intergroup differences were not detected for diastolic blood pressure and peripheral oxygen saturation ($p > 0.05$).

No intergroup difference was encountered regarding intraoperative fentanyl consumption (group L: 94.66 ± 45.08 μg; group E: 82.50 ± 28.36 μg) ($p = 0.298$). Additional fentanyl was required in both the lidocaine ($n = 10$) and esmolol ($n = 9$) groups.

Postoperative systolic blood pressures (mmHg) did not differ between groups in all measurement periods ($p > 0.05$). Hypotension developed in one patient in the lidocaine group,
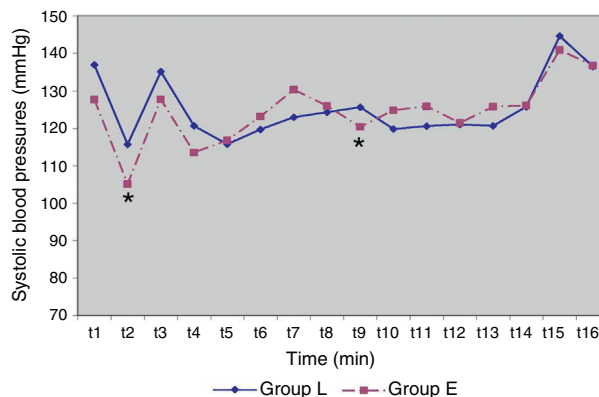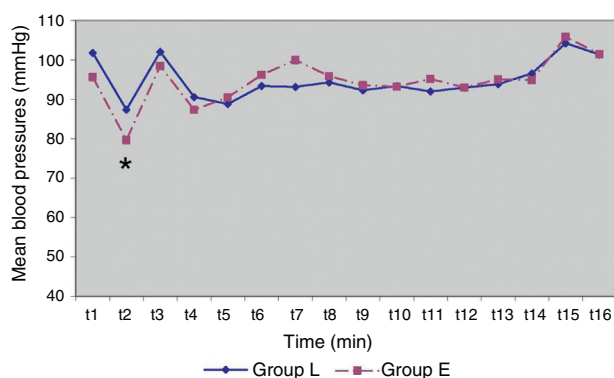

Figure 1 Systolic blood pressures (mmHg). *$p < 0.05$.

Figure 2　Mean blood pressures (mmHg). *p < 0.05.

Table 1　Ramsay Sedation Scores (mean ± SD).

Time	Group L	Group E	p
t17	2.76 ± 0.62	2.33 ± 0.80	0.015
t18	2.26 ± 0.52	2.03 ± 0.55	0.105
t19	2.00 ± 0.00	1.93 ± 0.25	0.154
t20	2.00 ± 0.00	2.00 ± 0.00	1.000
t21	2.00 ± 0.00	2.00 ± 0.00	1.000
t22	2.00 ± 0.00	2.00 ± 0.00	1.000
t23	2.00 ± 0.00	2.00 ± 0.00	1.000
t24	2.00 ± 0.00	2.00 ± 0.00	1.000

while hypertension occurred in both the lidocaine (n = 1) and esmolol (n = 2) groups.

Postoperative diastolic, mean arterial blood pressures and heart rates were not different between the groups in all measurement periods (p > 0.05).

The recovery times (min) of the cases were significantly shorter in the esmolol group (group L: 6.55 ± 1.84 and group E: 4.56 ± 1.40) (p = 0.0001).

In intergroup comparisons, the Ramsay Sedation Scores estimated 10 min after extubation (t17) were lower in the esmolol group (p = 0.015) (Table 1).

The modified Aldrete scores during the recovery period were significantly lower in the lidocaine group (p < 0.05) (Table 2).

The modified Aldrete scores of ≥9 points were attained in a significantly shorter time (min) in the esmolol group (group L: 14.76 ± 3.82 and group E: 12.46 ± 4.80) (p = 0.006).

Postoperative VAS values calculated at rest and 10 (t17) and 20 (t18) min after extubation were found to be significantly higher in the lidocaine group (p = 0.017 and p = 0.006, respectively).

Table 2　Modified Aldrete scores (mean ± SD).

Time	Group L	Group E	p
t17	8.23 ± 0.43	8.53 ± 0.51	0.018
t18	9.00 ± 0.00	9.27 ± 0.52	0.006
t19	9.30 ± 0.46	9.70 ± 0.46	0.002
t20	9.7 ± 0.46	9.93 ± 0.25	0.002

Postoperative dynamic VAS values detected 10 (t17) and 20 (t18) min after extubation were significantly higher in the lidocaine group relative to the esmolol group (p = 0.021 and p = 0.003, respectively).

The number of demands for postoperative PCA, the amount of analgesics administered, and the time to the first requirement of analgesia estimated in all measurement periods were not statistically significantly different between the groups (p > 0.05).

Fewer patients in the lidocaine group required additional analgesics [group L: 2 (6.7%) and group E: 11 (36.7%)] (p = 0.005).

Any statistically significant intergroup difference was not detected regarding intra- and postoperative side effects (p > 0.05). During the operation, one patient in the lidocaine group and two patients in the esmolol group developed bradycardia responsive to 0.5 mg atropine. In the lidocaine group, two patients developed hypertension, which responded to 100 μg nitroglycerine. During the postoperative period, hypotension developed in one patient in the lidocaine (n = 1) group, while hypertension was noted in the lidocaine (n = 1) and esmolol (n = 2) groups. Nausea and vomiting were seen in four patients in each group and treated with 10 mg metochlopramide.

Discussion

Though laparoscopic cholecystectomy offers the possibility of relatively early discharge from the hospital, postoperative pain, nausea, and vomiting induced by opioids are frequent complaints.[13,14] Multimodal analgesic techniques and adjuvant agents employed to decrease the incidence of these side effects might be useful in reducing dosages of systemic opioids.[13,14]

Chia et al.[15] administered esmolol infusions at a rate of 50 μg/kg/min following a loading dose of 0.5 mg/kg before the induction of anesthesia in 49 patients who had undergone abdominal hysterectomy, while 48 patients received normal saline infusions. They also demonstrated that the response of the heart rate and blood pressure to surgical incision and extubation was significantly suppressed in the esmolol group. White et al.[16] administered esmolol infusions at a rate of 5 μg/kg/min following a loading dose of 50 mg before the induction of anesthesia in 15 patients undergoing gynecologic laparoscopic surgeries, while 15 patients received only 50 mg esmolol IV and then esmolol infusions (5 μg/kg/min) following the administration of 1 mg nicardipine. Still, 15 patients received saline infusions. They concluded that esmolol infusions per se or in combination with nicardipine were sufficiently effective in suppressing intraoperative acute hemodynamic responses. Keskin et al.[17] compared esmolol and lidocaine in the prevention of hemodynamic responses developed secondary to laryngoscopy, intubation, and extubation. To that end, they initially delivered IV esmolol infusions at a rate of 0.5 mg/kg for 1 min to 50 patients scheduled for laparotomy; then, the dose of IV infusion was increased to 200 μg/kg, delivered for 4 min. However, 50 patients received only lidocaine IV at a dose of 1.5 mg/kg for 1 min, whereas 50 patients were given equal volumes of physiological saline infusions. They stated that esmolol and lidocaine had equipotently depressed

hemodynamic responses that developed during intubation but failed to adequately suppress hemodynamic responses that evolved during extubation.

We think that differences among these outcomes are related to the application of premedication (if any), drugs used in induction, and doses of the study drugs. In addition, in our study, lidocaine and esmolol equally depressed hemodynamic responses to intubation. Even though hemodynamic responses to extubation were suppressed more effectively in the lidocaine group relative to the esmolol group, doses of both agents we used could not completely attenuate hemodynamic responses to extubation. Chia et al.[15] delivered esmolol infusions at a rate of 50 μg/kg/min following a loading dose of 0.5 mg/kg in patients scheduled for abdominal hysterectomy and found significantly lower intraoperative opiate and volatile agent consumption compared with the control group. Topçu et al.[18] stated that the total consumption of remifentanil and propofol was significantly lower in the group of patients scheduled for elective abdominal surgery under total intravenous anesthesia who also received osmolol infusion at a rate of 250 μg/kg/min compared with the control group. Lauwick et al.[7] investigated the effects of intraoperative lidocaine infusion in patients scheduled for laparoscopic cholecystectomy and indicated lesser consumption of intraoperative fentanyl and desflurane in the group that received lidocaine infusion at a rate of 2 mg/kg/h following a loading dose of 1.5 mg/kg compared with the control group. They also stated that esmolol and lidocaine infusions led to lesser intraoperative opiate and volatile agent consumption relative to the control group. However, no study has compared both of these agents in this respect. In our study, we could not detect any significant difference between the total amounts of intraoperative fentanyl consumed by the groups.

Koppert et al.[19] investigated the effects of perioperative lidocaine infusion in major abdominal surgeries and initiated lidocaine infusion at a rate of 1.5 mg/kg/h following a loading dose of 1.5 mg/kg lidocaine IV 30 min before surgical incision in 20 patients undergoing major abdominal surgeries. Infusion was discontinued 1 h after the termination of surgery. The authors also stated that, when they had infused the same volume of physiologic saline to the control group, they could not find any intergroup difference in sedation scores. Collard et al.[11] analyzed the effects of intraoperative esmolol infusion on the postoperative consumption of fentanyl in laparoscopic cholecystectomies. The investigators delivered esmolol to 30 patients at a rate of 5–15 μg/kg following a loading dose of 1 mg/kg, while another 30 patients received esmolol infusions at a rate of 0.1–0.5 μg/kg/min after a loading dose of 1 μg/kg. Furthermore, 30 patients were given physiological saline solutions, and shorter recovery times were detected in the esmolol group compared with the other groups. Many studies have demonstrated that beta adrenergic blockers that exert depressive effects on the central nervous system also decrease the need for intraoperative anesthetic agents, leading to rapid recovery from anesthesia.[11,16,20] In the literature, we encountered no study comparing esmolol and lidocaine regarding awakening times and recovery scores. In our study, awakening times were shorter in the esmolol group. Ramsay Sedation Scores estimated 10 min after extubation were found to be higher in the lidocaine group relative to the esmolol group. However,

no significant intergroup difference was found at other measurement time points. Modified Aldrete recovery scores in the esmolol group were significantly higher in all measurement periods. Similarly, the time to achieve a score of ≥9 points was also shorter in the esmolol group.

Chia et al.[15] investigated the effects of beta blockers on postoperative pain in patients who had undergone abdominal hysterectomies and found that the VAS scores of patients who received IV esmolol infusion at a rate of 50 μg/kg/min following a loading dose of 0.5 mg/kg before the induction of anesthesia were similar to those of the control group with significantly lower requirements for postoperative morphine supplementations in the esmolol group. Öztürk et al.[21] administered esmolol infusions at a rate of 5–15 μg/kg/min following a loading dose of 1 mg/kg, while their control group received equal volumes of ringer lactate infusions. In the esmolol group, the postoperative need for analgesics was significantly lower relative to the control group. Collard et al.[11] investigated the effects of intraoperative esmolol infusions on postoperative fentanyl consumption in patients undergoing laparoscopic cholecystectomy and administered esmolol infusions to 30 patients at a rate of 5–15 μg/kg/min following a loading dose of 1 mg/kg. Whereas 30 patients received remifentanil infusion (0.1–0.5 μg/kg/min) after a loading dose of 1 μg/kg, another 30 patients were given only physiological saline infusions. The authors demonstrated that the group that received esmolol infusion during the postoperative period required lesser amounts of fentanyl. Koppert et al.[19] analyzed the effects of perioperative lidocaine infusion in major abdominal surgeries and found that, in patients who had received lidocaine infusion at a rate of 1.5 mg/kg/h following a loading dose of 1.5 mg/kg 30 min before surgical incision up to the end of surgery demanded fewer numbers of PCA and less morphine administered via PCA, and the total consumption of morphine was relatively lower compared with the control group. In our study, we found no difference between groups in the time to the first requirement for an analgesic, the number of demands for PCA, and the amount of fentanyl delivered by PCA. In both groups, even though the total amount of postoperative opioid consumption was nearly equal, we detected lower requirements for additional analgesics in patients who had received lidocaine infusion. Early postoperative resting and dynamic VAS scores in the esmolol group were comparatively lower, but in the long term, the VAS scores determined in all measurement periods did not differ between the esmolol and lidocaine groups. It has been recognized that the intravenous administration of sodium channel blockers such as lidocaine has antinociceptive effects via its impact on dorsal spinal horn neurons.[22] However, some studies have revealed that esmolol decreased the requirement for anesthetic agents and ensured rapid recovery from anesthesia through its depressive effects on the central nervous system.[11,16,20] Sympathomietic drugs acting on the central nervous system are known to alter the need for anesthetic agents. The detection of lower VAS scores at 10 and 20 min after extubation can be explained by the antagonistic effects of esmolol on catecholamine synthesis in the brain and spinal cord.

In laparoscopic surgeries, the incidence of postoperative nausea/vomiting is 40–75%, and it is especially more frequently seen on the first and second postoperative days.[23]

Nausea and vomiting, residual effects of anesthetic drugs and opioids, and gastric distension might become apparent with ambulation and hypotension.[23] Opioids can induce nausea and vomiting not only by stimulating the chemoreceptor trigger zone in the brain stem but by delaying gastric emptying and their hypotensive effects.[23] In comparison with the remifantil group, Coloma et al.[12] detected significantly lower incidence of nausea and vomiting in the esmolol group undergoing laparoscopic gynecologic surgeries. Similarly, in a study investigating the effects of lidocaine in laparoscopic cholecystectomies, Lauwick et al.[7] observed lower rates of nausea and vomiting relative to the control group. In our study, we also noted treatment-requiring nausea and vomiting with similar degrees of severity in the lidocaine and esmolol groups.

Conclusion

We found that intraoperative lidocaine and esmolol infusions in laparoscopic cholecystectomies exert comparatively similar suppressive effects on hemodynamic responses to tracheal intubation and surgical incision, and they are not superior to each other regarding the need for intraoperative and postoperative opioid analgesics and the development of side effects. We also noted that lidocaine infusion was comparatively superior in the suppression of the response to tracheal extubation and postoperative need for additional analgesia; however, esmolol infusion was more advantageous regarding awakening time, early postoperative pain score, modified Aldrete recovery (MAS) score, and time to achieve a MAS of 9 points. In the comparison of the efficacy of these two adjuvant agents, in various types of surgery, we think that further controlled studies to evaluate the consumption of anesthetic agents using different drug dosages should be conducted.

Conflicts of interest

The authors declare no conflicts of interest.

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