Original Article

Intraoperative Esmolol®: Can It Reduce Need of Postoperative Analgesia (Opioid) in Laparoscopic Cholecystectomy Patients?

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Abstract

Background: Laparoscopic cholecystectomy may be associated with postoperative pain mandating rescue analgesics; intraoperative β-blocker (Esmolol) might improve analgesia and spare opioids. This study was performed to test this potentially beneficial effect of intraoperative Esmolol in patients undergoing general anesthesia for laparoscopic cholecystectomy.

Materials and Methods: A total of 100 patients of the American sociological association (ASA) physical status-1 scheduled for laparoscopic cholecystectomy under general anesthesia were included. Patients receiving Esmolol were assessed for its effect on postoperative analgesia concerning those who did not receive Esmolol. Esmolol was administered as a bolus dose (0.5mg/kg) just before induction of anesthesia followed by an infusion rate of 0.05mg/kg/min until the completion of surgery.

Results: Patients in the Esmolol group and the control group were compared. A significant difference in postoperative visual analog scale ($p<0.001$), need for opioid analgesics ($p<0.001$), and the time for rescue analgesia ($p<0.001$) was observed, with the Esmolol group performing better. We also observed a better hemodynamic profile in patients receiving Esmolol as compared to the control group in the postoperative period. The difference in postoperative complications was not statistically significant ($p=0.374$).

Conclusion: intraoperative Esmolol significantly reduced the postoperative opioids (analgesia) consumption and improved analgesia. The hemodynamic profile of the patients who received intraoperative Esmolol was significantly better. There was no statistically significant difference between study groups regarding intra- and postoperative complications. No major adverse event is noted with the use of Esmolol.

Keywords: Heart rate, Noninvasive blood pressure, Respiratory rate, Electrocardiography, EtCO2 end-tidal carbon dioxide, Visual analog scale

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Introduction

Laparoscopic cholecystectomy has become the gold standard for the treatment of cholecystectomy throughout the world. Although it offers better pain dynamics and decreased hospital stay in comparison to open procedure, it is not completely pain-free. Inadequate pain control can result in prolonged hospital stays leading to increased morbidity and healthcare costs (1-4). Opioids have been traditionally used for the management of post-operative pain, however, they can lead to side effects like post-operative nausea and vomiting, urinary retention, respiratory depression, and even opioid-induced hyperalgesia thereby causing an increase in hospital stay (5).

There is an increasing need to formulate an opioid-sparing multimodal approach for the management of post-operative pain to avoid opioid-associated side effects (5). Beta-blockers have been traditionally used for maintaining hemodynamic stability and cardiac protection, however recently they have also been used as a perioperative anesthetic adjuvant showing promising results concerning post-operative pain and hemodynamic stability (6).

Using beta-blockers like Esmolol has been found to significantly reduce the need for postoperative analgesics and also decrease the incidence of postoperative nausea and vomiting. An earlier discharge is possible in patients of laparoscopic cholecystectomy improving cost-effectiveness and patient satisfaction. Also, the short half-life and predictable onset of action of beta-blocker like Esmolol make it a safe drug to be used in multimodal postoperative pain management protocols (7, 8). However, the use of Esmolol in developing countries remains a dilemma as a significant experience. Our study was aimed at exploring the use of Esmolol in postoperative pain management in patients undergoing laparoscopic cholecystectomy in our setting and to assess its safety as a perioperative anesthetic adjuvant drug.

Methods

We included 100 patients aged 18-60 years with American sociological association (ASA) physical status-1 scheduled for laparoscopic cholecystectomy under general anesthesia in our observational study conducted in SMHS Hospital, an associated hospital of GMC, Srinagar. Patients allergic to opioids, with opioid dependence, those with severe comorbidity, and those in which the procedure was converted to open cholecystectomy were excluded. The patients were divided into Esmolol and control groups.

Patients to be taken for the procedure underwent a thorough pre-anesthetic check-up and were kept fasting for at least 6 hours. Vital parameters like heart rate (HR), noninvasive blood pressure (NIBP), respiratory rate (RR), pulse oximetry (SpO2), electrocardiography (ECG), blood pressure (BP), and end-tidal carbon dioxide (EtCO2) were recorded and observed during and following the surgery.

Before induction, all patients received fentanyl 1.5mcg/kg intravenously after preoxygenation with 100% oxygen for 3 min, followed by a bolus dose of Esmolol (0.5mg/kg) dissolved in 30ml isotonic saline over 10 minutes and then Esmolol infusion at the rate of 0.05mg/kg/min in Esmolol group of patients. Immediately after giving the bolus dose of Esmolol, anesthesia was induced with IV propofol 1-2mg/kg. Tracheal intubation was facilitated by injection atracurium intravenously (0.5mg/kg). Anesthesia was maintained using controlled ventilation with isoflurane 0.5-1% and O2:N2O in the ratio of 50%:50%.

Bradycardia defined as HR <50-beats/min and hypotension defined as MAP <70 mmHg was managed with IV atropine 0.01 mg/kg and IV ephedrine 0.05 mg/kg respectively.

The duration of surgery was recorded in all cases. After surgery, the Esmolol infusion was discontinued. Residual neuromuscular blockade was reversed with neostigmine (0.5mg/kg) and glycopyrrolate 10 mcg/kg intravenously. After extubation, patients were shifted to the post-anesthesia care unit wherein Pain, HR, NIBP, RR, and SpO2 were monitored every 15 min for the first hour, and then every 4 hourly for 24 hrs. The pain was assessed by a visual analog scale (VAS). Visual analog scale≥3 was treated with a supplemental dose of tramadol 50 mg intravenously and the trend of VAS scores in the postoperative period (24hrs) was recorded. Time of rescue analgesia, as well as the

total dose of postoperative analgesic administered, was noted for all the patients in both groups for the first 24 hours.

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to the data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). The student's independent t-test was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. A P-value of less than 0.05 was considered statistically significant.

Results

Patient profile: We included 100 patients in our study dividing them into the Esmolol group (A) and control group (B) with 53 and 47 patients respectively. The mean age of the patients in group A was 51.8±6.67 with a range of 25-60 years while that of patients in group B was 51.2±6.42 with a range of 29-60 years. Male/female ratio in group A was 23 (43.4%)/30 (56.6%). while in group B it was 19 (40.4%)/28 (59.6%).

Preoperative vitals: In group A, the mean values of pre-operative vitals were HR 81.3±3.59, SBP 119.8±2.90, DBP 78.5±3.16 MA 92.3±2.57, RR 14.0±1.20, and Spo2 97.9±0.94. In group B the mean values of pre-operative vitals were HR 82.1±3.71, SBP 120.1±3.04, DBP 79.2±3.57, MAP 92.8±2.67, RR 14.1±1.20, and Spo2 98±1.11 (Fig. 1).

VAS at various intervals of time: The VAS scores in group A patients were consistently less than those in group B at different time intervals in the postoperative period up to 24hrs (Table 1 & Fig. 2).

Table 1: Comparison based on VAS in two groups at various intervals of time; It Showing VAS scores in the 2 groups at various time intervals in the postoperative period.

Time Interval	Group A		Group B		p-value
	Mean	SD	Mean	SD	
15 M	0.42	0.50	1.89	0.89	<0.001*
30 M	0.64	0.48	2.64	0.90	<0.001*
45 M	0.96	0.52	3.70	1.47	<0.001*
60 M	1.23	0.61	1.66	1.13	0.017*
4 HR	3.98	0.97	2.11	0.94	<0.001*
8 HR	1.74	2.06	4.04	1.46	<0.001*
12 HR	1.26	0.62	2.47	1.36	<0.001*
16 HR	3.57	1.68	3.94	1.54	0.256
20 HR	0.92	1.21	1.98	1.70	<0.001*
24 HR	0.89	0.67	1.02	0.71	0.331

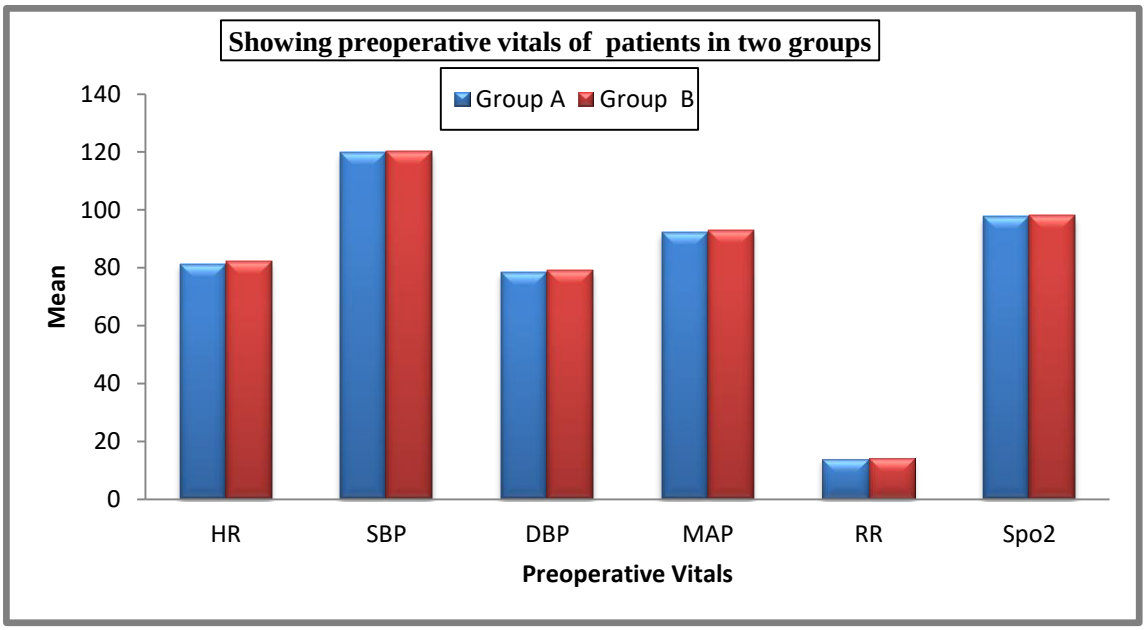

Figure 1. Showing preoperative vitals of patients in two groups that are comparable with no significant difference.

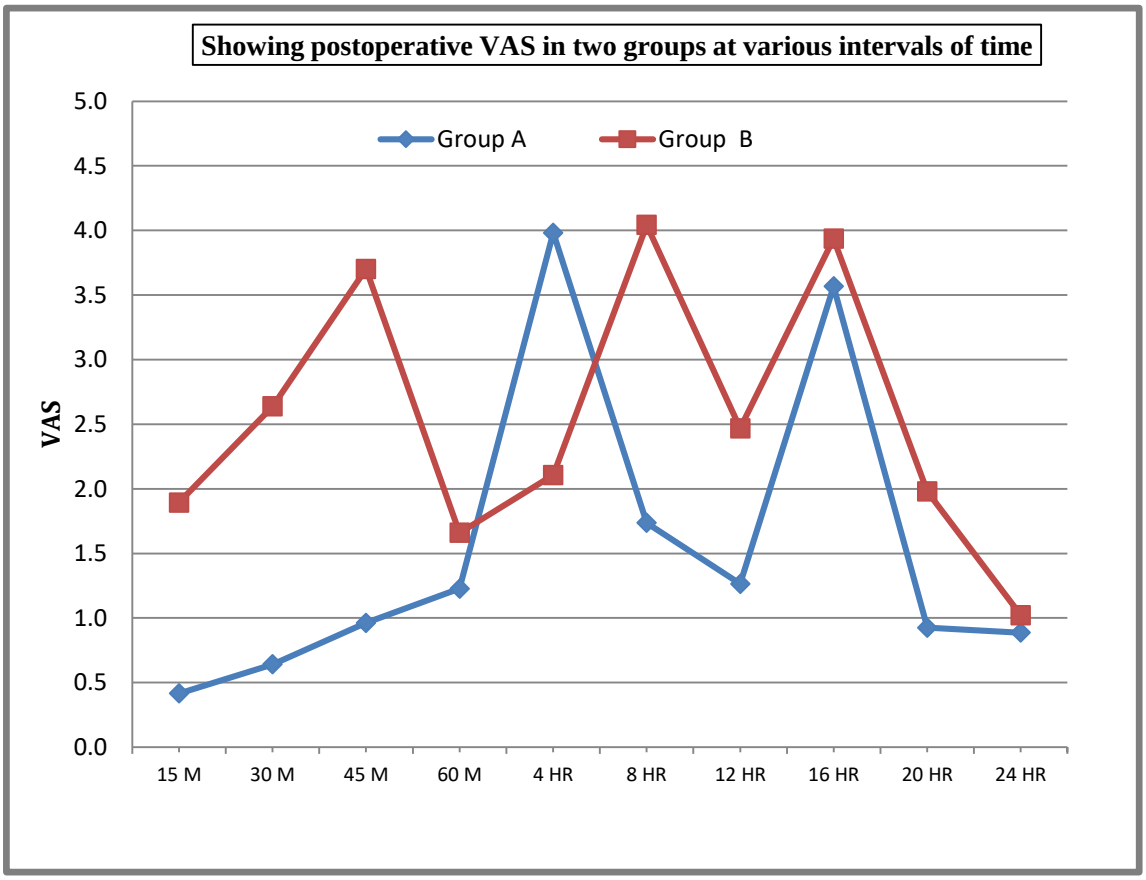

Figure 2. Showing postoperative VAS in two groups at various intervals of time.

Time to first rescue analgesia (minutes): The mean time interval after surgery when the patients required an opioid owing to increasing VAS score (>3) was 307.9 ± 109.1 mins in group A (range 240-480 mins) and 42.8±10.36 mins in group B patients (range 15-60 min).

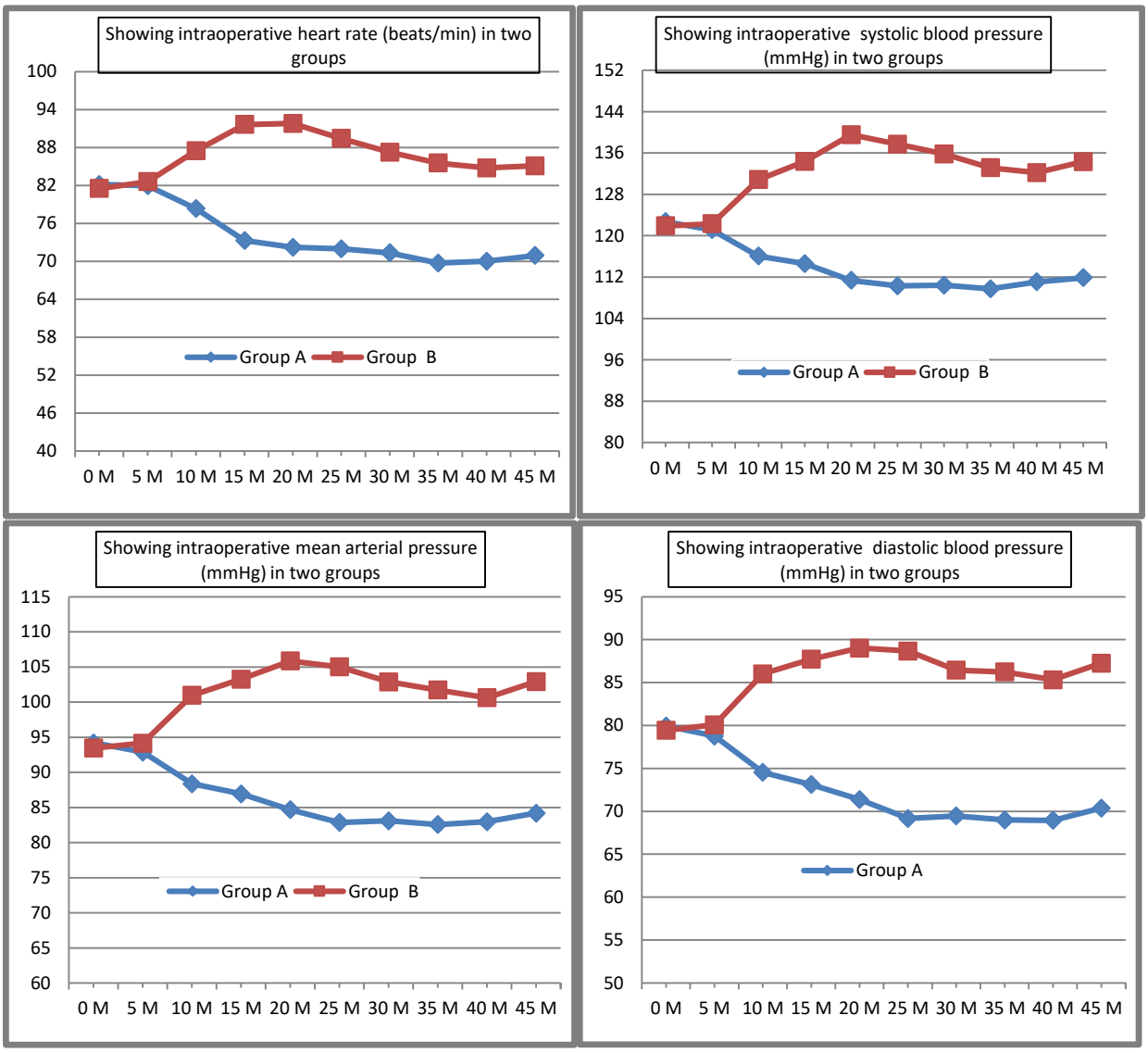

Figure 3. Showing intraoperative mean HR, SBP, DBP, and MAP in the two groups of patients at various time intervals.

Postoperative tramadol consumption (mg)

The mean total dose of tramadol used (over 24 hours) in group A patients was 89.62±20.47 mg (range 50-100 mg) while in group B it was 156.4±16.87 mg (range 150-200 mg).

Intraoperative vitals: We recorded the mean heart rate (HR), mean systolic blood pressures (SBP), mean diastolic blood pressures (DBP), mean values of mean arterial pressures (MAP), and oxygen saturation (SpO2) at various time intervals in the two groups. All these variables were less in Group A patients as compared to Group B patients except SpO2 which was comparable (Fig. 3).

Postoperative vitals: The mean heart rate (HR), mean systolic blood pressures (SBP), mean diastolic blood pressures (DBP), mean values of mean arterial pressures (MAP), and oxygen saturation (SpO2) at various times intervals in the two groups were recorded in the postoperative period. A significant difference was observed in all variables among the two groups except for SpO2 (Fig 4).

Intraoperative and postoperative complications: Intraoperative bradycardia and hypotension occurred only in 1 patient each in Group A which was

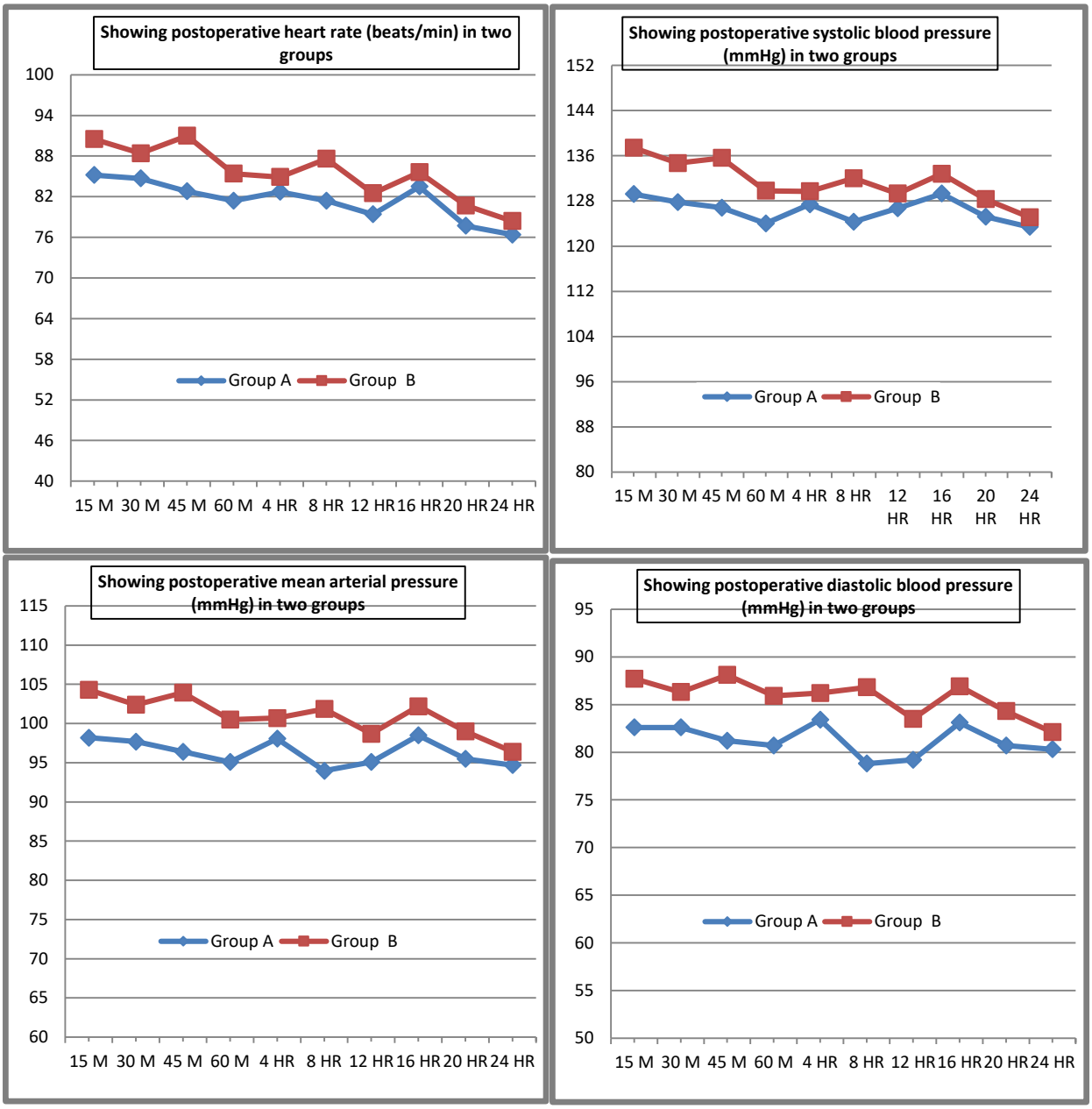

Figure 4. Showing postoperative mean HR, SBP, DBP, and MAP in the two groups of patients at various time intervals.

successfully treated. Postoperative complications in Group A included 3 patients with nausea and 1 patient developing vomiting. In Group B, 6 patients developed nausea and 3 patients developed vomiting. None of the patients in either group developed postoperative bradycardia or hypotension.

Discussion

This study was conducted over a period of 2 years in our center and included 100 patients undergoing laparoscopic cholecystectomy selected according to inclusion and exclusion criteria. The patients were divided into Esmolol group A including 53 patients

and control group B with 47 patients. The age and body mass index (BMI) of the patients in the two groups were comparable. A female predominance was seen in both the groups and is probably due to the preponderance of gallstone disease in females especially middle-aged ones. The demographic profile of our patients is comparable to that of Coloma et al (9) and Bhawna et al (10).

The mean duration of surgery was also comparable between the groups (group A 39.9±5.68 mins and group B 40.3 ± 5.41mins) indicating Esmolol had no significant effect on the duration of surgery. This observation was also made by Chia et al (11) with the duration of surgery (min) in the Esmolol group being 122 min (54 patients) and 138 min (50 patients) (p-value 0.835).

The analgesic effect of Esmolol in our study was assessed by evaluating postoperative pain in the form of VAS score at various time intervals, the need and mean dose of tramadol required, and the time after surgery to rescue analgesia. Visual analog scale scores in patients group A were consistently less than those in group B indicating the good postoperative analgesic effect of Esmolol plus opioids. As patients in the control group required opioid top-ups earlier than the Esmolol group patients, the VAS score at 4 hours in the Esmolol group was more than that of the control group. In the Esmolol group, the mean VAS score showed an increase beyond VAS=3 at 4 hrs and 16 hrs requiring the administration of top-up analgesia in the form of opioids (Fig 2). Patients in the control group on the other hand showed an increase in the VAS score more than 3 at 45 min, 8 hrs, and 16 hrs requiring top analgesia at an earlier time and a total of 3 doses. Owing to the better pain control in the Esmolol group, hemodynamic parameters and VAS scores were consistently lower than the control group. These results are in concordance with the studies conducted by Dhir et al (12), Vahabi et al (13), Celebi et al (14), and Shukla et al (15). The mean time interval after surgery when the patients required an opioid owing to increasing VAS score (>3) was 307.9±109.15 mins in group A with a range of 240-480 mins and 42.8±10.36mins in group B patients with a range of 15-60 min. The difference in the time to first rescue analgesia was statistically significant ($p<0.001$). This shows that the use of intraoperative Esmolol enhances postoperative analgesia and reduces the need for postoperative analgesics in the form of opioids. Needing for a top-up analgesic in the Esmolol group was not required until 4 hrs postoperatively while as all the patients in the control group required it in the 1st hr. These observations were also made by Dhir et al (12) and Celebi et al (14) who in their studies found that the time to rescue analgesia postoperatively was significantly more in the Esmolol group as compared to the control group. The mean of the total amount of tramadol used in Esmolol group patients was 89.62±20.47 mg with a range of 50-100 mg while in the control group it was 156.4±16.87 mg with a range of 150-200 mg. This corresponded to a statistically significant difference in the postoperative tramadol requirement. This indicates the postoperative analgesia sparing effect of Esmolol. The opioid-sparing effect of Esmolol becomes important as it has been found that the high dosage of perioperative opioids or their continuous IV infusion can increase opioid tolerance and bring about severe postoperative pain (16). The increased requirement of tramadol in the control group was also observed by Bhawna et al (10), Chia et al (11), Vahabi et al (13), Celebi et al (14), and Lee et al (17) in their studies.

We also evaluated the intraoperative and postoperative hemodynamic profiles of our patients to assess the hemodynamic effects of Esmolol. The intraoperative HR, SBP, DBP, and MAP was found to be consistently lower in the Esmolol group as compared to the control group in our study (Fig 3). The difference was statistically significant and was observed beyond 10 mins following Esmolol administration indicating the effect of beta-blocker (Esmolol) on the hemodynamic status of the patients in Group A. These observations were also made by Dhir et al (12), VAHABI et al (13) and Shukla et al (15) in their studies.

The post-operative parameters also showed a similar trend in our study. The HR, SBP, DBP, and MAP in group A patients were consistently less than those in group B. This was due to good post-operative analgesia supplementation provided by Esmolol in group A patients. In the Esmolol group, a rise in the hemodynamic parameters was observed at 4 Hr and 16 Hr which corresponded to an increase in VAS

scores (>3) at these times and required top-up analgesia in the form of opioids (Tramadol) (Fig 4). In the control group the hemodynamic parameters showed a rise at 45 min, 8 Hr, and 16 Hr which corresponded to an increase in VAS (>3) indicating an earlier requirement for opioids and an overall increased VAS score than that in the Esmolol group. These findings are concordant with the studies conducted by Chia et al (11), Dhir et al (12), and Vahabi et al (13).

There was no significant difference in the intraoperative complications (Bradycardia and hypotension) between the 2 groups of patients. Bradycardia and hypotension occurred only in 1 patient each in Group A which was successfully treated by injecting 0.01mg/kg intravenous atropine and 0.05mg/kg intravenous ephedrine, respectively. Postoperative complications like nausea, vomiting, bradycardia, and hypotension were sought in both groups of patients. In group A (Esmolol), only 3(5%) patients developed nausea, and 1(2%) patients developed vomiting. In group B (control), 6(13%) patients developed nausea and 3(6%) patients developed vomiting. None of the patients in either group developed postoperative bradycardia or hypotension. The difference in postoperative complications between the two groups was statistically insignificant ($p>0.05$), however, the incidence of postoperative nausea and vomiting was less in the Esmolol group. This is probably due to better pain control and hemodynamic profile of Esmolol patients. These results are similar to those observed by VAHABI et al (13), Celebi et al (14), and Hwang et al (18).

Limitations of our study included the fact that postoperative pain is a subjective experience and can be difficult to quantify objectively when comparing various treatment options. Besides, further studies with different doses of Esmolol are needed to derive maximal benefit in terms of postoperative pain relief with minimal adverse effects after laparoscopic surgeries.

Conclusion

Using intraoperative Esmolol could significantly reduce the need for postoperative opioids and improve the quality of postoperative analgesia. The hemodynamic profile of the patients receiving intraoperative Esmolol was significantly affected during the intra- and postoperative period. Besides, Esmolol did not significantly affect the incidence of postoperative complications or major adverse events.

Acknowledgment

None.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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