IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 5 Ser.16 (May. 2020), PP 25-29
www.iosrjournals.org

Effect of Esmolol in Perioperative Hemodynamic and Analgesic Requirement in Adult Patients Undergoing Laparoscopic Surgeries

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Abstract: *Esmolol plays important role in surgical pain response modulation in addition to good perioperative hemodynamic control. The ability of Esmolol to rapidly achieve steady-state β-blockade also makes it ideal to attenuate the intraoperative adverse sympathetic hemodynamic effects and improve the postoperative recovery by reducing postoperative pain intensity and intraoperative anesthetic and opioid requirements. The aim of this study was to evaluate the influence of Esmolol on perioperative hemodynamic and postoperative pain management.*

Material and method: *A prospective double blind randomized controlled trial was conducted in a tertiary care hospital over a period of one year. ASA status I or II, aged 16 to 60 years, undergoing laparoscopic surgeries of up to two hours duration under general anesthesia after taking consent, were enrolled. The study drug Esmolol was given 0.5mg/kg preoperatively and intraoperative Esmolol infusion at the rate 0.05 mg/kg/minute was administered in group A and compared with saline group B. Perioperative hemodynamic and postoperative pain and complications were recorded.*

Result: *In Esmolol and Control groups mean arterial pressure was raised from baseline after intubation i.e. 94.40, 105.67 mmHg; at skin incision 90.02, 102.60 mmHg and at extubation 92.03, 104.32 mmHg respectively ($p<0.05$). Heart rate was also raised in both groups at intubation, skin incision and extubation ($p<0.05$)77.34, 88.42; 75.62, 87.03; 76.61, 89.01 respectively. The difference in mean arterial pressure and heart rate in both the groups was significant. Intraoperative fentanyl consumption in control group (143.78mcg) was higher than in Esmolol group (94.52mcg). Postoperative tramadol requirement was significantly higher in control group (72.10mg) as compared to Esmolol group (61.52mg). Postoperative nausea vomiting was also higher in patients of control group (9 versus 4).*

Conclusion: *Esmolol reduces Intraoperative hemodynamic changes and decreases perioperative analgesic requirements, postoperative pain.*

Key words: *Esmolol, intraoperative hemodynamic, tramadol, perioperatively analgesia*

Date of Submission: 16-05-2020 Date of Acceptance: 31-05-2020

I. Introduction

Beta-blockers have recently been investigated for the management of postoperative pain. These drugs are increasingly being used to reduce perioperative cardiac complications [1]. There is evidence that beta-blockers reduce neuronal stimulation responses of the cingulate cortex in rats. Esmolol is a selective short-acting β antagonist with a half life of 9.2 ± 2 min. It shows its' maximal effect on heart rate and blood pressure in 1-2 min after intravenous injection. It appears that Esmolol may have beneficial effects during surgery including stabilizing the patient's intraoperative hemodynamic status and may also result in reduced postoperative opioid consumption[2]. When used as an adjunct, it has been shown to reduce intraoperative anesthetics and opioid requirement and postoperative pain intensity and thus improves the postoperative recovery[3, 4, 5] .

The present study has been planned with an aim to evaluate use of Esmolol in intraoperative attenuation of stress response and reduced perioperative analgesia requirement and postoperative complication to allow early ambulation and hasten recovery.

II. Material And Method

After approval of the Hospital Ethics Committee, 60 adult patients of either sex, of ASA status I or II, undergoing laparoscopic cholecystectomy or laparoscopic hernioplasty under general anaesthesia were studied in this randomized double blinded study protocol. The anticipated duration of surgery was upto two hours.

Exclusion Criteria-

1. Ischemic heart disease
2. Heart block
3. Pulmonary diseases, Liver disease
4. Being using β blockers or calcium channel blockers
5. Obese or underweighted (body mass index >30 or <18.5), diabetes mellitus,
6. History of chronic opioid usage.
7. Not given consent

After obtaining written and informed consent, patients were randomly allocated into one of the two groups.

Group I (Esmolol Group)

15 minutes before the induction of anaesthesia, patients in the Esmolol group received a loading dose of Esmolol (0.5 mg/kg in 50 ml normal saline) over a period of 5 minutes followed by an I.V. infusion of Esmolol (0.05mg/kg/min) until the end of surgery.

Group 2 (Control Group)

Patients in control group received the same volume of normal saline for loading and continuous infusion. Perioperatively standard monitors were applied and baseline parameters were recorded. Balanced general anaesthesia was given in both groups and maintained using controlled ventilation with isoflurane 0.5-1.0% and O_2:N_2O in the ratio of 50:50. Neuromuscular blockade was achieved with vecuronium 0.1 mg/kg IV. Paracetamol 1 gram (100ml) IV was given 45 minutes prior to extubation. Injection ondansetron 4 mg slow IV was given 30 minute prior to the extubation. Anaesthesia was reversed with inj. Neostigmine (0.04 mg/kg) and inj. Glycopyrrolate (0.01 mg/kg). In the Esmolol group, Esmolol infusion was discontinued at the end of surgery.

Intraoperative hypotension and bradycardia was treated with intermittent inj. Ephedrine 5 mg IV and inj. Atropine 0.6 mg IV respectively.

After surgery, patients received 1mg/ kg Tramadol in 100 ml normal saline IV infusion if needed as postoperative analgesia. Pain intensity was evaluated using a visual analogue scale for movement (VASM) and at rest (VASR), at postoperative 2, 3, 4, 8, 12, 24 and 48 hours after the operation. A pain </=3 represented satisfactory pain relief. Total tramadol consumption and side effect as nausea, emesis were recorded hourly for first 6 hour and then at 12, 24 hrs. Each patient was asked to grade satisfaction (Yes/No) at different interval for 2 days.

For analysis of data, we used Independent t-test, chi square test and Mann- Whitney U Test. A value of $p<0.05$ was considered to represent statistical significance.

III. Observation And Result

Written informed consent was obtained from sixty adult patients fulfilling the inclusion criteria scheduled to undergo laparoscopic surgery (cholecystectomy and hernioplasty). The difference in mean age and weight of patients of Group I (46.53±12.08 years, 61.20±9.03kg) and Group II (45.71±10.70 years, 62.67±10.33 kg) was not found to be statistically significant. Patients of above two groups were found to be statistically comparable for gender and anthropometric parameters. Difference in Physical (ASA Grade) and Nutritional Status (BMI) of patients of above two groups were not found to be statistically significant. The study was conducted over a period of one year. Initially 60 patients were recruited in the study (30 patients in each group).

TABLE No. 1-Demographic Data

Groups	GROUP I	GROUP II
Mean age(yrs) (SD)	46.53 (12.08)	45.71 (10.7)
Mean weight(kg) (SD)	61.20 (9.03)	62.67 (10.33)
Male	16	14
Female	14	16
ASA I	24	23

ASA II	**6**	**7**

Table No.2- CHANGES IN MEAN ARTERIAL PRESSURE (mmHg) (Mean±SD.)

Time	Case		Control	
	Mean	SD	Mean	SD
Baseline	**90.02**	**8.53**	**94.03**	**9.58**
Intubation	**94.40**	**8.54**	**105.67**	**9.32**
5min.	**90.09**	**7.97**	**100.25**	**8.46**
10	**88.62**	**8.61**	**97.41**	**8.81**
15	**90.02**	**8.25**	**102.60**	**8.22**
20	**89.42**	**7.76**	**99.08**	**9.84**
25	**87.82**	**7.63**	**96.69**	**8.08**
30	**86.85**	**7.84**	**95.14**	**8.67**
45	**86.78**	**8.20**	**94.35**	**7.16**
60	**84.02**	**8.64**	**93.44**	**7.99**
75	**83.50**	**9.65**	**92.55**	**6.48**
90	**81.89**	**8.76**	**90.60**	**16.4**
105	**82.94**	**7.60**	**93.81**	**6.35**
120	**83.45**	**6.88**	**98.96**	**11.56**
Extubation	**92.03**	**8.16**	**104.32**	**8.56**

The baseline value of mean arterial pressure in Esmolol and control groups were 90.02±8.53 (mmHg) and 94.03 ±9.58 (mmHg) respectively (p >0.05). Mean heart rate of patients in Esmolol and control groups were 73.23 ± 7.28 per minute and 75.61 ±6.16 per minute respectively (p >0.05).

Table No.3 CHANGES IN HEART RATE (per minute)(Mean±SD)

Time	Case		Control	
	Mean	SD	Mean	SD
Baseline	**73.13**	**7.28**	**75.61**	**6.16**
Intubation	**77.34**	**7.11**	**88.42**	**7.34**
5min.	**74.34**	**8.10**	**85.22**	**7.99**
10	**74.76**	**8.19**	**84.39**	**8.76**
15	**75.62**	**7.46**	**87.03**	**9.15**
20	**73.98**	**7.96**	**87.20**	**8.52**
25	**73.03**	**7.46**	**82.28**	**8.80**
30	**72.18**	**7.31**	**82.61**	**7.43**
45	**70.83**	**7.53**	**83.27**	**7.25**
60	**68.92**	**9.53**	**81.26**	**8.20**
75	**68.55**	**8.48**	**81.08**	**6.26**
90	**68.95**	**6.01**	**80.81**	**6.61**
105	**69.84**	**6.46**	**75.43**	**15.28**
120	**72.85**	**9.09**	**80.81**	**9.25**
Extubation	**76.61**	**7.31**	**89.01**	**7.32**

MAP and heart rate variation in case and control group was significant at intubation, skin incision and extubation. Intraoperatively, in Esmolol group mean arterial pressure and heart rate variability were less than in control group (p<0.05) (Table-2, 3).

Table 4 -INTRAOPERATIVE FENTANYL CONSUMPTION

	Groups	Mean	SD
Fentanyl (µg)	**Esmolol**	**120.73**	**35.45**
	Control	**163.78**	**49.65**

Intraoperative use of fentanyl high in control groups (163.78 µg) as compared to Esmolol group(p<0.05).

Table 5- POSTOPERATIVE TRAMADOL USED

	Groups	Mean	SD
Tramadol(mg)	**Control(41)**	**72.10**	**10.98**
	Case(33)	**61.52**	**9.57**

Requirement of tramadol for postoperative pain relief in the first two days was found to be significantly lower in Esmolol group (Table-5) (p<0.05).Total number of patients needing tramadol was higher in control group (41) than Esmolol group (33). First dose of Tramadol was used earlier in group II as compared to Esmolol group.

Table 6 -POSTOPERATIVE MEAN VISUAL ANALOGUE SCORE AT REST AND MOVEMENT

Post op period(Hr.)	Esmolol		CONTROL	
	VASR	VASM	VASR	VASM

2	**1.46**	**1.51**	**2.26**	**2.64**
3	**1.80**	**2.00**	**3.53**	**3.70**
4	**2.03**	**2.10**	**2.20**	**2.40**
8	**2.73**	**2.91**	**2.95**	**3.51**
12	**2.53**	**2.61**	**2.75**	**2.84**
24	**1.21**	**1.52**	**2.00**	**2.20**
48	**1.33**	**1.35**	**1.60**	**1.67**

Post operative VAS score was recorded and found to be significantly different in both groups at rest and at movement.
Incidence of post operative nausea and vomiting were less in Esmolol group.

Intraoperative ephridine (5mg) IV was given in two patient of Esmolol group but not used in the control group.
Intraoperative atropine (0.6mg) IV was used in one patients of Esmolol group but was not used in the control group.

IV. Discussion

Opioid free anaesthesia (OFA) is a recent trend which has gained immense popularity in good hemodynamic control. [6] Esmolol could mask signs of sympathetic activity due to pain. [7]

Efficient intraoperative hemodynamic stability and postoperative analgesia are very important factors that affect complication rates in patients. [8] PONV has an incidence of 40-75% and usually delays early ambulation and patient discharge.[9]

In this study, intraoperative Esmolol infusion contributes opioid sparing effect and low VAS scores in entire postoperative period. Bhawna et al reported that in lower abdominal surgery addition of Esmolol to isoflurane might decrease both anaesthetic and postoperative analgesic requirements [10].

Change in Mean arterial pressure and heart rate during intubation, skin incision is higher in the control group as compared to the Esmolol group, similar studied was done by Serpil et al 2016 [11].

Intraoperative fentanyl used and postoperative opioid requirement in control group was higher as compared to Esmolol group. VAS score at rest and on movement was higher in control group on 12th and 24th hours as compared to Esmolol group. Same results were also observed by Haghighi M et al in 2015 [12].

Ozturk et al reported that both PONV incidence and analgesic requirements decrease in laparoscopic cholecystectomy patients by adjuvant Esmolol [13]. A similar effect on PONV was reported from an earlier systematic review on the safety of Esmolol when Esmolol was compared with opioids in attenuating the hemodynamic response to intubation and extubation. [14] The reduction in PONV that we observed is probably an indirect consequence of opioid and volatile-sparing effect, although there is some evidence that β-blockade may have a direct antiemetic effect[15].

Postoperative sedation was low in Esmolol group as compared to control group; hence the patients were ready to go home earlier. Coloma et al 2001 used intraoperative continuous infusion of Esmolol and reported postoperative opioid sparing effect [16]. Postoperative nausea vomiting was lower in Esmolol group (4 patients) as compared to control group (9 patients)

The mechanism by which Esmolol modulates the pain response is unclear. β-Adrenergic antagonist regulation of voltage-gated Ca^{2+} channels that stimulate inhibitory G proteins in the cell membrane may control the release of neurotransmitters leading to a state of central analgesia, like clonidine. [17, 18] Another proposed mechanism involves blocking hippocampal activation by adrenergic pathways that may then attenuate the perception of pain via N-methyl-D-aspartate subtype glutamate receptors.[19]

V. Conclusion

As a conclusion we observed that using adjuvant Esmolol during anesthetic maintenance of laparoscopic cholecystectomy patients decreases anesthetic-analgesic requirements, postoperative pain and PONV without causing any hemodynamic instability.

Acknowledgement
Author would like to acknowledge Dr. Pavan Nayar for guiding us during this study.
Financial support and sponsorship: NIL
Conflicts of Interest: There are no known conflicts of interest.
1. Consultant, 2.Senior Consultant and corresponding author, 3. Consultant & Professor, 4.Senior consultant, 5. Consultant Public health, 6.Consultant

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