Original Research Paper

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TO EVALUATE THE EFFECT OF ESMOLOL ON PERIOPERATIVE ANALGESIC REQUIREMENT IN PATIENTS UNDERGOING LAPAROSCOPIC SURGERY UNDER GENERAL ANESTHESIA.

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ABSTRACT

BACKGROUND: Esmolol is a short acting beta blocker. Esmolol is primarily used in the treatment of hypertension and tachycardia during anesthesia, but some study claim that it can be used to modulate pain. The main objective of this study was to evaluate the effect of esmolol on perioperative analgesic requirement in patients undergoing laparoscopic surgery.

METHOD: It was a prospective, randomized, double blind interventional study. Total number of participants was 60. The study was carried out for a period of 3 years from 2015- 2017 in the department of Anesthesiology, Jawaharlal Nehru Medical College, Aligarh Muslim University. Informed consent was taken from all the participants included in this study.

RESULT: In Group E, 27/30 patients had VAS score ≤ 3 compared to 8/30 patients in the Group C at 15 minutes. Similarly at 30 minutes and next 24 hours, all of 30 patients in Group E had VAS score of≤ 3 compared to 18/30 patients in Group C.

CONCLUSION: Esmolol decreases perioperative analgesic requirement and postoperative pain. The visual analogue score for pain assessment was found to be significantly lower in the esmolol group.

KEYWORDS : Esmolol, Perioperative analgesic, Laparoscopic surgery.

INTRODUCTION:

Esmolol is a selective β1-adrenoceptor antagonist. The action of esmolol is both rapid and transient, with an elimination half-time of approximately 9 minutes. This beta adrenergic receptor antagonist has a sympathetic nerve blocking effect. Although esmolol is primarily used in the treatment of hypertension and tachycardia during anesthesia, but some study claim that it can be used to modulate pain.[1]

Esmolol has been postulated to reduce anesthetic requirements via a direct antinociceptive property. Use of esmolol and nicardipine in patients undergoing gynecological laparoscopic procedures attenuated the increase in HR and MAP intra-operatively, facilitated faster emergence from anesthesia and significantly decreased postoperative analgesic requirements and time to discharge, without increasing any side effects.[2]

The mechanisms of analgesic effects of esmolol remain largely unidentified, some studies indicated that esmolol might exert its antinociceptive effect via blockage of tetrodotoxin (TTX)-resistant Na^+ channels involved in nociceptive signaling in the dorsal root ganglion and by activation of G proteins in isolated cell membranes; suggesting that this property of esmolol resembles mechanism of central analgesia as induced by clonidine.[3]

In 1901, George Kelling of Germany, performed first laparoscopic procedure in dogs, and in 1910, Hans Christian Jacobaeus of Sweden performed first laparoscopic operation in humans. Laparoscopic surgeries is an essential part of surgical practice because of its magnification, skillfulness, less cosmetic scar, less postoperative pain, and decreased hospital stay along with less morbidity and mortality.[4]

The well-known visual analogue scale (VAS) and numeric rating scale (NRS) for assessment of pain intensity are equally sensitive in assessing acute pain after surgery, and they are both superior to a four-point verbal categorical rating scale (VRS).[5]

METHOD:

It was a prospective, randomized, double blind interventional study. The study was carried out in the department of Anaesthesiology, Jawaharlal Nehru Medical College, Aligarh Muslim University for a period of 3 years from 2015-2017.Informed consent was taken from all the participants included in this study. Total number of participants was 60. 60 patients of either sex scheduled for elective laparoscopic surgery under General anaesthesia were included in this study.60 patients were randomly divided into two groups: Group E (esmolol) and Group C (control) with 30 patients in each group. Patients with cardiovascular disease, renal disease, and respiratory disease and with history of intake of analgesic drug like paracetamol, NSAID or opioids and beta blockers were excluded from the study. Parameters to be recorded in perioperative period are Postoperative VAS score, total amount of used analgesic, total amount of esmolol given, and hemodynamic parameters.

Inclusion Criteria:

- ASA I & II patients of either sex
- Age between 20-60 years
- Patients planned for laparoscopic surgery

Exclusion Criteria:

- Patients with cardiovascular, renal and respiratory comorbidities.
- Patients with history of intake of analgesic drug like paracetamol, NSAIDS, opioids and beta blockers.

Patients were randomly divided into two groups (Group E and Group C) of 30 patients each by computer generated random number (www.randomization.com). Patients in Group E (esmolol group) received esmolol in the loading dose of 0.5mg/kg and 3mg/kg/hr. infusion, while group C (control group) received the same volume of normal saline. Both patient and the anaesthetist in charge were blinded for the study as the drug was given and assessed by different anaesthetist.

After a thorough preoperative evaluation an informed consent was taken from the patient about anaesthetic technique and esmolol. The patients were shifted to the operating room, intravenous line established and monitors attached for continuous monitoring of electrocardiography, heart rate, non-invasive blood pressure, and oxygen saturation.

All the patients were premedictated with inj. ondensetron 0.1 mg/kg, inj. midazolam 0.03 mg/kg, inj. tramadol 2 mg/kg.After that patients were pre-oxygenated with 100% oxygen for 3 to 5 min and then induced with propofol 2-2.5 mg/kg (titrated dose). Relaxation was achieved with inj. succinylcholine 1.5 mg/kg following which laryngoscopy was attempted using standard technique. Patients were intubated by using an appropriate sized cuffed ETT . Patients were

subsequently maintained with 60% N_2O in oxygen with inj vecuronium (intermittently) on IPPV. Both group received 1.5mg/kg diclofenac sodium bolus IV. Aqueous preparation as per requirement in intraoperative period. Patients in Group E received loading dose of injection esmolol 0.5mg/kg in 30 ml isotonic saline before induction of anaesthesia, followed by an IV Infusion of esmolol 3mg/kg/hr till the completion of surgery. While patient from the group C received the same volume of normal saline for loading and continuous infusion as the esmolol group till the completion of surgery. Heart rate (HR), systolic BP and diastolic BP were recorded at the start of slow bolus esmolol injection and throughout the procedure. Residual neuromuscular blockade was reversed with neostigmine 0.05mg/kg and glycopyrrolate 0.01mg/kg IV. When patient's spontaneous respiration was considered sufficient and patient was able to obey simple commands, suction of throat was done and trachea was extubated. Patient was shifted to PACU, HR and BP was monitored till the patient was shifted to ward. Patient with >3 VAS score was treated with 30mg ketorolac. Patient shifted to PACU and HR, BP, oxygen saturation and VAS score were monitored till the patient was shifted to ward.

RESULT:

Table 1: Age Distribution Of The Patients In Group E (esmolol) And Group C (control).

Patient Group	Age in years Mean (SD)	Standard error	P value (t-test)	Mean difference	95% CI
Group E (N=30)	33.07 (7.32)	1.34	0.876	0.3	-3.545 to 4.145
Group C (N=30)	32.77 (7.55)	1.38			

N=number of patients, SD= Standard deviation ≤ 0.05 is significant, I=Confidence interval.

Table 2: Gender Distribution Of Patients In Group E (esmolol) And Group C (control)

Patient Group	Male Number (%)	Female Number (%)	P value (Fisher's exact)
Group E (N=30)	2 (6.7)	28 (93.3)	0.254
Group C (N=30)	6 (20)	24 (80)	

Table 3: Comparison Of Mallampati Grades (MP 1-4) In Patients Of Group E (esmolol) And Group C (control)

MP Grade	Group E Number (%)	Group C Number (%)	P value
1	12 (40)	9 (30)	0.188
2	16 (53.3)	14(46.7)	
3	2 (6.7)	7(23.3)	
4	0	0	
Total	30 (100)	30 (100)	

Table 4: Comparison Of American Society Of Anesthesiologist Score (ASA I and II) In Patients Of Group E (esmolol) And Group C (control).

ASA Score	Group E Number (%)	Group C Number (%)	P value
I	25 (83.3)	20 (66.7)	0.132
II	5 (16.7)	10 (33.3)	
Total	30 (100)	30 (100)	

Table 5: Comparison Of Pain Sensation (visual Analogue Scale) At 15, 30 Minutes And Next 24 Hours Postoperatively In Group E (esmolol) And Group C (control).

VAS score	Group E (N=30) Number (%)	Group C (N=30) Number (%)	P value (chi-square)
≤3 at 15 minute	27 (90)	8 (26.7)	0.00
>3 at 15 minute	3 (10)	22 (73.3)	
≤3 at 30 minute and next 24 hours	30 (100)	18 (60)	0.00
>3 at 30 minute and next 24 hours	0	12 (40)	

The pain sensation test was assessed at three time points: at 15, 30 minutes and next 24 hours postoperatively, using Visual analogue scale (VAS). In Group E, 27/30 patients had VAS score ≤ 3 compared to 8/30 patients in the Group C at 15 minutes. The difference was significant with p value 0.00. Similarly at 30 minutes and next 24 hours, all of 30 patients in Group E had VAS score of≤ 3 compared to 18/30 patients in Group C. The difference was significant with p value 0.00.

DISCUSSION:

Lee S J et al studied the effect of perioperative esmolol infusion on the postoperative nausea, vomiting and pain after laparoscopic appendectomy and pain was assessed at 30 minute, 6 hours and 24 hours after surgery. They found significantly higher pain response in patients of control group in the 1st 24 hours of postoperative period.[6]

Salman E A et al studied the role of very low dose of intravenous esmolol in reducing propofol injection pain and during the injection of both pre-treatment solutions. Propofol pain was assessed by using four point scales. The incidence of pain on injection of propofol in the control group was maximum (90%) followed by 50% in lidocaine group and least in esmolol group (33.3%).[7]

Korpinen R et al studied the effect of alfentanil and esmolol and their half-dose combination on the increment of heart rate and arterial pressure and on the prolongation of the QTc interval of the ECG occurring during anaesthetic induction. They found that the half-dose combination of alfentanil and esmolol is as effective as alfentanil and superior to esmolol in the prevention of hemodynamic responses to the tracheal intubation.[8]

White et al conducted their study in forty-five healthy female patients undergoing gynecologic laparoscopy procedures. They were randomly assigned into 3 treatment groups: Group 1 (control, n=15) received normal saline 5 ml and 1 ml, followed by a saline infusion at a rate of 0.005 ml/kg/min. Group 2 (n=15) received esmolol 50 mg and saline 1 ml, followed by an esmolol infusion 5µg/kg/min and Group 3 (n=15) received esmolol 50 mg and nicardipine 1 mg, followed by an esmolol infusion 5µg/kg/min. The study drugs were administered after the induction of anesthesia with fentanyl 1.5 g/kg and propofol 2 mg/kg i.v.They concluded that the adjunctive use of esmolol alone or in combination with nicardipine during the induction of anesthesia reduced the hemodynamic response to tracheal intubation and esmolol infusion as an adjuvant to desflurane-N_2O anesthesia for maintenance period also improved the recovery profile after outpatient laparoscopic surgery.[9]

Celebi N et al observed that intravenous infusion of esmolol reduced intraoperative and postoperative analgesic consumption and visual analogue scale scores in the early postoperative period and prolonged the time to need for first analgesia; however it did not influence the depth of anaesthesia.[10]

CONCLUSION:

We conclude that esmolol influences the analgesic requirement by modulation of sympathetic component of the pain.Esmolol decreases perioperative analgesic requirement and postoperative pain. The visual analogue score for pain assessment was found to be significantly lower in the esmolol group at all three points (15 min, 30 min, and next 24 hours) post-surgery. Despite previous studies comparing esmolol with placebo and other analgesic suggesting effective reduction in the postoperative analgesic requirement with esmolol use, further studies with large sample size, open surgery, cardiac diseases etc. need to be done to generalize its outcome.

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