INFLUENCE OF ESMOLOL ON REQUIREMENT OF INHALATIONAL AGENT USING ENTROPY AND ASSESSMENT OF ITS EFFECT ON IMMEDIATE POSTOPERATIVE PAIN SCORE

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ABSTRACT

AIM
This study aims to know the influence of esmolol on requirement of inhalational agent using entropy and also to assess the effect on immediate postoperative pain score.

MATERIALS AND METHODS
This study was conducted in 60 healthy ASA I and II patients.

INCLUSION CRITERIA
Body mass index (BMI) which is less than 25, age between 25 to 60 years of either sex who underwent lower abdominal surgeries.

EXCLUSION CRITERIA
Patients with history of allergy to opioids or halogenated anaesthetics, or taking drugs known to influence anaesthetic requirement including beta blockers, opioids, pregnant women and those who had cardiovascular, pulmonary, renal, hepatic diseases were excluded. Patients were divided into two groups, Group A and Group B depending on the infusion being used, esmolol in Group A and saline in Group B.

RESULTS
Age, body weight, ASA physical Status, total duration of surgeries (min.) and total isoflurane used was compared in both the groups and was non-significant (P>0.05). Pain was assessed in all the patients when they reached the postoperative room after extubation. VAS0 being the pain score at the time when they reached the postoperative room and VAS5, 10, 15, 20, 25 and 30 being the pain scores at respective time intervals which revealed a statistically significant difference in the VAS score between the groups at 5 and 10 min. intervals. Dose of morphine used at 5, 10, 15, 20, 25 and 30 min. for pain relief was calculated for both the groups and compared. Similarily, there was a statistically significant difference in morphine consumption at 5, 10, 25 and 30 min. intervals (P<0.05). Total dose of morphine used in 30 min. was also significantly less in Group A as compared to Group B (P<0.05).

CONCLUSION
Esmolol has no effect on requirement of isoflurane, but it decreases the postoperative requirement of morphine and postoperative pain without increasing the risk of awareness as concluded from this study.

KEYWORDS
Esmolol Entropy, Inhalational Agent.

HOW TO CITE THIS ARTICLE: Rajendra G, Shiva PV, Bias D. Influence of esmolol on requirement of inhalational agent using entropy and assessment of its effect on immediate postoperative pain score. J. Evid. Based Med. Healthc. 2016; 3(58), 3063-3066. DOI:10.18410/jebmh/2016/666

INTRODUCTION: During preoperative procedures like intubation, laryngoscopy, tracheal extubation and surgical stimulation, when anaesthesia is administered, beta-blockers like esmolol are used to blunt the adrenergic response to various stimuli.

Financial or Other, Competing Interest: None.
Submission 24-06-2016, Peer Review 30-06-2016, Acceptance 08-07-2016, Published 21-07-2016.
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DOI: 10.19410/jebmh/2016/666

During surgery, to achieve the dual aims of the transient autonomic changes which is due to noxious surgical stimuli and recovery after ambulatory anaesthesia administration is still debatable.¹ Potentiation of hypnotic effects of anaesthesia and reduction of the dose requirement of intravenous and inhalational anaesthetics is done by β-blockers.² Whether these objectives are achieved to the best by use of opioid analgesics, sympatholytic drugs, sedative-hypnotics or other adjuvant drugs is still unclear. The depth of anaesthesia has been measured by many clinical and physical modalities like end tidal anaesthesia concentration,
minimum alveolar concentration (MAC), bispectral index system (BIS).

Due to insensitivity to measure accurately anaesthetics like N₂O, BIS has been questioned by various studies, discrepancies between clinical signs and measurement of BIS¹. Entropy which is derived from electroencephalography (EEG) has been considered a modality which is a quantifiable measure of the sedative and hypnotic effects of anaesthesia drugs.² It consists of two variables of EEG, namely state entropy and response entropy which is used to measure the cortical state and adequacy of analgesia.³ This study aims to know the influence of esmolol on requirement of inhalational agent using entropy and also to assess the effect on immediate postoperative pain score.

MATERIALS AND METHODS: This study was conducted in 60 healthy ASA I and II patients.

Inclusion Criteria: Body mass index (BMI) which is less than 25, age between 25 to 60 years of either sex who underwent lower abdominal surgeries.

Exclusion Criteria: Patients with history of allergy to opioids or halogenated anaesthetics, or taking drugs known to influence anaesthetic requirement including beta blockers, opioids, pregnant women and those who had cardiovascular, pulmonary, renal, hepatic diseases were excluded. Patients were divided into two groups - Group A and Group B depending on the infusion being used; esmolol in Group A and saline in Group B. One day prior to surgery, preoperative check up of all patients was done and informed consent was taken after explaining the anaesthetic procedure. No pre-anaesthetic medications were administered. 18G/20G intravenous cannula was placed in the operating theatre on arriving and 10 mL/kg of ringer lactate solution was preloaded.

After the standard monitoring was applied which included continuous electrocardiography (ECG), heart rate (HR), non-invasive mean arterial pressure (MAP), pulse oximetry (SpO₂), inspired oxygen concentration (FiO₂) and M Entropy, a loading dose of randomly selected study drug infusion (0.5 mg/kg) over 5 min., 20 min. before induction followed by a continuous infusion of the study drug at 0.5 mg/kg/min. till the closure of skin incision was received by every patient. The study drugs were prepared by an anaesthesia technician but was not aware about the design of the study who was given written instructions. Induction was carried out by administering intravenous fentanyl (3.0 mcg/kg) and propofol (1.25-2.0 mg/kg) which was titrated to bring entropy between 40 and 60 and muscle relaxation was achieved with Atracurium (0.5 mg/kg).

Patients were hand-ventilated with oxygen in air through face mask with fresh gas flow of 4 litres/min. and keeping the inspiratory fraction of oxygen (FiO₂) at 0.4. Laryngoscopy with Macintosh laryngoscope and subsequent intubation with Portex PVC cuffed endotracheal tube of appropriate size was carried out in all the patients after adequate relaxation. From the start of ventilation, the fresh gas flow was kept at 4 litres per min. keeping the fractional inspired oxygen concentration at 0.4 for 10 min.

Fresh gas flow was reduced to 1 litre per min., again keeping the FiO₂ 0.4 after 10 min. The percentage (%) volume dial of isoflurane was set and changed to target both the RE and SE of the entropy monitor between 40 and 60. Using tidal volume of 10 mL/kg and ventilatory rate was adjusted to keep PaCO₂ at 30–40 mmHg. Relaxation was maintained by bolus doses of Atracurium (0.15 mg/kg) as and when required, controlled ventilation was achieved. Doses of fentanyl (1.0 mcg/kg) every 60 min., intraoperative analgesia was maintained by bolus. All these parameters were monitored continuously like baseline readings of HR, ECG, MAP, End tidal carbon dioxide (EtCO₂), pulse oximetry (SpO₂) and entropy were noted just prior to induction and thereafter at 1 min. intervals for the first 5 min. and at 5 min. intervals starting from induction till extubation.

Peak airway pressures were monitored continuously during the operation and were always kept below 30 cm H₂O. Isotec 5 vapouriser was used as vapouriser outside the circuit and its dial settings were changed to target the entropy readings of both RE and SE between 45 and 55. Dial setting was recorded at the start and at all the times when it was changed from the initial setting. The absolute value of MAC delivered to each patient was calculated every 3 min. and noted and was compared later between the two groups. Consumption of isoflurane was calculated by formula: Consumption=CFTM/d 2412 Where C=agent dial setting consumption, M=molecular weight, T=time (min.), F=fraction of inspired oxygen (FIO₂), d=agent density in kg/m³, T=time (min.). At the time of closure of skin and maintaining the fresh gas flow at 1.5 litre/min., vapouriser was switched off. After administration of injection reversal and establishment of spontaneous rhythmic breathing, patients were extubated.

The patients were transferred to postoperative recovery ward and observed till fully awake. All the patients were followed up in the postoperative room for 30 min. to assess visual analogue scale for pain and managed with morphine boluses. The patients were examined after 24 h. and were also asked about any kind of awareness during the peri-operative period. P<0.05 was considered statistically significant and P<0.001 as highly significant.

RESULTS:

<table>
<thead>
<tr>
<th>Demographic Data</th>
<th>Group A (n=30)</th>
<th>Group B (n=30)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years) Mean±SD</td>
<td>45.23±6.890</td>
<td>45.43±7.451</td>
<td>0.487</td>
</tr>
<tr>
<td>Body Weight (in Kgs) Mean±SD</td>
<td>64.89±7.998</td>
<td>65.214±8971</td>
<td>0.725</td>
</tr>
<tr>
<td>ASA physical status (I/II)</td>
<td>14:10</td>
<td>13:12</td>
<td>0.616</td>
</tr>
<tr>
<td>Total duration of surgeries (min.)</td>
<td>141.00±32.333</td>
<td>140.77±22.987</td>
<td>0.281</td>
</tr>
<tr>
<td>Total isoflurane used (mL)</td>
<td>20.854±7.521</td>
<td>21.257±7.144</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table 1: Shows Demographic Parameters
From the above table, age, body weight, ASA physical Status, total duration of surgeries (min.) and total isoflurane used was compared in both the groups and non-significant (P>0.05).

<table>
<thead>
<tr>
<th>Time (min.)</th>
<th>Group A</th>
<th>Group B</th>
<th>P value (Mann Whitney Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>0.39±1.088</td>
<td>2.17±1.258</td>
<td>0.000**</td>
</tr>
<tr>
<td>10</td>
<td>1.57±1.659</td>
<td>2.67±0.200</td>
<td>0.000**</td>
</tr>
<tr>
<td>15</td>
<td>1.10±1.350</td>
<td>0.87±1.587</td>
<td>0.982</td>
</tr>
<tr>
<td>20</td>
<td>1.04±1.879</td>
<td>2.07±1.984</td>
<td>0.478</td>
</tr>
<tr>
<td>25</td>
<td>0.85±1.425</td>
<td>1.27±1.286</td>
<td>0.020*</td>
</tr>
<tr>
<td>30</td>
<td>0.00±1.350</td>
<td>0.78±1.579</td>
<td>0.002*</td>
</tr>
<tr>
<td>Total dose</td>
<td>3.40±1.657</td>
<td>8.27±1.875</td>
<td>0.000**</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time (mins)</th>
<th>Group A</th>
<th>Group B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS 5</td>
<td>3.28±1.977</td>
<td>4.23±1.782</td>
<td>0.002*</td>
</tr>
<tr>
<td>VAS 10</td>
<td>4.28±1.258</td>
<td>6.78±0.158</td>
<td>0.000**</td>
</tr>
<tr>
<td>VAS 15</td>
<td>3.24±0.351</td>
<td>4.12±1.797</td>
<td>0.200</td>
</tr>
<tr>
<td>VAS 20</td>
<td>4.44±1.749</td>
<td>4.97±1.741</td>
<td>0.702</td>
</tr>
<tr>
<td>VAS 25</td>
<td>4.35±1.225</td>
<td>4.17±1.200</td>
<td>0.071</td>
</tr>
<tr>
<td>VAS 30</td>
<td>3.21±1.347</td>
<td>3.78±1.511</td>
<td>0.638</td>
</tr>
</tbody>
</table>

Pain was assessed in all the patients when they reached the postoperative room after extubation. VAS0 being the pain score at the time when they reached the postoperative room and VASS, 10, 15, 20, 25 and 30 being the pain scores at respective time intervals which revealed a statistically significant difference in the VAS score between the groups at 5 and 10 min. intervals. Dose of morphine used at 5, 10, 15, 20, 25 and 30 min. for pain relief was calculated for both the groups and compared. Similarly, there was a statistically significant difference in morphine consumption at 5, 10, 25 and 30 min. intervals (P<0.05). Total dose of morphine used in 30 min. was also significantly less in Group A as compared to Group B (P<0.05).

DISCUSSION: Many studies have been reported related to this study. Bhawna et al7 in their study, fifty American Society of Anaesthesiologists (ASA) I and II patients, between 25 and 65 years of age who underwent lower abdominal surgeries were randomly allocated to two groups: Group E and Group S of 25 patients each were selected. Group E received esmolol infusion while Group S received the same volume of saline infusion. Demographic data, haemodynamics, amount of isoflurane used, end-tidal isoflurane concentration, postoperative pain score and total dose of morphine consumed in immediate postoperative period of 30 min. were analysed by using appropriate statistical tests.

Value of P<0.05 was considered significant and P<0.001 as highly significant. The two groups were comparable with respect to age, weight, ASA physical status, duration of surgery and amount of isoflurane used during anaesthesia. Assessment of postoperative pain was assessed by visual analogue scale (VAS) which showed significant difference at 30 min. The total dose of morphine consumption was significantly less (P<0.05) in Group E for relief of postoperative pain. They concluded that in light of depth of anaesthesia monitor, esmolol has no effect on requirement of isoflurane, but it decreases the postoperative pain as well as postoperative requirement of morphine without increasing the risk of awareness. Necla Dereli et al7 from their study, sixty patients have been included, propofol, remifentanil and vecuronium were used for induction.

Study groups were as follows: I-- Esmolol infusion was added to maintenance anaesthetics (propofol and remifentanil), II-- Only propofol and remifentanil was used during maintenance, III-- Esmolol infusion was added to maintenance anaesthetics (desflurane and remifentanil), IV-- Only desflurane and remifentanil was used during maintenance. They have been followed up for 24 h. for PNV and analgesic requirements. Visual analogue scale (VAS) scores for pain has also been evaluated. VAS scores were significantly lowest in group I (p=0.001--0.028). PNV incidence was significantly lowest in group I (p = 0.026). PNV incidence was also lower in group III compared to group IV (p=0.032). Analgesic requirements were significantly lower in group I and was lower in group III compared to group IV (p=0.005). Heart rates were significantly lower in esmolol groups (group I and III) compared to their controls (p=0.001); however, blood pressures were similar in all groups (p=0.594). Comparison of esmolol groups with controls revealed that there is a significant decrease in anaesthetic and opioid requirements (p=0.024--0.03).

It concluded that using esmolol during anaesthetic maintenance significantly decreases anaesthetic- analgesic requirements, postoperative pain and PNV. Urban M K et al8 in their study, they concluded that perioperative myocardial ischaemia (MI) is associated with postoperative cardiac morbidity. Postoperative sympathetic may reduce the incidence of MI. This study evaluated such reduction postoperatively with the administration of prophylactic beta-blockers in patients undergoing elective total knee arthroplasty with epidural anaesthesia and postoperative epidural analgesia. One hundred seven patients were preoperatively randomised into two groups, control and beta-blockers, who received postoperative esmolol infusions on the day of surgery and metoprolol for the next 48 h. to maintain a heart rate less than 80 bpm. Patients were followed for ST segment depression by using a Holter monitor and adverse cardiac outcomes. Postoperative electrocardiographic ischaemia was significantly more prevalent in the control group compared with the beta-blocker group during esmolol blockade (0 of 52 vs. 4 of 55; P=0.04) and tended to be more common in the control group the next two days (8 of 55 vs. 3 of 52; P =0.135).
In addition, the number of ischaemic events (control, 50; beta-blockers, 16) and total ischaemic time (control, 709 min.; beta-blocker, 236 min.) were also significantly different from the control group. Myocardial infarctions and cardiac events were more common in the control group, but these differences were not significant. Our results suggest that the use of prophylactic beta-blocker therapy may reduce the incidence of postoperative MI. Fuhrman T M et al conducted a randomised, double blinded, placebo controlled study at general surgery operating rooms at University hospitals. Forty-two ASA physical status I and II patients without history of cardiac or pulmonary disease undergoing surgery not involving the cranium or thorax were selected.

Patients were given either a bolus dose of normal saline followed by an infusion of normal saline, a bolus dose of alfentanil 5 micrograms/kg followed by an infusion of normal saline, or a bolus dose of esmolol 500 micrograms/kg followed by an infusion of esmolol 300 micrograms/kg/min. Emergency and extubation resulted in significant increases in heart rate (HR) and blood pressure (BP) in the placebo group. Alfentanil controlled the responses to emergence but prolonged the time to extubation (p < 0.05). Esmolol significantly controlled the responses to emergence and extubation (p < 0.05). Emergency and extubation resulted in significant increases in heart rate (HR) and blood pressure (BP) in the placebo group. Alfentanil controlled the responses to emergence but prolonged the time to extubation (p < 0.05). Esmolol significantly controlled the responses to emergence and extubation (p<0.05).

CONCLUSION: Esmolol has no effect on requirement of isoflurane, but it decreases the postoperative requirement of morphine and postoperative pain without increasing the risk of awareness as concluded from this study.

REFERENCES