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Attenuation of sympathetic response to laryngoscopy and endotracheal intubation in patients undergoing laparoscopic cholecystectomy: a comparative study between esmolol and dexmedetomidine

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ABSTRACT

Introduction: Attenuation of sympathetic response in response to laryngoscopy and intubation is vital for smooth induction of general anaesthesia in patients undergoing a surgical procedure. Various methods have been used by the anaesthetist to control this sympathetic response with varying degree of success. The drug profile of esmolol and dexmedetomidine seems to be ideally suited to attenuate this haemodynamic response and hence have been considered for this study.

Aim: to compare the effectiveness of esmolol and dexmedetomidine in attenuating the haemodynamic response to laryngoscopy and endotracheal intubation when used in bolus dosing regimen in surgical patients undergoing laparoscopic cholecystectomy under general anaesthesia.

Materials and Methods: ASA I&II patients between the age of 20 -60 years undergoing laparoscopic cholecystectomy under general anaesthesia were enrolled in the study after obtaining written consent from them. A sample size of 80 patients was drawn which was randomly divided into two groups (E &D) of 40 patients each. Group E received esmolol in a dose of 1mg/kg which was injected slowly over 30 seconds while Group D received dexmedetomidine in a dose of 0.75ug/kg given over 10 minutes. Induction of anaesthesia was done once the study drug was given. The recording was done for changes in haemodynamic parameters during laryngoscopy and intubation and any incidence of adverse events arising as a result of administration of study drug. Data of the two groups were analysed using student t-test and chi-square test with p-Value of <0.05 statistically significant.

Results: Both esmolol and dexmedetomidine are capable of attenuating the sympathetic response to laryngoscopy and intubation. However, compared to esmolol, dexmedetomidine was able to produce statistically significant attenuation of this sympathetic response. Data for haemodynamic parameters at 2minutes and 4 minutes after giving the study drug was statistically significant for Group D compared to Group E, during which time laryngoscopy and endotracheal intubation were being done. The incidences of adverse events were negligible in Group D compared to Group E.

Conclusion: There is greater attenuation of haemodynamic response to laryngoscopy and endotracheal intubation with Dexmedetomidine given in a dose of 0.75ug/kg given over 10 minutes compared to esmolol given in a dose of 1mg/kg.

Key words: attenuation–sympathetic response–laryngoscopy–smooth induction–haemodynamic response

1 INTRODUCTION

Perhaps the biggest hindrance to ensuring a smooth induction of general anaesthesia in patients undergoing a surgical procedure is the activation of sympathetic response that takes place during laryngoscopy and endotracheal intubation to secure the airway [1]. Although brief and transient, still such is the rise in heart rate and blood pressure in response to the noxious stimulus of laryngoscopy that if it is not controlled adequately, it may lead to fatal complications like myocardial ischemia or intraventricular haemorrhage in susceptible individuals.

This tricky scenario has always been a challenge for practising anesthesiologist and various methods have been used to combat the impending disaster. This includes the use of sedatives as premedication, intubating the patient in a deep plane of anaesthesia and use of drugs which lower heart rate and blood pressure like beta-blockers, calcium channel blockers, glyceryl trinitrate and lidocaine. All these methods have been able to control this sympathetic response with varying degree of success.

Being a highly selective α_2 agonist, dexmedetomidine is a central sympatholytic drug which also has a peripheral vasoconstrictive effect and as a result causes a decrease in heart rate and blood pressure in a dose-dependent effect.[2,3]

Esmolol, a cardio-selective β_1 blocker has a rapid onset and short duration of action and also inhibits the action of endogenous catecholamines on the heart thereby decreasing the heart rate and blood pressure. [4]

The profile of these two drugs in consideration seems ideally suited to attenuate the sympathetic response to laryngoscopy and endotracheal intubation.

Patient with cholelithiasis tends to have a higher body mass index compared to other patients. [5] As a result of which securing the airway of these patients without causing too much sympathetic stimulation while performing laryngoscopy and endotracheal intubation becomes a challenge to the anesthesiologist. We intended to achieve this smooth induction of general anaesthesia using a prescribed dosage of either esmolol 1mg/kg bolus [6] given slowly over 30 seconds or dexmedetomidine 0.75Ug/kg given over 10 minutes.[7]

The aim of this study was to compare the effectiveness of esmolol and dexmedetomidine in attenuating the haemodynamic response to laryngoscopy and endotracheal intubation when used in bolus dosing regimen in surgical patients undergoing laparoscopic cholecystectomy under general anaesthesia.

2 MATERIALS AND METHODS

After obtaining clearance from the institutional ethical committee, this prospective randomized clinical trial was conducted at Sikkim Manipal Institute of Medical Sciences, Gangtok. Prior to enrolling patient into the study, written informed consent was taken from the patient. Unwilling patients, patient with a history of allergy to the study drug and patients with multiple co-morbidities were excluded from the study.

All patients underwent pre-anaesthetic check-up and only ASA I & II patients of either sex between the ages of 20 – 60 years were included in the study. Based on a previous study [8] and using Medcalc software version 19.0.7 with an alpha error of 0.5% and the power of study $\geq$ 0.8, a sample size of 80 patients divided into two groups of 40 patients each was enrolled into the study.

Patients were randomly divided into two groups of 40 patients each. Randomization was done using a computer-generated random table (www.randomizer.org). Group D received dexmedetomidine in a dose of 0.75μg/kg diluted in 20 ml 0.9% normal saline and given as an infusion over 10 minutes prior to induction of anaesthesia and Group E received a bolus dose of esmolol in a dose of 1mg/kg to be given slowly over 30 seconds. Although the patient was blinded from the study, the investigating anaesthetist could not be blinded due to the method of administration of the drug.

On receiving the patient in the operation theatre, a 20G intravenous line was secured and baseline vitals recorded which included non-invasive blood pressure, heart rate and oxygen saturation (SpO2) using an automated multichannel monitor. The patient was made comfortable by verbal assurance to allay the anxiety of undergoing a surgical procedure and once the patient was settled, the study drug was started in prescribed dose. Once the study drug was given, all the patients were induced with a standardized anaesthetic regimen comprising of injection thiopentone given in a dose of 5mg/kg body weight and airway secured with an appropriate sized endotracheal tube using a McIntosh laryngoscope after giving injection fentanyl 2μg/kg and injection Succinylcholine 2mg/kg as a muscle relaxant. Successful place of the endotracheal tube was confirmed by 5 point auscultation of chest and detection of end tidal carbon dioxide graph on the multi channel monitor. Anaesthesia was maintained during intra operative period using inhalational anaesthetic agent Isoflurane along with admixture of oxygen and nitrous oxide in equal ratio to maintain a minimum alveolar concentration of 1.0 for Isoflurane and patient rendered immobile by using an intermediate acting muscle relaxant injection atracurium in the appropriate dose. Patient was extubated at the end of surgical procedure upon return of spontaneous respiration and reversal of the residual effect of muscle relaxant using injection neostigmine and patient shifted to post operative recovery room for further care.

After recording the baseline hemodynamic parameters, the further recording was done immediately after giving the study drug in prescribed dose and then every 2 minutes after induction of anaesthesia for 10 minutes post induction of anaesthesia.

Tachycardia was defined as a rise in heart rate to $\geq$30% of the baseline value while hypertension was defined as a rise in mean blood pressure to $\geq$30 % of the baseline value.

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Similarly, bradycardia was defined as a fall in heart rate to < 60 beats per minute while hypotension was defined as a fall in mean blood pressure to < 30 % of the baseline value.

Data recording was done for patients in each group to compare the age, weight, height, body mass index (BMI), changes in hemodynamic parameters between the two groups and any adverse events arising as a result of administration of study drug.

STATISTICAL ANALYSIS

Data analysis was done using IBM SSPE statistical software version 25.0. Mean ± S.D and unpaired t test was used for comparison and analysis of age, weight, height, BMI, haemodynamic parameters and incidence of adverse events between the two groups (p Value <0.05). Qualitative data analysis (sex, ASA grading) was done using Chi square test.

3 RESULTS

After clearance from the ethical committee, 94 patients were enrolled in the study. However, 14 patients had to be excluded from the study and a sample size of 80 patients was drawn and divided into two groups of 40 patients each.

The patients in the two groups were similar when compared for age, sex, weight, height, Body mass index (BMI) and ASA status. [TABLE/FIGURE 2].

The mean body mass index of the patients chosen for the study was 26.584 kg/m^2 which have been defined by World health organization nutritional status to be in pre-obesity range. [TABLE/FIGURE 3]. [9]

Although the sympathetic response to laryngoscopy and intubation was attenuated by both esmolol and dexmedetomidine in the prescribed dosage, dexmedetomidine was able to achieve better control of heart rate and blood pressure compared to esmolol. The data for haemodynamic parameters after giving study drug, at 2 minutes and 4 minutes after giving the study drug was statistically significant for dexmedetomidine compared to esmolol. This holds significance as laryngoscopy and intubation were taking place within the first 4 minutes of induction of patient and there was no surge in heart rate and blood pressure during this phase. [TABLE/FIGURE 4, 5, 6& 7].

Among the patients who received dexmedetomidine, 3 patients developed hypotension while 5 patients had bradycardia with the same drug (statistically insignificant). No patient complained of nausea and vomiting. There was no incidence of any adverse events in patients who received esmolol. [TABLE/FIGURE 8].

4 DISCUSSION

At the end of our study, we found out that both esmolol and dexmedetomidine are capable of attenuating the sympathetic response to laryngoscopy and intubation. Given as a bolus dose of 0.75ug/kg diluted in 0.9% normal saline and infused over 10 minutes [7], dexmedetomidine was able to

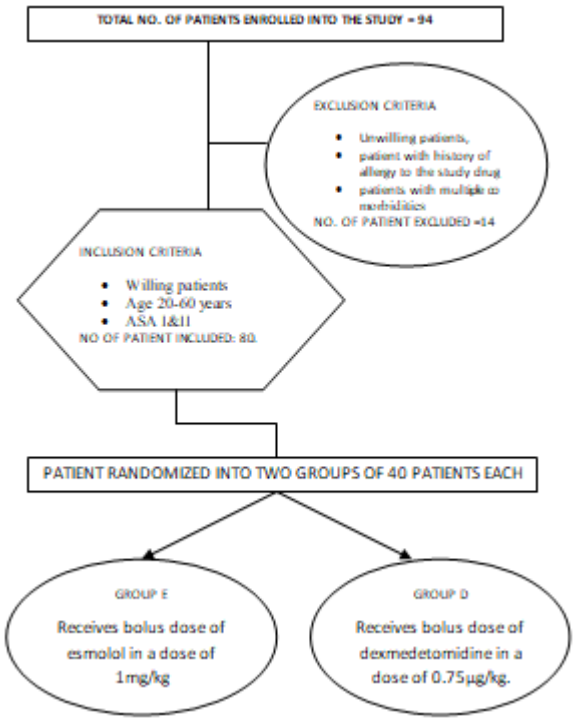

Figure 1. INCLUSION/EXCLUSION CRITERIA OF PATIENTS

Table 1. Demographic profile of the two groups

CRITERIA	GROUP E	GROUP D	P Value (<0.05)
AGE (years)	36.32± 8.65	37.16 ± 7.51	0.71559
Sex (M:F)	9:31	11:29	NA
Weight (Kgs)	69.44± 10.81	70.08 ± 9.24	0.822912
Height (meters)	1.6088± 0.62	1.6284 ± 0.70	0.301027
BMI (kgs/m2)	26.808± 3.79	26.36 ± 2.45	0.623005

Table 2. WORLD HEALTH ORGANIZATION NUTRITIONAL STATUS FOR ADULTS OVER 20 YRS OLD [9]

BODY MASS INDEX (KG/M2)	NUTRITIONAL STATUS
Below 18.5	Underweight
18.5-24.9	Normal weight
25.0- 29.9	Pre-obesity
30.0- 34.9	Obesity Class 1
35- 39.9	Obesity Class II
Above 40	Obesity Class III

Table 3. COMPARISON OF MEAN HEART RATE BETWEEN THE TWO GROUPS

Mean Heart Rate (bpm)	GROUP E	GROUP D	P Value(<0.05)
Baseline	81.08 ± 15.24	85.48 ± 13.43	0.1626
After giving study drug	77.68 ± 14.31	72.2 ± 10.62	0.1313
After 2 minutes	80 ± 15.46	71.32 ± 9.42	0.0213
After 4 minutes	86.2 ± 14.08	77 ± 7.98	0.0072
After 6 minutes	81.4 ± 15.13	85.12 ± 8.42	0.2899
After 8 minutes	80.92 ± 12.54	77.2 ± 7.60	0.2122
After 10 minutes	78.16 ± 12.70	73.36 ± 6.08	0.0973

Table 4. COMPARISON OF MEAN SYSTOLIC BLOOD PRESSURE (SBP) BETWEEN THE TWO GROUPS

Mean SBP (mmHg)	GROUP E	GROUP D	P Value(<0.05)
Baseline	127 ± 10.83	127.96 ± 8.83	0.7329
After giving study drug	115.76 ± 8.72	109.2 ± 7.36	0.0061
After 2 minutes	117.2 ± 12.32	106.6 ± 6.75	0.0005
After 4 minutes	125.08 ± 13.81	113.6 ± 6.48	0.0006
After 6 minutes	121.2 ± 12.48	119.96 ± 5.97	0.6568
After 8 minutes	106.52 ± 12.11	110.84 ± 7.34	0.1112
After 10 minutes	106.28 ± 10.97	107.6 ± 5.11	0.5890

Table 5. COMPARISON OF MEAN DIASTOLIC BLOOD PRESSURE (DBP)BETWEEN THE TWO GROUPS

Mean DBP (mmHg)	GROUP E	GROUP D	P Value(<0.05)
Baseline	78.84 ± 9.95	76.24 ± 8.21	0.3190
After giving study drug	70.52 ± 7.50	61.68 ± 9.57	0.0007
After 2 minutes	70.56 8.32	61.76 ± 9.20	0.0008
After 4 minutes	75.4 ± 9.26	67.76 ± 7.28	0.0023
After 6 minutes	76.12 ± 14.21	72.28 ± 6.90	0.2324
After 8 minutes	70.2 ± 9.63	65.92 ± 7.97	0.0938
After 10 minutes	68.2 ± 10.72	62.44 ± 6.04	0.0132

Table 6. COMPARISON OF MEAN ARTERIAL BLOOD PRESSURE (MAP)BETWEEN THE TWO GROUPS

Mean MAP (mmHg)	GROUP E	GROUP D	P Value(<0.05)
Baseline	91.56 ± 9.62	93.48 ± 8.58	0.4601
After giving study drug	84.96 ± 6.59	76.72 ± 8.28	0.0003
After 2 minutes	84.64 ± 8.77	75.04 ± 6.45	0.0001
After 4 minutes	90.96 ± 9.21	82.8 ± 5.72	0.0005
After 6 minutes	89.12 ± 12.23	87.96 ± 5.91	0.6720
After 8 minutes	80.4 ± 9.29	80.44 ± 6.94	0.9863
After 10 minutes	79.32 ± 10.00	76.6 ± 5.49	0.2409

Table 7. COMPARISON OF ADVERSEEVENTS BETWEEN THE TWO GROUPS

ADVERSE EVENTS	GROUP E	GROUP D	P Value(<0.05)
NAUSEA	0	0	-
VOMITING	0	0	-
HYPOTENSION	0	3	0.1615
HYPERTENSION	0	0	-
BRADYCARDIA	0	5	0.0830
TACHYCARDIA	0	0	

prevent the rise in blood pressure and heart rate to catastrophic level and ensure smooth induction of anaesthesia. The same response was noted with esmolol given as a bolus dose of 1mg/kg [6] given slowly over 30 seconds. However, compared to esmolol, dexmedetomidine was able to produce statistically significant attenuation of this sympathetic response.

Dexmedetomidine produces a dose-dependent reduction in heart rate and blood pressure as it is a selective α_2 agonist and has a central sympatholytic and peripheral vasoconstrictive effect.[2,3] Esmolol a cardio-selective β_1 blocker decreases the force of cardiac muscle contraction and heart rate and produces a reduction in blood pressure and heart rate. It also inhibits the action of endogenous catecholamines on the heart.[4]

Since cholelithiasis is commonly seen in obese patients,[5] laryngoscopy and endotracheal intubation in these patients can be challenging for the anaesthetist owing to the short neck and increased fat collection around the neck and face. Hence it is necessary to ensure a smooth anaesthetic induction in these patients without too much sympathetic stimulation while handling the potentially difficult airway. Both esmolol and dexmedetomidine has proved to be effective in blunting this sympathetic response. Body mass index, which is defined as patients body weight in kilogram divided by square of patients height in metres (kg/m^2), is used as an indicator to assess patients nutritional status. [9]. In our study, the mean body mass index of patients was 26.584 kg/m^2 which have been defined by World health

organization nutritional status to be in pre-obesity range.

Sandeep Sharma et al. [8] Compared the haemodynamic attenuating response of esmolol and dexmedetomidine in patients undergoing elective general surgery under general anaesthesia and found both esmolol and dexmedetomidine to be effective than the control group in controlling heart rate and blood pressure. However, dexmedetomidine was the most effective of the three groups in attenuating the sympathetic response. The findings of our study are similar to the study by Sandeep Sharma et al.

Vinit K Srivastava et al. [10] compared esmolol and dexmedetomidine for attenuation of haemodynamic re-sponse to laryngoscopy and intubation in neurosurgical pa-tients and found dexmedetomidine to be more effective than esmolol in attenuating this haemodynamic response. The findings of our study were similar to the study quoted above.

Arti Rathore et al [9] studied the haemodynamic attenuating effect o f e smolol u sing d ifferent do sing an d found bolus dose of 150mg given 2 minutes prior to induction of anaesthesia to be significantly e ffective in bl unting blood pressure response compared to a bolus dose of 50mg and 100mgs. In our study, we chose a standard dose of esmolol of 1mg/kg [6] to avoid drug overdose or under-dosing and found it to be effective i n a ttenuating t he haemodynamic response to laryngoscopy and intubation, without any adverse events.

Bon Sebastian et al. [7] compared two different doses of dexmedetomidine with regard to attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation and found a dose of 0.75ug/kg given over 10 minutes prior to induction on anaesthesia to be most effective than 0.5ug/kg. Based on this study, we choose a dose of 0.75ug/kg for dexmedetomidine for our study and found it to be very effective in controlling the rise in heart rate and blood pressure during laryngoscopy and intubation. The number of patients developing the noted side effects of dexmedetomidine namely bradycardia and hypotension was statistically insignificant while comparing it with esmolol.

LIMITATIONS

The findings of difficult airway in the patients included in the study could not be studied in detail to know the degree of difficulty in securing the airway and the haemodynamic response in those patients with difficult airway and effectiveness of the study drug in attenuating this response.

5 CONCLUSION

Based on the findings of o ur study, we concluded t hat both esmolol and dexmedetomidine are capable of attenuating the haemodynamic response to laryngoscopy and intubation. However, dexmedetomidine is more effective t han esmolol in attenuating this response and may be more useful in difficult airway scenario.

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