A COMPARATIVE STUDY OF ATTENUATION OF STRESS RESPONSE DURING INTUBATION WITH ESMOLOL AND PROPOFOL

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ABSTRACT

BACKGROUND

Endotracheal intubation for giving anaesthesia and for other purposes have become integral part of anaesthesiology. Tracheal intubation provides a patent airway for unconscious person. For endotracheal intubation, direct laryngoscopy is a tool. Direct laryngoscopy and passage of endotracheal tube are noxious stimuli that can provoke adverse responses in cardiovascular system. To prevent adverse responses different drugs are used in different methods. In the present study, we are comparing the effects of esmolol and propofol to obtund adverse responses in the cardiovascular system.

MATERIALS AND METHODS

Hospital-based prospective randomised comparative study, which includes 70 normotensive patients aged 15 to 60 years of either sex belonging to ASA I and II, Mallampati class 1 and 2 posted for various elective non-cardiac surgeries. In this study, the group 1 patients received esmolol 1 mg/kg bolus and in group 2 propofol 1 mg/kg bolus after 1 minute of induction. Haemodynamic parameters were recorded (SBP, DBP, MAP and HR) before and after intubation and compared.

RESULTS

The mean heart rate in both group 1 and 2 reduced significantly from preoperative value after 2 minutes of drug administration. The mean values of the haemodynamic parameters HR, SBP, DBP and MAP were compared in group 1 and 2 after 5 minutes of intubation. There is no statistically significance between the two groups as the p value >0.05.

CONCLUSION

Both esmolol and propofol were effective in attenuation of haemodynamic response to laryngoscopy and intubation.

KEYWORDS

Laryngoscopy, Intubation, Esmolol, Propofol.

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BACKGROUND

Tracheal intubation provides a patent airway, thus preventing obstruction as a result of either loss of consciousness, oedema or compression. Direct laryngoscopy and passage of endotracheal tube are noxious stimuli that can provoke adverse responses in the cardiovascular, respiratory, cerebrovascular and other physiological systems. Laryngoscopy and tracheal intubation have been associated with haemodynamic changes such as transient hypertension, tachycardia and arrhythmias. These haemodynamic changes are of little consequence in healthy individuals, but maybe more severe and life-threatening in patients with hypertension, coronary artery diseases and cerebrovascular diseases. Reflex changes in the cardiovascular system are most marked after laryngoscopy and intubation and lead to an average increase in blood pressure by 40-50% and 20% increase in heart rate (Savio et al, 2011).[1] An increase in arterial pressure and heart rate following laryngoscopy and intubation can have deleterious effects on the heart as shown by Stoelting (1978).[2] Significant hypertension and tachycardia are associated with tracheal intubation under light anaesthesia. The elevation in arterial pressure typically starts within 5 seconds of laryngoscopy, peak in 1 to 2 minutes and return to control levels within 5 minutes. Pharmacological approaches to attenuate the stress response to laryngoscopy and intubation include the use of opioids like fentanyl, remifentanil, morphine and buprenorphine; beta blockers like esmolol, labetalol and metoprolol; calcium channel blockers like diltiazem, verapamil and nicardipine; alpha 2 agonists like clonidine and dexmedetomidine; and vasodilators like nitroglycerin and other agents like lidocaine, propofol, etc. Propofol with certain actions like hypnosis, suppression of airway reflexes, myocardial depression and vasodilatation can be used to attenuate intubation response. It is short-acting, extensively studied and routinely used.

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Esmolol is considered appropriate to attenuate haemodynamic changes during endotracheal intubation as it is cardioselective, short-acting and it reduces heart rate as well as blood pressure.

Our present study is to compare the effectiveness of propofol and esmolol in attenuation of intubation response.

The aim of our study is to compare the efficacy of propofol and esmolol in attenuation of stress response and haemodynamic changes during laryngoscopy and tracheal intubation.

MATERIALS AND METHODS

This is hospital-based prospective randomised comparative study, which includes 70 normotensive patients aged 15-60 years of either sex belonging to ASA I and II, Mallampati class I and II posted for various elective non-cardiac surgeries in Department of Anaesthesiology, S.V.R.R. Government General Hospital, Tirupati, between 2015 to 2016.

The patients are randomly selected and made into 2 groups of 35 each. Group I received esmolol and group II propofol to compare their action mentioned in the aim of study.

Preanaesthetic check-up with detailed history and thorough examination was done a day before surgery. Basic investigations such as CBP, blood sugar, blood urea, serum creatinine, chest x-ray and complete urine examination were done. The study was undertaken after obtaining ethical committee clearance as well as written informed consent from all patients.

Adult patients of age 15-60 years of ASA grade I and II posted for elective surgeries under general anaesthesia were included in the study.

Patients with history of drug abuse, sensitivity to study drug and patients with anticipated difficult intubation were excluded in the study.

All the patients were given alprazolam 0.5 mg at bedtime on the day before surgery and were kept fasting for 12 hours.

On the day of surgery, patients were brought into the operation theatre and intravenous access was established. Blood pressure monitored by non-invasive blood pressure monitor and SpO2 by pulse oximetry. ECG leads applied and connected to the monitor.

All the medications like premedication, induction and neuromuscular blockers except the study drug are standardised.

The patients were premedicated with tramadol 2 mg/kg, glycopyrrolate 4 micrograms/kg, ondansetron 0.08 mg/kg and ranitidine 1 mg/kg intravenously.

Preoperative vitals (T0) including heart rate, systolic and diastolic blood pressure and mean arterial pressure were noted in all the patients.

Patients in both the groups received thiopentone 5 mg/kg and vecuronium 0.1 mg/kg. After 1 minute of induction, the patients in group I received esmolol 1 mg/kg bolus and propofol 1 mg/kg bolus in group II. Controlled ventilation was continued manually with 100% oxygen. Vitals were recorded 1 minute (T_1) and 2 minutes (T_2) after the study drug was administered.

Laryngoscopy was done with Macintosh curved blade laryngoscope and intubation was done with appropriate size cuffed PVC endotracheal tube. The duration of laryngoscopy did not exceed 30 seconds.

Vital data were recorded 1 minute (T_3), 3 minutes (T_4) and 5 minutes (T_5) after intubation. The patients were connected to closed circuit and controlled ventilation given with 67% nitrous oxide and 33% oxygen throughout the surgical procedure. Monitoring was continued and patients were extubated and shifted after complete recovery. Patients were observed for 2 hours postoperatively.

The variables taken under study are heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure.

Statistical analysis was done using unpaired t-test.

Time of Study	Represents
T_0	Preoperative vitals
T_1	Vitals studied 1 minute after administration of study drug
T_2	Vitals studied 2 minutes after administration of study drug
T_3	Vitals studied 1 minute after intubation
T_4	Vitals studied 3 minutes after intubation
T_5	Vitals studied 5 minutes after intubation

OBSERVATION AND RESULTS

Parameter	Group I	Group II
Age	38.14 (± 10.75)	37.28 (± 9.18)
Weight	53.8 kg (± 5.9)	52.71 kg (± 3.81)
Gender distribution	17 M and 18 F	19 M and 16 F

Table 1. Demographic Profile

In the present study, both the groups were comparable with respect to the demographic profile as shown in Table 1.

There was no statistically significant difference among the above variables between the two groups (p-value >0.05).

General surgery, ENT and neurosurgery and surgical procedures were compared in both the groups shown in the Table 2.

Type of Surgery	Group I	Group II
General surgery	13	15
ENT	18	17
Neurosurgery	4	3

Table 2. Types of Surgical Procedures

Preoperative vitals were monitored in both the groups and mean values with standard deviations were calculated, there is no statistically significant difference between two groups (p-value >0.05).

Variables	Group - I	Group - II	P value
Heart rate (beats/minute)	88.34 (± 13.32)	88.4 (± 12.53)	0.49
Systolic blood pressure (mm of Hg)	123.94 (± 9.8)	124.29 (± 9.33)	0.45
Diastolic blood pressure (mm of Hg)	84.57 (± 4)	84.11 (± 3.72)	0.3
Mean arterial pressure (mm of Hg)	98.99 (± 3.99)	97.5 (± 4.21)	0.07

Table 3. Intergroup Comparison of Mean Values of Preoperative Vitals

The mean HR preoperatively in group I was 88.34 bpm. It is reduced to 81.6 bpm after one minute of esmolol administration and to 75.6 bpm after 2nd minute. In group II, HR has reduced from a preoperative value of 88.4 bpm to 84.86 bpm after 1 minute of propofol and to 82.51 bpm after 2nd minute.

In Group - I, SBP, DBP and MAP reduced from preoperative values of 123.94 mm of Hg, 84.57 mm of Hg and 98.99 mm of Hg to 114.34 mm of Hg, 79.89 mm of Hg and 91.9 mm of Hg after 1 minute of esmolol and to 111.71 mm of Hg, 75.8 mm of Hg and 88.3 mm of Hg after 2nd minute, respectively.

In Group - II, SBP, DBP and MAP reduced from a preoperative values of 124.29 mm of Hg, 84.1 mm of Hg and 97.5 mm of Hg to 110.74 mm of Hg, 80.57 mm of Hg and 92.63 mm of Hg after 1 minute of propofol and to 112 of Hg, 77.6 mm of Hg and 89 mm of Hg after 2nd minute, respectively.

Variables	Group - I	Group - II	'P' Value
HR (beats per minute)	81.6 (± 12.93)	84.86 (± 11.79)	0.14
SBP (mm of Hg)	114.34 (± 7.78)	116.74 (± 9.19)	0.12
DBP (mm of Hg)	79.89 (± 3.69)	80.57 (± 3.61)	0.22
MAP (mm of Hg)	91.9 (± 3.88)	92.63 (± 3.93)	0.22

Table 4. Comparison of Mean Values of Vitals at One Minute of Study Drug Administration

	Group - I	Group - II	'P' Value
HR (beats/minute)	75.6 (± 12.47)	82.51 (± 11.78)	0.008
SBP (mm of Hg)	111.71 (± 7.78)	112 (± 8.53)	0.44
DBP (mm of Hg)	75.83 (±4.07)	77.6 (± 3.72)	0.203
MAP (mm of Hg)	88.3 (± 4.03)	DBP (mm of Hg)	0.227

Table 5. Comparison of Mean Values of Vitals at Two Minutes of Study Drug Administration

Regarding heart rate, the values obtained preoperatively in group 1 and group 2 at 1 minute after drug administration in group 1 and 2, there is no statistically significant difference (p-value >0.05). But, at 2 minutes of drug administration in group 1 and 2, the values are statistically significant (p-value <0.05). Regarding SBP, DBP and MAP in group 1 and 2 preoperatively and 1 minute, 2 minutes of drug administration, the values obtained are statistically not significant (p-value >0.05).

Haemodynamic parameters at 1 minute, 3 minutes and 5 minutes after intubation.

	Group - I	Group - II	'P' Value
HR (beats/minute)	83.7 (± 12.66)	91.08 (± 11.48)	0.005
SBP (mm of Hg)	126.28 (± 9.5)	126.11 (± 9.29)	0.47
DBP (mm of Hg)	86.86 (± 4)	86.28 (± 3.88)	0.27
MAP (mm of Hg)	101.02 (± 3.83)	99.56 (± 4.34)	0.07

Table 6. Comparison of Mean Values of Vitals at One Minute of Intubation

	Group - I	Group - II	'P' Value
HR (beats/minute)	81 (± 12.64)	86.06 (± 12.32)	0.04
SBP (mm of Hg)	120.11 (± 9.95)	115.94 (± 9.34)	0.076
DBP (mm of Hg)	83.54 (± 3.79)	82.23 (± 4.54)	0.091
MAP (mm of Hg)	97.16 (± 3.67)	96.14 (± 4.52)	0.145

Table 7. Intergroup Comparison of Mean Values of Vitals at Three Minutes of Intubation

	Group - I	Group - II	'P' Value
HR (beats/minute)	77.26.68 (± 12.3)	82.17 (± 12.36)	0.04
SBP (mm of Hg)	113.89 (± 9.39)	111.37 (± 8.65)	0.123
DBP (mm of Hg)	79.6 (± 3.69)	78.34 (± 4.27)	0.093
MAP (mm of Hg)	91.71 (± 3.55)	90.69 (± 4.29)	0.123

Table 8. Intergroup Comparison of Mean Values of Vitals at Five Minutes of Intubation

The heart rate in group 1 and 2 at 1 minute, 3 minutes and 5 minutes after intubation, the values obtained are comparable and statistically significant (p-value <0.05). Regarding SBP, DBP and MAP, the values obtained in group 1 and 2 at 1 minute, 3 minutes and 5 minutes after intubation are not statistically significant (p-value <0.05).

DISCUSSION

The haemodynamic responses during laryngoscopy and intubation play vital role in intraoperative and postoperative period, especially in hypertensive, coronary heart diseases and other vascular disease patients.

The usual circulatory response to laryngeal and tracheal stimulation is tachycardia, hypertension and arrhythmias (Prys Roberts 1971, Stoelting R.K. 1977).[2] Hypertension seen in these patients is mostly due to increased cardiac output rather than due to increased systemic vascular resistance (Prys Roberts 1971).

Several studies have shown that there is increased incidence of myocardial infarction when intraoperative heart rate increases above 110 beats/minute (Stone et al, 1988; Slogoff and Keats, 1989).

Forbes et al in their study on normotensive subjects concluded that mean arterial pressure increases by 20-25 mm of Hg in response to laryngoscopy and intubation. They also suggested that this hypertensive response maybe dangerous especially in patients with ischaemic heart disease or hypertension.[3]

The haemodynamic changes occurring during laryngoscopy and endotracheal intubation are well evident (Bostana and Eroglu, 2012).[4] The changes observed are transient hypertension (Manjunath et al, 2008),[5] tachycardia (Moon et al, 2012),[6] arrhythmias (Bae et al, 2007),[7] myocardial ischaemia or infarction (Landesberg et al, 2009).[8]

Reflex changes in the cardiovascular system are most marked after laryngoscopy and intubation and lead to an average increase in blood pressure by 40-50% and 20% increase in heart rate. Perioperative myocardial infarction is a leading cause of postoperative morbidity and mortality in normotensive patients due to hypertension and tachycardia (Savio et al, 2011)[1] following laryngoscopy and intubation.

The predominant response to laryngoscopy and intubation under anaesthesia are hypertension, tachycardia and depression of left ventricular ejection fraction

(Takeshima et al, 1964).[9] These changes are at their approximately 30-45 seconds after laryngoscopy.

The magnitude of the response is greater with increasing force and duration of laryngoscopy. The elevation in arterial pressure typically starts within 5 seconds laryngoscopy peak in 1 to 2 minutes and return to control levels within 5 minutes. Haemodynamic changes start within seconds of direct laryngoscopy and there is a further increase in heart rate and blood pressure with passage of endotracheal tube.

To attenuate the pressor response to laryngoscopy and tracheal intubation, laryngoscopy should be done within 30 seconds. When laryngoscopy is prolonged, laryngotracheal rather than intravenous lignocaine is necessary to attenuate circulatory response to intubation.

These haemodynamic changes are associated with increased catecholamines due to reflex sympathetic discharge resulting from epipharyngeal and laryngopharyngeal stimulation.

The mechanical stimulation of upper respiratory tract induced reflex cardiovascular response is associated with enhanced neuronal activity in cervical sympathetic fibres (Tomori Z et al 1969).[10]

In normotensive patients, there is a moderate increase in noradrenaline level, whereas in hypertensive patients, there is a three-fold increase of noradrenaline and also a rise in adrenaline levels (Low J M et al 1986).[11]

Pharmacological approaches involving the use of lidocaine (Manjunath et al, 2008),[5] remifentanil (Kaygusuz et al, 2007),[12] nitroglycerin (Fassoulaki and Kaniaris, 1983),[13] esmolol (Figueredo and Garcia, 2004),[14] fentanyl (Bostana and Eroglu, 2012)[4] and a combination of esmolol and nicardipine (Moon et al, 2012)[6] have been utilised to attenuate the pressure responses to laryngoscopy and tracheal intubation.

In our present study, we have compared the effectiveness of esmolol with propofol in attenuation of haemodynamic response to intubation. Esmolol has on action on efferent blockade and propofol has all the above three mentioned mechanism of action.

Esmolol is a cardioselective beta blocker with rapid onset and very short duration of action (t½ - 9 minutes).

Suman Sharma et al[15] studied that esmolol is effective as well as safe in blunting the haemodynamic responses to laryngoscopy and tracheal intubation in treated hypertensive patients.

Donald Oxorn et al[16] studied on esmolol and concluded that bolus dose of esmolol is useful for the prevention of perioperative hypertension and tachycardia.

Helfman et al[17] studied that lidocaine or fentanyl was effective in blunting the increase in systolic blood pressure associated with laryngoscopy and tracheal intubation, but heart rate is not influenced, but esmolol decreases both heart rate and systolic blood pressure.

Menkhaus PG, Reves et al studied that esmolol blunts the haemodynamic response to intubation of trachea.[18]

Propofol is an alkyl phenol compound. Propofol has short duration of action and rapidly metabolised in the liver. It is a hypnotic agent.

Rouby et al[19] studied that propofol produces decrease in systemic blood pressure that are greater than those evoked by comparable doses of thiopental.

Robinson et al[20] studied that the relaxation of vascular smooth muscle produced by propofol is primarily due to inhibition of sympathetic vasoconstrictor nerve activity.

A. J. Ogles did studies on propofol and concluded that it is a potent suppressor of pharyngeal, laryngeal and tracheal reflexes. It reduces systemic vascular resistance and arterial pressure.

Harris C E et al studied on thiopentone, etomidate and propofol and concluded propofol alone is effective in obtunding haemodynamic response to laryngoscopy and intubation.

Usha et al in a study on pressor response and hypertension confirmed that the use of IV propofol prior to laryngoscopy to be effective. The duration of laryngoscopy is also very important. We limited the duration of laryngoscopy to less than 15 seconds as this was thought to be a powerful stimuli for haemodynamic response.

Though attenuation of blood pressure due to intubation was effective with both esmolol and propofol, it was better with propofol than esmolol.

In both the groups, we have not encountered any complications like bradycardia, hypotension, bronchospasm and delayed recovery, etc.

CONCLUSION

In our study of comparing esmolol and propofol in attenuation of intubation response, we conclude that both esmolol and propofol were effective in attenuation of haemodynamic response to laryngoscopy and intubation. Esmolol caused more fall in heart rate than the preoperative value and was also very effective than propofol in minimising the rise in heart rate after intubation, which it was statistically significant. Both esmolol and propofol were effective in obtunding the rise in blood pressure (SBP, DBP and MAP), but the results are statistically not significant in both the groups.

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