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Original Research Article

A Comparative Study between Intravenous Dexmedetomidine and Intravenous Esmolol in Attenuating Haemodynamic Stress Response to Laryngoscopy and Intubation

Siva Shanmugam[1], Aishwarya S[2*], Rallen Jacob[3]

[1,2,3]Department of Anesthesiology, Trichy SRM Medical College Hospital and Research Centre

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Corresponding Author: Dr. Aishwarya S
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Abstract:

Background: Laryngoscopy and endotracheal intubation cause an intense reflex which produces a significant increase in heart rate, blood pressure, due to an increased sympathoadrenalic pressor response. Various agents are being tried to combat the intubation response. The objective of the study is to compare the efficacy of dexmedetomidine which is a highly selective alpha-2 agonist with an ultrashort-acting beta blocker esmolol in attenuating the haemodynamic stress response secondary to laryngoscopy and endotracheal intubation.

Methods: After obtaining an approval from Institutional Ethics Committee and after having informed and written consent from each patient, 60 adult patients scheduled for elective surgery under general anaesthesia were selected and provided general anaesthesia with endotracheal intubation for all patients. Patients were randomly allocated into two groups, Group Dexmedetomidine and Group Esmolol with 30 cases in each group. Group Dexmedetomidine received infusion of Dexmedetomidine 1 µg/kg diluted in 20 mL 0.9% normal saline (NS) over 10 minutes, and Group Esmolol received infusion of Esmolol 0.5 mg/kg diluted in 20 mL NS over 10 minutes. Patient's heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) was recorded at baseline, after infusion of study drug, after induction of anaesthesia, immediately and 1, 3 and 5 minutes after intubation.

Results: All the study parameters were collected and documented by a single anaesthesiologist in all cases. The percentage change of all haemodynamic parameters from baseline was similar in both the dexmedetomidine group and the esmolol group at all-time points of measurement. Hence, no statistically significant difference was observed at any time points after tracheal intubation**.**

Conclusion: Both dexmedetomidine 1 µg/kg and Esmolol 0.5 mg/kg were equally effective in controlling the heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressures following laryngoscopy and intubation.

Keywords: Dexmedetomidine, Esmolol, Haemodynamics, Endotracheal Intubation, Laryngoscopy.

Introduction

Direct laryngoscopy and endotracheal intubation frequently induce a cardiovascular stress response characterized by hypertension and tachycardia due to reflex sympathetic stimulation. The response is transient, occurring 30 seconds after intubation and lasting for less than 10 minutes.[1] The arterial hypertension is due to increase in cardiac output rather than an increase in systemic vascular resistance, and is associated with the transient rise in central venous pressure.

Arrhythmias also tend to occur.[2] It may be well tolerated in healthy people, but may be hazardous in patients with hypertension, coronary artery disease, cerebrovascular disease, myocardial infarction and thyrotoxicosis.[3] Numerous agents like opioids, calcium channel blockers, beta blockers, α 2 agonists, magnesium sulphate, local anesthetics etc. have been used to blunt it.[4,5] Esmolol is an ultra-short acting, β1 -cardioselective adrenergic receptor blocker with a distribution half-life of 2 min and an elimination half-life of 9 minutes. Esmolol appears quite suitable for use during a short-lived stress such as tracheal intubation.[4]

Dexmedetomidine, the pharmacologically active d-isomer of medetomidine, is a selective α2-adrenoceptor agonist has been used currently for obtunding sympathoadrenal stimulation by tracheal intubation has sympatholytic properties with minimal respiratory depression. Its short half-life makes it an ideal drug for intravenous (IV) titration for blunting haemodynamic response.[6] Thus, this

study is aimed to compare the efficacy between intravenous dexmedetomidine and intravenous esmolol in attenuating haemodynamic stress response to laryngoscopy and intubation for surgical procedures under general anaesthesia.

Materials and Methods

A randomized controlled, double-blinded study with preinduction dose of Dexmedetomidine and Esmolol was conducted among 60 patients after the approval of the Institutional Ethics Committee. The calculated sample size was 27 patients in each group. It was found that from previous study comparing these drugs, a sample of at least 27 in each group is needed to detect a MAP effect size of 10.4 mmHg and standard deviation (SD) of 12.7 with a power of 90% and an alpha error of 0.05.[7]

Hence, we have included 30 patients in each group with an expected drop rate of 10%. Totally, 60 adults belonging to the age group of 18 - 60 years of both sexes scheduled for elective procedures requiring general anaesthesia were divided into two groups, Dexmedetomidine group and Esmolol group of thirty each. Double blinded randomization followed with 1:1 ratio based on computer generated random numbered list and allocation be concealed by serially numbered sealed envelopes.

Patients in the age group 18 to 60 years of both sexes with ASA grade I scheduled for elective surgical procedures requiring general anesthesia were included in the study. Whereas patients with ASA grade II and above, anticipated difficult airway, BMI >30, Laryngoscopy time >20 seconds, emergency surgeries, and patients who required more than one attempt of intubation were excluded from the study. The overall study protocol was designed in the form of Flow chart (Figure 1).

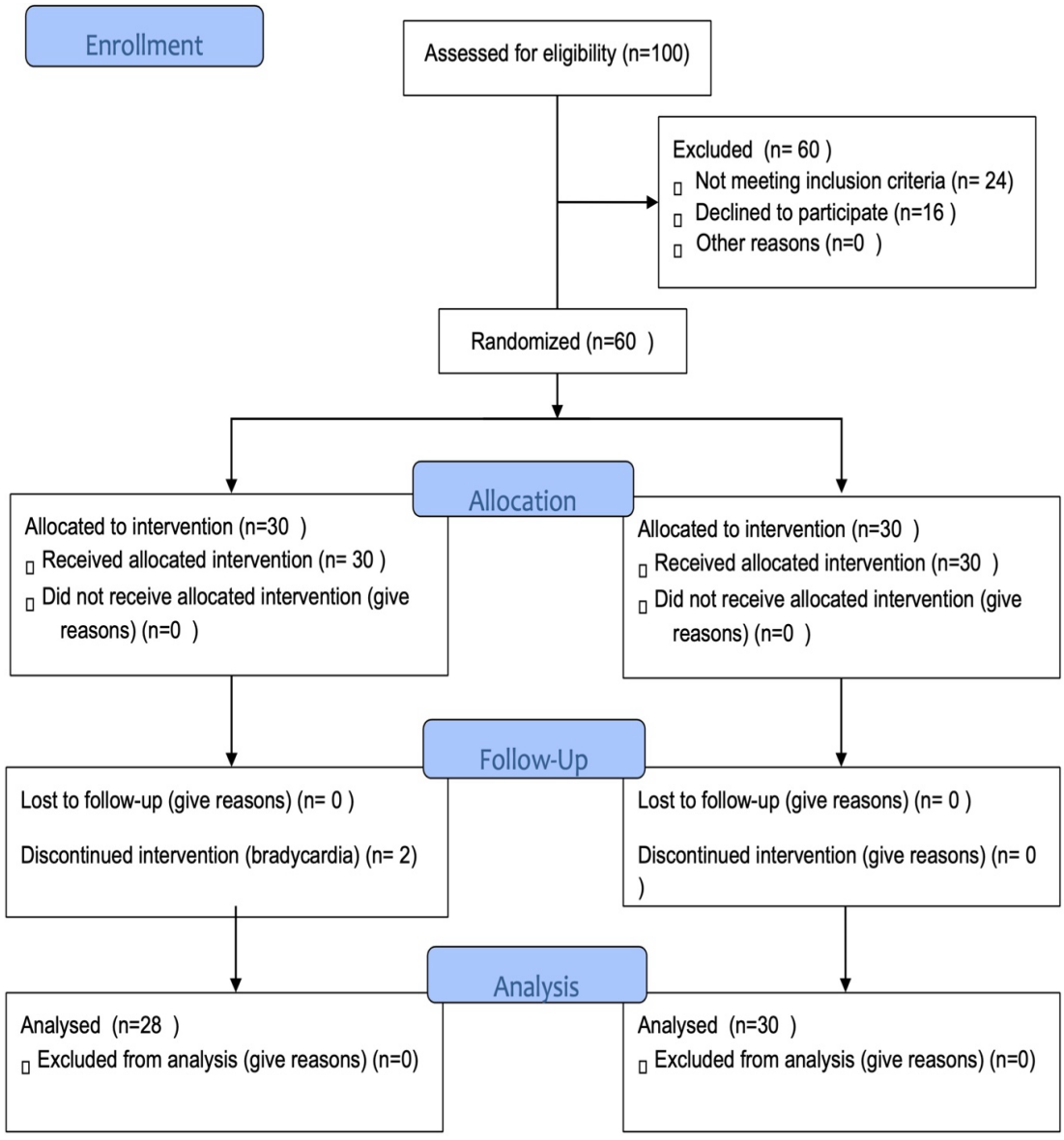

Figure 1: Overall study methods

Data Collection Tool

Patients were kept nil per-oral (NPO) for 8h prior to surgery. Patients were given Tablet Alprazolam 0.25mg and Tablet Ranitidine 150mg at bed on the previous night and one hour before shifting to operation theatre.

Procedure

On the day of surgery, after confirmation of NPO status patients were shifted to operation theatre and connected to multi-para monitor. Baseline parameters including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP), SpO2 were recorded. A peripheral intravenous line was secured using appropriately sized intravenous cannula in holding area.

Dexmedetomidine group - Received dexmedetomidine 1 μg/kg made into 50 ml with normal saline infused intravenously over 10 minutes before induction in a 50 ml syringe and a bolus of 20 ml of normal saline loaded in a 20 ml syringe given slowly (over 30 seconds) IV 2 min before intubation.

Esmolol group - Received 50 ml of normal saline infused intravenously over 10 min before induction in a 50 ml syringe and a bolus of esmolol 0.5 mg/kg diluted into total volume of 20 ml with normal saline in a 20 ml syringe given slowly (over 30 seconds) IV 2 minutes before intubation.

Syringe infusion pump was used for infusion of drugs. The infusion and the bolus syringes were loaded by anesthesiologist who was not aware of the study protocol and not involved in the recording of study parameters or performance of laryngoscopy. The study parameters were recorded before infusion of 50 ml study drug (taken as baseline), before intubation, at 1, 3, 5 minutes and 10 minutes (marked as time interval BL, T0, T1, T3, and T5 respectively) after endotracheal intubation. Conventional method of induction with Inj. Glycopyrrolate 4μg/kg i.v, Inj. Midazolam 0.05mg/kg i.v, Inj. Fentanyl 2 μg/kg, Inj. Propofol 2mg/kg and muscle relaxant Inj. Succinyl choline 2mg/kg were administered.

SBP, DBP, MAP, HR and SpO_2 were recorded before intubation. Patients were intubated with the appropriate size endotracheal tube & after confirmation of bilateral equal air entry; cuff was inflated and connected to mechanical ventilation. Anaesthesia was maintained with isoflurane in oxygen (33%) and nitrous oxide (66%) in controlled fashion with muscle relaxant Inj. Vecuronium 0.08mg/kg. Parameters i.e. SBP, DBP, MAP, HR & SpO2 were recorded at 1 min, 3min, and 5 min following laryngoscopy & intubation. At the end of surgery, when patient showed respiratory attempts, residual neuromuscular blockade was reversed with Inj. Neostigmine 0.05mg/kg & Inj. Glycopyrrolate 10μg/kg. Following adequate recovery, extubation was done after thorough oropharyngeal suction.

Statistical Analysis

The data was entered and analyzed using statistical software Epiinfo 3.

1. The study data was analyzed statistically by using chi-square test, student 't' test
2. Quantitative results are expressed as mean ±SD
3. p value <0.05 was considered as significant

Results

A total of 60 participants were included in the study, 30 participants received dexmedetomidine and 30 received esmolol. There were about, 41 (68.3%) male and 19 (31.7%) females. The average age of the participants was found to be 38 years. ASA 1 status was found in 46 (76.7%) participants. All the baseline characteristics of study participants such as age, weight, gender and ASA status were found to be comparable in both the groups Table 1 and 2).

Table 1: Analysis of age and weight of the study subjects

Groups	Number	Age groups		Weight	
		Mean±SD	p value	Mean±SD	p value
Dexmedetomidine	30	38.77±13.1	0.644	68.30±10.4	
Esmolol	30	37.20±13.1		64.60±7.7	0.124

Table 2: Gender and ASA Grade of the study groups

Descriptions		Groups		Chi-square value	p value
		Dexmedetomidine	Esmolol		
Gender	Female	10 (52.6%)	9 (47.4%)	0.077	0.7814
	Male	20 (48.8%)	21 (51.2%)		
ASA Grade	1	24 (52.2%)	22 (47.8%)	0.3727	0.542
	2	6 (42.9%)	8 (57.1%)		

The mean heart rate (HR) was different between the 2 groups before the start of the procedure and also at the different time points when the data were collected. However they were not found to be significantly different from each other.

Table 3: Comparison of mean Heart Rate at different time points between the groups

Heart Rate (bpm)	Mean±SD values		p value
	Dexmedetomidine (n=28)	Esmolol (n=30)	
Pre procedure	82.07±12.5	78.5±11.9	0.273
Pre induction	86.21±16.9	81.03±13.9	0.212
HR at 0 min	85.36±10.5	85.33±17.9	0.995
At 1 minute	88.93±14.2	89.17±15.7	0.952
At 3 minutes	83.75±13.6	84.67±15.5	0.812
At 5 minutes	80.86±12.3	80.40±15.1	0.900

The mean SBP, DBP and MAP were different between the 2 groups before the start of the procedure and also at the different time points when the data were collected. However they were not found to be significantly different from each other.

Table 4: Evaluation of mean arterial pressures (MAP) [(systolic pressure (SBP) + double the diastolic pressure (DBP) divided by three)] at different time points between the groups

Heart Rate (bpm)	Mean Arterial pressure	Mean±SD values		p value
		Dexmedetomidine (n=28)	Esmolol (n=30)	
Pre procedure	SBP	125.96±13.2	124.17±13.2	0.608
	DAP	81.21±8.3	78.50±9.5	0.250
	MAP	96.09±8.1	93.69±9.7	0.308
Pre induction	SBP	131.43±21.7	126.20±20.8	0.354
	DAP	80.82±11.2	78.50±12.3	0.455
	MAP	97.77±14.9	94.89±14.9	0.465
At 0 min	SBP	120.64±26.6	120.70±23.2	0.993
	DAP	76.54±23.6	76.73±16.2	0.971
	MAP	93.82±20.3	90.94±16.5	0.559
At 1 minute	SBP	129.21±25.8	130.97±23.8	0.789
	DAP	82.21±15.2	83.80±14.4	0.685
	MAP	98.16±17.6	100.49±17.5	0.616
At 3 minutes	SBP	117.86±17.7	120.87±17.7	0.521
	DAP	76.46±13.1	75.37±11.8	0.739
	MAP	90.35±14.1	90.11±11.8	0.943
At 5 minutes	SBP	109.32±18.1	111.63±11.9	0.571
	DAP	70.07±11.4	69.40±10.0	0.814
	MAP	82.69±11.9	82.68±9.6	0.997

The mean age among the study participants was found to be 38.77±13.082 years in Dexmedetomidine group and 37.2 ±13.069 years in Esmolol group with no statistical difference (p value >0.05) between the two groups. The gender distribution among the patients, ASA status and body weight were also comparable in both groups with no statistical significance between them.

Therefore our study groups were equally matched demographically.

Discussion

The mean heart rate between the two groups at pre procedure, pre induction, immediately after intubation and then at 1 minute, 3 minute and 5 minutes were compared and analyzed. Our study did not show any statistically significant difference between the two groups at any time points (p value of 0.393). However, in a study where the usage of Dexmedetomidine 1 μg/kg and Esmolol 0.5 mg/kg found that Dexmedetomidine was better in controlling the heart rate response to laryngoscopy and intubation.[4,8]

In our study, we observed that both dexmedetomidine and esmolol equally attenuated the rise in HR after intubation. However, when the mean heart rate within each group was analyzed using repeated measures analysis of variance (ANOVA). By using post hoc tests with Bon ferroni correction, it was found that the mean heart rate at 1 minute after intubation was higher compared to the heart rate at 5 minutes which was statistically significant(p value <0.001) in both groups. Similarly, the mean systolic blood pressure between the two groups at pre procedure, pre induction, immediately after intubation and then at

1 minute, 3 minute and 5 minutes were compared and analyzed.

Our results when analyzed using Student's unpaired t test, did not show any statistically significant difference between the two groups at any of the time points (p value of 0.750). Comparative another study revealed both Dexmedetomidine 1 μg/kg and Esmolol 2 mg/kg attenuated the pressor response to laryngoscopy and intubation, Of which, Dexmedetomidine provided a more consistent and reliable attenuation of pressor responses compared to Esmolol.[9] Similarly another study found that dexmedetomidine 1 μg/kg was more effective than esmolol 1.5 mg/kg in suppressing the laryngoscopic pressor response.[10]

In our study, even though we used only 0.5 mg/kg of Esmolol, we did not find any statistical difference in SBP between the two groups. The mean systolic blood pressure within each group was analyzed using repeated measures analysis of variance (ANOVA). By using post hoc tests with Bon ferroni correction it was found that there was a statistically significant reduction in SBP at 5 minutes as compared to all other time points (p value <0.001) in both groups.

The mean diastolic blood pressure between the two groups at pre procedure, pre induction, immediately after intubation and then at 1 minute, 3 minute and 5 minutes were compared and analyzed. Our results when analyzed using Student's unpaired t test, did not show any statistically significant difference between the two groups at any time points (p value of 0.801)

Previous literature also suggested the usage of dexmedetomidine (1 μg/kg) and esmolol (0.5mg/kg) for the suppression of laryngoscopic response.[8] Dexmedetomidine group showed statistically significant reduction in all the study parameters at all study time intervals following intubation whereas esmolol group showed significant attenuation of HR, SBP, and MAP following intubation. But, however, they found that Esmolol failed to produce significant reduction in DBP when compared to other hemodynamic variables.

In our study when the mean diastolic blood pressure within each group was analyzed using repeated measures analysis of variance (ANOVA), By using post hoc tests with Bon ferroni correction, it was found that there was a statistically significant reduction in DBP at 5 minutes as compared to all other time points (p value <0.001) except at 0 minutes in both groups. The mean arterial blood pressure between the two groups at pre procedure, pre induction, immediately after intubation and then at 1 minute, 3 minute and 5 minutes were compared and analyzed. Our results when analyzed using Student's unpaired t test, did not show any statistically significant difference between the two groups at any of the time points (p value of 0.729).

The comparative effects of dexmedetomidine (1 μg/kg) and esmolol (1 mg/kg) and they could conclude that Esmolol was more effective than dexmedetomidine in attenuating the hemodynamic response to laryngoscopy and intubation. In our study, we used Esmolol 0.5 mg/kg only compared to the study by Alagol who used 1 mg/kg of Esmolol.[6,11] This may be the reason why Esmolol did not prove to be superior to Dexmedetomidine in our study.

However, when the mean arterial pressure within each group was analyzed using repeated measures analysis of variance (ANOVA), by post hoc tests (using Bon ferroni correction) it was found that there was a statistically significant reduction in MAP at 5 minutes following both the drugs as compared to all other time points. There was also a statistically significant reduction in MAP at 3 minutes as compared to MAP at 1 minute (p value <0.001). No desaturation was noted at any time points between the two groups and all patients maintained 100% saturation throughout the study period.

Higher doses of dexmedetomidine have been associated with the risk of bradycardia and hypotension and 1 μg/kg dexmedetomidine was considered as a safer dose. However, we encountered bradycardia in 2 patients for whom dexmedetomidine 1 μg/kg was given which was treated with inj. atropine 0.6 mg. Baseline characteristics such as age, gender, ASA status, weight were found to be comparable in both the groups.

Conclusion

Dexmedetomidine at 1 μg/kg is equally effective to Esmolol given at 0.5 mg/kg in attenuation of haemodynamic stress response to laryngoscopy and endotracheal intubation in patients under general anaesthesia.

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