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The effect of Dexmedetomidine versus Esmolol on attenuation of stress response to endotracheal intubation in patients undergoing elective off pump Coronary artery bypass grafting

Nikhil Mudgalkar[1], K.Ravinder Reddy[2], Lanka Siva rama prasad[3]

[1]Associate Professor, Department of Anaesthesiology, [2] Professor, Department of General Medicine and Consultant Cardiologist , [3]Associate Professor, Department of General Surgery and Consultant Cardiac Surgeon, Prathima Institute of Medical Sciences, Karimnagar, Telangana, India.

Address for Correspondence: Dr. Nikhil Mudgalkar, Associate Professor, Department of Anaesthesiology Prathima Institute of Medical Sciences, Karimnagar, Telangana, India.

Email: drniks200@yahoo.com

ABSTRACT

Introduction: Laryngoscopy and intubation are associated with massive hemodynamic changes which can be detrimental to patients with cardiac disease. Very few studies tried to compare Dexmedetomidine and Esmolol for prevention of this response in off pump coronary artery disease. The designs of the study are biased towards one agent as these two drugs have to be given by different forms. We tried to compare these two agents with different design so as to take advantage of most appropriate dosage form.

Materials & Methods: The present study is a prospective, double blind, parallel group, randomized study done on eighty patients divided in two groups. After randomization, patients received Dexmedetomidine 0.5 microgram/kg vs. Esmolol 2 mg/kg. Anaesthesia was induced in routine manner after invasive monitoring. Blood pressure, heart rate were assessed prior to induction and at the time of induction,1 min,3 min,5 min and 10 minute post induction and intubation.

Results: Demographic characters were comparable in both the groups with non significant p values. Both the drugs controlled heart rate, systolic blood pressure and diastolic blood pressure well in first 3 minutes indicating effectiveness. Dexmedetomidine scored over Esmolol after 3rd minute and prevented the heart rate and blood pressure from rising in a sustained manner even at 10th minute.

Conclusion: Dexmedetomidine and Esmolol are appropriate for attenuation of hemodynamic control in off pump coronary artery bypass patients for up to 3rd minute. Dexmedetomidine provides more sustained hemodynamic stability up to 10th minute and suitable for long term control.

Keywords: Dexmedetomidine, Esmolol, intubation, coronary artery bypass grafting.

INTRODUCTION

During general anaesthesia, airway control is generally achieved by laryngoscopy and intubation. Direct laryngoscopy and endotracheal intubation following induction of anaesthesia is associated with haemodynamic changes due to reflex sympathetic discharge caused by epipharyngeal and laryngopharangeal stimulation. Mechanical stimuli causes reflex response in cardiovascular and respiratory systems[1]. The sympathoadrenal response is in the form of hypertension, tachycardia and arrhythmias. This response reaches its maximum limit in one minute and ends in 5-10 minutes. This sympathoadrenal response is probably less significant in healthy adults but it may take significant toll on the life of patient who has already compromised myocardium[2]. tachycardia generates more powerful stimulant for myocardium as it increases oxygen consumption of the myocardium, decreases diastolic filling and finally reduces coronary blood supply. This sympathoadrenal response is deleterious in patients with coronary artery disease, myocardial insufficiency, and cerebrovascular disease[3, 4]. There is need to control this response to have better patient outcome.

The magnitude of the reflex response to laryngoscopy and intubation is related with type of anaesthesia, deepness of anaesthesia, age of the patient, and presence of heart disease[5].The common drug categories used to control this response are narcotic analgesics, local anaesthetics, beta blockers, calcium channel blockers and vasodilators. Dexmeditomidine is highly selective alpha 2 adrenergic agonist, most often used for short term sedation in patients in intensive care[6,7]. The main advantage of this drug is opiod sparing effect.

From anaesthesiologist point of view, neuronal hyperpolarisation is a key element in mechanism of action of alpha 2 adrenergic agonist. In general, presynaptic activation of alpha 2 adrenargic receptor inhibit the release of

norepinephrine, terminating the pain signals and inhibit sympathetic activity and thus can reduce the systemic blood pressure and heart rate[8].

The present study compares the effect of single bolus dose of dexmedetomidine 0.5microgram/kg verses 2 mg/kg esmolol on hemodynamic parameters of patients undergoing off pump coronary artery bypass grafting.

MATERIALS & METHODS: This was prospective, double blind, parallel group, randomized clinical trial of Dexmeditomidine verses Esmolol for attenuation of hemodynamic response to laryngoscopy and intubation in 80 cases who underwent elective off pump coronary artery bypass graft. The study protocol was approved by ethical committee of the institute. Written valid and informed consent was obtained from all the patients prior to procedure. Inclusion criteria included all patients posted for elective off pump coronary artery bypass surgery. Exclusion criterion included were anticipated difficult intubation, emergency surgery, left ventricular ejection fraction less than 40%, left ventricular aneurysm, combined valvular surgery, left main coronary artery disease or left main equivalent disease, severe systemic disease including hepatic and renal, preoperative bundle branch block, history of smoking or bronchial asthma.

Patients were identified by primary investigator one day prior to surgery in preanaesthesia clinic. Aspirin,clopidogrel were stopped five days prior to surgery while calcium channel blockers, angiotensine convergting enzyme inhibitor or angiotensin receptor blockers were stopped one day prior to surgery as per institutional protocol. Beta blockers and nitogycerines were continued. All patients received pantoprazole 40 mg and alprazolam 0.25 mg prior night of surgery.

Patients were randomized by computer generated random number table. All patients received injection midazolam 0.04mcg/kg and fentanyl 2 mcg/kg. Patients were put with 20 gauge left radial canula and 7 French 16cm right internal jugular venous catheter under all aseptic precautions and local anaesthetic effect. Invasive monitoring was started with the monitor. Patients received cefoperazone tazobactem 1.250 grams at this stage. Patient monitoring included electrocardiogram, pulse oximetry, intraarterial blood pressure, central venous pressure, nasopharyngeal temperature, end tidal carbon dioxide concentration, and capnography.

Before induction of anaesthesia, a single dose of Dexmedetomidine 0.5microgram/kg was administered by syringe pump over 10 minutes. Induction of general anaesthesia was done with intravenous midazolam 0.1mg/kg,fentanyl 4 mcg//kg,and propofol 2 mg/kg. Lack of response to verbal command is considered as the end point of induction.Veuronium bromide 0.1mg/kg was administered intravenously to facilitate intubation. Second group received esmolol 2mg/kg 1 minute prior to intubation. At this time anaesthesiologist was changed to facilitate blinding and primary anaesthesiologist intubated the patient. Haemodynamic variables were recorded immediately before intubation, 1st, 3rd, and 5th minute after intubation. Time of hemodynamic measurement was as follows- Baseline HV1-, 1 Minute prior to intubation, HV0-At the time of intubation, HV1-1 min after intubation,HV3 – 3minutes after intubation,HV5-5 minutes after intubation (HV – Haemodynamic Variable).

Statistical analysis:

Data expressed at mean +/- standard deviation. Student t test was applied to compare study group a and b. Paired t test was used to compare variable before and after the intervention.P value less than 0.05 was considered significant. SPSS 19 was used for statistical analysis.

RESULTS

Demographic characteristics of the patients are presented in Table 1.There was no significant difference in demographic characters which included age, sex, number of coronary vessels involved and ejection fraction of the patients. Patient risk factors are presented in Table 2, which also do not show any change in two groups as assessed by non significant p values.

When we compare heart rate changes as shown in Table 3, baseline heart rate was similar in both the cases along with heart rate at the time of induction as well as first minute after the intubation assessed by non significant p values. While heart rate at 3rd minute, 5th minute, and 10th minute there is statistically significant difference between the values of the two groups.

A statistically significant difference was noted in systolic blood pressure in the two groups at 5th and 10th minute post induction favouring Dexmedetomidine.

There was no significant difference in the diastolic blood pressure in the two groups at pre induction, 1st minute and 3rd minute post intubation. However a statistically significant difference was noted in 5th and 10th minute post induction again favouring Dexmedetomidine.

Table 1: Patients characteristics

Variable	Dexmedito-midine	Esmolol	P Value
Age in years	56+/_10	57+/_12	0.4
Male sex	28	27	0.332
Ejection fraction	52+/_12	51+/_10	0.102
Number of diseased vessels	2.4	2.2	0.874

Table 2: Risk factor of the patients

Variable	Group Dexemeditomidine	Group Esmolol
NYHA grade 2 angina	25	27
Hypertension	36	37
Diabetes	22	21
Old myocardial infarction	21	23
Old cerebrovascular accident	5	6

Table 3: Effect of Dexmedetomidine and Esmolol on heart rate and blood pressure

Variable	Time of measurement	Group Dexemeditomidine	Group Esmolol	P value
Heart rate	HV1-	72.22+/_12	75.1+/_10.11	0.28
	HV0	70.13+/-10.9	74.1+/_8.4	0.32
	HV1+	74.33+/_12.1	73.2+/_9.8	0.22
	HV3+	78.14+/_8.2	84.1+/_7.6	0.03
	HV5+	80.1+/_8.6	92.1+/_10.1	0.028
	HV10+	77.1+/_8.6	94+/_10.22	0.042
Systolic blood pressure	HV1-	142+/_13.7	141.32+/_10.1	0.44
	HV0	143.22+/_11.1	143.11+/_10.18	0.324
	HV1+	140.12+/_8.6	144.12+/_9.2	0.454
	HV3+	145.1+/_8.1	149.11+/_9.1	0.212
	HV5+	143.27+/_8.6	125.11+/_8.81	0.0134
	HV10+	145.0+/_10.11	155.1+/_8.88	0.0322
Diastolic blood pressure	HV1-	85.11+/_8.2	84.12+/_10.1	0.233
	HV0	88.1+/_10.8	85.11+/_8.44	0.432
	HV1+	84.12+/_8.2	86.11+/_8.5	0.313
	HV3+	86.2+/_12.1	92.11+/_8.62	0.03
	HV5+	87.1+/_8.22	98.11+/_8.88	0.02
	HV10+	82+/_10.11	100.1+/_1.11	0.001

DISCUSSION

Laryngoscopy and endotracheal intubation is the most excited period both for the anaesthesiologist and the patient as far as cardiac indices are concerned. It is absolutely necessary to control blood pressure and heart rate during intubation. The importance again increases if the case is cardiac case with multiple blockages. Many drugs were studied and found effective, though studies prove that opiods, beta blockers and vasodilators score over other agents. There are very few studies to prove effectiveness of these drugs in cardiac patients who are posted for off pump coronary artery bypass, in which absolute control on hemodynamic is essential.

Esmolol is an ultra-short acting, ß1-cardioselective adrenergic receptor blocker with a distribution half-life of 2 min and an elimination half-life of 9 min. It has a rapid onset (60 seconds) and short duration of action (10 to 20 minutes). Dexmedetomidine is a2-adrenergic agonist which produces its action by decreasing the catecholamine release from locus cereleus in the brain. Various studies[9,10,11] have used different doses of dexmedetomidine ranging from 0.5 to 10 µg/kg/h with not so much certain data but definitely associated with a significant incidence of bradycardia and hypotension in high doses.[12].

Our study shows both the drugs controlled hypertension and tachycardia well in initial minutes, while from third minute,dexmedetomidine scored above esmolol in preventing tachycardia with significant P values , the esmolol could prevent tachycardia upto 3 minutes while dexmedetomidine prevented it in sustained manner. Similar trends were observed with regards to systolic blood pressure and diastolic blood pressure, where dexmedetomidine controlled blood pressure in a sustained manner, effect lasting up to 10 minutes, whereas esmolol could control blood pressure up to 3-5 minutes.

There are conflicting results in various studies which compare both these drugs. Alagol et al.[13] found that esmolol was found to control hemodynamic better than dexmedetomidine, while others report superiority of dexmedetomidine over esmolol[14,15]. Most of these studies have been biased towards onset of action of primary drug esmolol. Esmolol has very fast onset of action, (2 min) while dexmedetomidine has little delayed onset of action and also has to be given by infusion. To make double blinding possible, majority of authors who studied these drugs gave esmolol also in similar fashion as dexmedetomidine, but this may decrease the efficacy of esmolol, as it is rapidly cleared from the body. This is the major drawback of other studies. To negate this bias, rather than making the drug less effective by giving it in non effective form, we changed the anaesthesiologist in last minute after giving one drug in bolus form and one drug in infusion form, which is a preferred technique.

CONCLUSION

Dexmedetomidine is widely used agent in general anaesthesia, but uncommonly used in cardiac patients because of fear of having sudden bradycardia, we did not find bradycardia with this agent with the dose of 0.5microgram/ kg, and it effectively suppressed cardiac response to intubation in the doses and forms that are most suitable for the drug.The effect is comparable to bolus dose of esmolol for first 3 minutes and after that, Dexmedetomidine scores over Esmolol.

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