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Panacea Journal of Medical Sciences

Journal homepage: http://www.pjms.in/

Original Research Article

To compare effects of pretreatment with two doses of dexmedetomidine on etomidate induced myoclonus and attenuation of stress response at intubation

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ARTICLE INFO

Article history:
Received 28-03-2022
Accepted 15-05-2022
Available online 17-08-2022

Keywords:
American Society of Anaesthesiologists (ASA)
Diastolic Blood Pressure (DBP)
Systolic Blood Pressure (SBP)
Mean Arterial Pressure (MAP)
Electrocardiogram (ECG)
Heart Rate (HR)

ABSTRACT

Introduction: Etomidate's haemodynamic stability is due to its unique lack of effect on the sympathetic nervous system and on baroreceptor function. Even in cardiac patients an induction dose of etomidate results in very stable haemodynamics. Etomidate also has minimal effects on respiratory system as compared to other induction agents. Since it causes minimal histamine release, this gives an advantage in patients with reactive airway disease, making it less likely that they will have bronchospasm. However, pain on injection and myoclonus are two most common side effects of this drug. Pain on injection has disappeared after the new fat emulsion of etomidate, but the new solvent has not reduced the incidence of myoclonus.

Objectives: 1): To compare the effects of pretreatment with two doses of Dexmedetomidine on the incidence of Etomidate induced myoclonus using numerical based grading; 2): To compare the effects of pretreatment with two doses of Dexmedetomidine on attenuation of stress response at laryngoscopy and intubation after induction with Etomidate.

Materials and Methods: Study area: The proposed study was carried out in the Department of Anesthesiology and Intensive care at a tertiary care teaching hospital, after seeking clearance from the college ethical committee and obtaining written informed consent from patient. Study design: Prospective Interventional Randomized Comparative Study Study period: 1 year

Results: It was a prospective and interventional randomized comparative study where 180 patients with age group 18-65 years, of either sex,ASA grade I & II, BMI, undergoing elective surgical procedures under general anaesthesia with endotracheal intubation were included in the study. They were divided into three groups where patients were randomly allocated into one of the three groups using Block Randomization with sealed envelope system. In Group 2 and 3, 78.3% and 76.6% patients did not have myoclonus during induction with etomidate. Stress response to intubation was suppressed by dexmedetomidine.

Conclusion: Based on the observations of our study, we conclude that pretreatment with 0.5μg/kg and1μg/kg Dexmedetomidine significantly reduce etomidate induced myoclonus and stress response at intubation. However, dexmedetomidine in dose of 0.5μg/kg is associated with fewer side effects of bradycardia and hypotension.

1. Introduction

Etomidate is a carboxylatedimidazole-derived, sedative hypnotic agent. It acts directly on GABA Receptor Complex, blocking neuroexcitation and producing anaesthesia. When introduced in 1973, it was considered a novel induction agent with a stable cardiovascular profile and minimal respiratory side effects and is still widely used for hemodynamically unstable patients. [1]

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https://doi.org/10.18231/j.pjms.2022.082

Etomidate's haemodynamic stability is due to its unique lack of effect on the sympathetic nervous system and on baroreceptor function. Even in cardiac patients an induction dose of etomidate results in very stable haemodynamics. Etomidate also has minimal effects on respiratory system as compared to other induction agents. Since it causes minimal histamine release, this gives an advantage in patients with reactive airway disease, making it less likely that they will have bronchospasm. However, pain on injection and myoclonus are two most common side effects of this drug.[2] Pain on injection has disappeared after the new fat emulsion of etomidate, but the new solvent has not reduced the incidence of myoclonus.[3]

A variety of drugs have been used in the past to decrease the incidence of myoclonus like

1. Opiods- Fentanyl, Sufentanyl, Alfentanyl and Remifentany[4–7]
2. Benzodiazapines – Midazolam[8–10]
3. Magnesium Sulphate[11]
4. Alpha 2 agonists-Dexmedetomidine[1,9,12]

2. Objectives

1. To compare the effects of pretreatment with two doses of Dexmedetomidine on the incidence of Etomidate induced myoclonus using numerical based grading.
2. To compare the effects of pretreatment with two doses of Dexmedetomidine on attenuation of stress response at laryngoscopy and intubation after induction with Etomidate.

3. Materials and Methods

3.1. Study area

The proposed study was carried out in the Department of Anesthesiology and Intensive care at a tertiary care teaching hospital, after seeking clearance from the college ethical committee and obtaining written informed consent from patient.

3.2. Study design

Prospective Interventional Randomized Comparative Study

3.3. Study period

1 Year.

3.4. Inclusion criteria

Adult patients of 18-65 years of age of either sex of ASA grade 1 and 2 undergoing elective surgery under general anaesthesia were included in study.

3.5. Exclusion criteria

Patients with history suggesting allergy to any of the study medications, anticipated difficult airway, known Psychiatric disorder, sepsis/systemic infections, pacemaker/on Beta Blockers/with Heart Blocks and Pregnancy.

4. Results

The present study "To compare the effects of pretreatment with two doses of Dexmedetomidine on Etomidate induced myoclonus and attenuation of stress response at intubation" was conducted in the Operation Theatres in the Department of Anaesthesia and Intensive Care, at a tertiary care teaching hospital after obtaining clearance from ethical committee.

It was a prospective and interventional randomized comparative study where 180 patients with age group 18-65 years, of either sex, ASA grade I & II, BMI, undergoing elective surgical procedures under general anaesthesia with endotracheal intubation were included in the study. They were divided into three groups where patients were randomly allocated into one of the three groups using Block Randomization with sealed envelope system.

Group 1 (n=60): This group received 10 ml Saline followed by Inj. Etomidate (0.3 mg/Kg).

Group 2(n=60): This group received pretreatment with Inj. Dexmedetomidine (0.5μg/Kg) in 10ml Saline followed by Inj. Etomidate (0.3 mg/Kg).

Group 3 (n=60): This group received pretreatment with Inj. Dexmedetomidine (1μg/Kg) in 10ml Saline followed by Inj. Etomidate (0.3 mg/Kg).

The intensity of myoclonus was grarded as follows

0-No myoclonus, 1- mild myoclonus, 2- moderate and 3-severe myocyonus.

In this study, there was no significant differences among three groups regarding age, weight, sex and ASA physical status.

In our study, incidence of myoclonus was maximum in Group 1(70%) while 47 out of 60 patients (78.3%) in Group 2 and 46 out of 60 patients (76.6%) in Group 3 had no myoclonus. It is shown in Table 2.

In our study, majority of patients in Group 1 had grade 2 myoclonus (31.67%), 30% had no myoclonus and 13.3% patients had grade 3 myoclonus compared to patients who were pretreated with dexmedetomidine. In Group 2 and 3 none of the patients had grade 3 myoclonus. Thus, showing the efficacy of dexmedetomidine in reducing incidence and severity of etomidate induced myoclonus as shown in Table 3.

Stress response to intubation was also attenuated in dexmedetomidine group. Both Heart rate and Systolic Bp were less post intubation in patients who were pretreated with injection dexmedetomidine compared to group 1 as shown in Figures 1 and 2.

Table 1: Comparison of age distribution between the groups

		Group			Total	P value
		1	2	3		
Age	<=20	6 (10.00%)	3 (5.00%)	7 (11.67%)	16 (8.89%)	0.327
	21-30	11 (18.33%)	18 (30.00%)	16 (26.67%)	45 (25.00%)	
	31-40	17 (28.33%)	13 (21.67%)	16 (26.67%)	46 (25.56%)	
	41-50	10 (16.67%)	17 (28.33%)	15 (25.00%)	42 (23.33%)	
	51-60	15 (25.00%)	8 (13.33%)	6 (10.00%)	29 (16.11%)	
	>60	1 (1.67%)	1 (1.67%)	0 (0.00%)	2 (1.11%)	
Total		60 (100.00%)	60 (100.00%)	60 (100.00%)	180 (100.00%)	

Table 2: Incidence of myoclonus

		Group			Total	P value
		1	2	3		
Myoclonus	No	18(30.00%)	47(78.33%)	46(76.67%)	111(61.67%)	<0.0001
	Yes	42(70.00%)	13(21.67%)	14(23.33%)	69(38.33%)	
Total		60(100.00%)	60(100.00%)	60(100.00%)	180(100.00%)	

Table 3: Distribution of myoclonus grade.

Grade of myoclonus	1	2	3	P value
0	18(30.00%)	47(78.33%)	46(76.67%)	<0.0001
1	10(16.67%)	9(15.00%)	11(18.33%)	
2	19(31.67%)	4(6.67%)	3(5.00%)	
3	13(21.67%)	0(0.00%)	0(0.00%)	
Total	60(100%)	60(100%)	60(100%)	

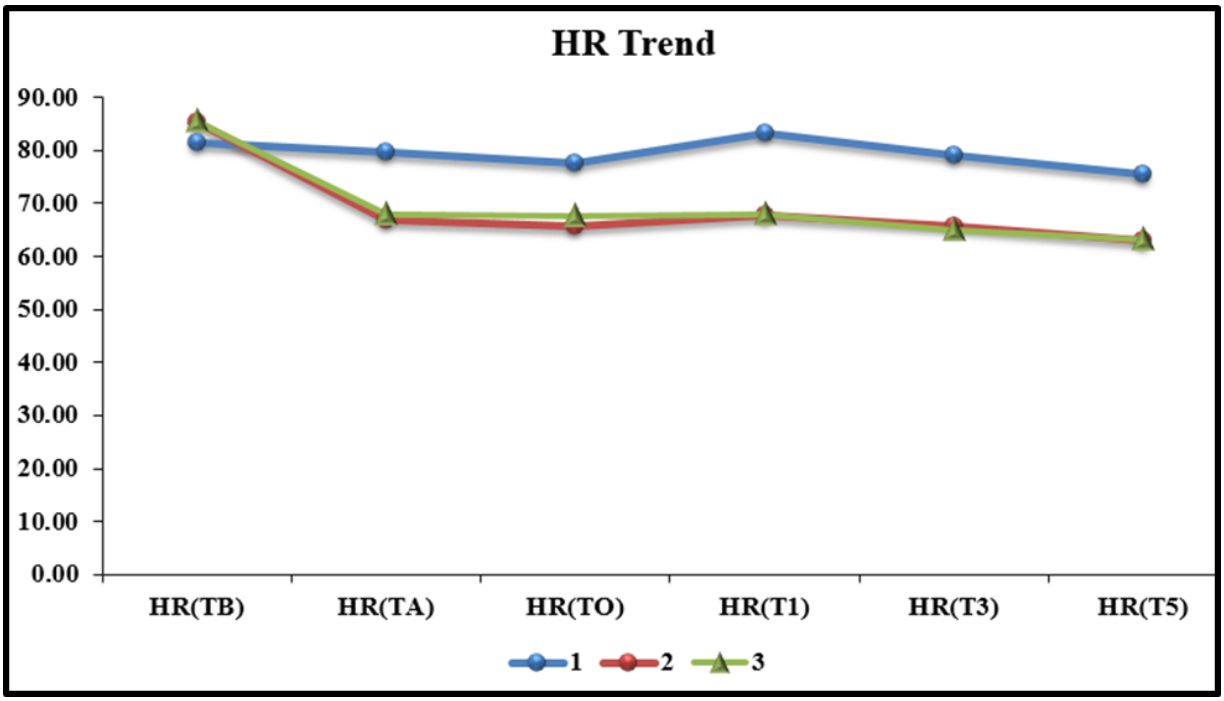

Fig. 1: HR Trend

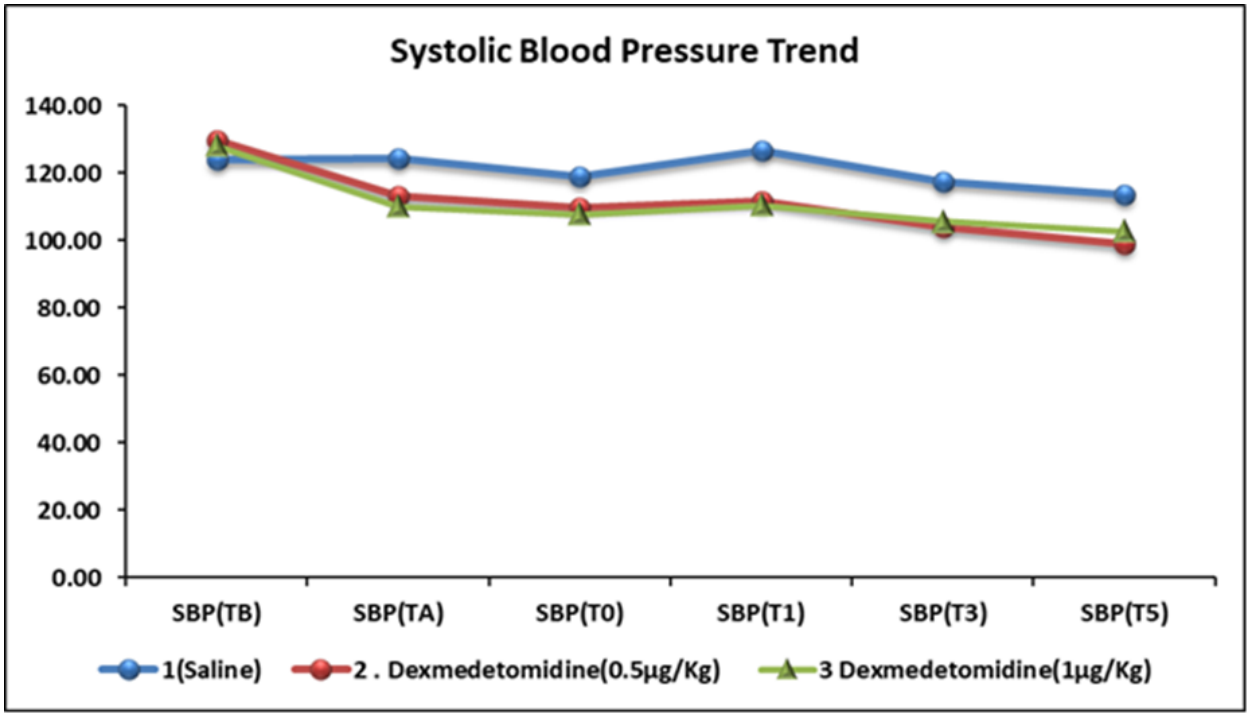

Fig. 2: Systolic blood pressure trend

5. Discussion

In this prospective randomized clinical study, we compared the effects of pretreatment with two doses of dexmedetomidine on the incidence of etomidate induced myoclonus and attenuation of stress response at intubation. This study was conducted in 180 adult patients (18-65 years) of ASA I or II undergoing elective surgery under general anaesthesia. These patients were randomly allocated to three groups, with each group having 60 patients each. Several studies have reported incidence of myoclonus in 50-80% patients receiving etomidate.[1,13,14]

Doenicke et al showed higher doses of etomidate were correlated with increased frequency of myoclonus, which was 83% with 0.3mg/kg etomidate. None of the patients had myoclonus in doses under 0.005 mg/kg.[13]

Mizrak et al (2010) concluded that pretreatment with dexmedetomidine or thiopental is effective in reducing the incidence and severity of etomidate-induced myoclonic muscle movements. Incidence of myoclonus was significantly low in Dexmedetomidine (0.5μg/kg) and Thiopental (1mg/kg) groups (34%,36%) than in control groups (64%) ($p<0.05$).[12]

Gunes Y et al (2010) conducted a study in 152 patients to compare effect of midazolam and dexmedetomidine for prevention of etomidate induced myoclonus and pain. They randomly allocated the patients into 3 groups, pretreated either with saline, or midazolam 0.5mg/kg or dexmedetomidine 1μg/kg and concluded that both groups pretreated with midazolam and dexmedetomidine showed significantly lower incidence of myoclonus as compared to group pretreated with saline. 37% patients in group pretreated with midazolam, 30% in group pretreated with dexmedtomidine and 90%in group pretreated with saline had myoclonus.[15]

Swarnendudey et al(2018) investigated effect of midazolam (0.015mg/kg) and dexmedetomidine (0.5μg/kg) in prevention of etomidate induced myoclonus in 80 adult patients. Incidence of myoclonus was much less in group receiving dexmedetomidine (45%) as compared to midazolam (52.5%). They also concluded that dexmedetomidine provides greater attenuation of stress response than midazolam.[10]

Sulaiman et al in 2012 studied the effects of dexmedetomidine on attenuation of stress response to endotracheal intubation. They concluded that dexmedetomidine provides good control of hemodynamics during laryngoscopy and endotracheal intubation. Dexmedetomidine at a dose of 0.5 mcg/kg as 10min infusion was administered prior to induction of general anaesthesia attenuated he sympathetic response to laryngoscopy and intubationin patients undergoing myocardial revascularization.[16]

Menda et al used dexmedetomidine in a dose of 1μg/Kg over 15 minutes before induction, to study its effects on attenuation of haemodynamic response to endotracheal intubation, found that the heart rate was significantly lower at all times as compared to the baseline values in the

intraoperative period.[17]

Scheinin et al (1992) concluded that dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and peroperative fentanyl.[18]

Koroglu et al. reported that a high dose of dexmedetomidine (bolus of 2-3μg/kg over 10 min or infusion of 1.5-3μg/kg/hr) in children undergoing MRI led to bradycardia in 16% of patients.[19]

H.F.Laun et al in their study reported incidence of bradycardia in group pretreated with dexmedetomidine 1μg/kg was significantly higher than groups using saline and dexmedetomidine 0.5μg/kg. In their study 24% patients in group III, 6.7% in group II, 0% in group I had bradycardia.[1]

6. Conclusions

1. Incidence and severity of etomidate induced myoclonus was signifinicantly lesser in patients who received pretreatment with dexmedetomidine compared to patients who received saline.
2. Both the doses (0.5μg/kg and 1μg/kg) dexmedetomidine are equally effective in prevention of incidence and severity of myoclonus induced by etomidate.
3. Compared to patients who received saline, pretreatment with dexmedetomidine (0.5μg/kg and 1μg/kg) attenuates the stress response to laryngoscopy and intubation.
4. Both the doses (0.5μg/kg and 1μg/kg) dexmedetomidine are comparable in attenuation of stress response during laryngoscpy and intubation.
5. Side effects like bradycardia and hypotension were more with dexmedetomidine 1μg/kg compared to 0.5μg/kg dexmedetomidine.

7. Source of Funding

No financial support was received for the work within this manuscript.

8. Conflict of Interest

The authors declare they have no conflict of interest.

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Cite this article: Gupta P, Kumari S, Chauhan R, Bhatia PS. To compare effects of pretreatment with two doses of dexmedetomidine on etomidate induced myoclonus and attenuation of stress response at intubation. *Panacea J Med Sci* 2022;12(2):436-441.