2
Original article
DOI: 10.48165/ijabms.2022.243802

2
Comparative Study of Dexmedetomidine vs Esmolol for Attenuation of Stress Responses to Laryngoscopy and Endotracheal intubation.

Dr. Manisha Kapdi (Ex Associate professor of Anaesthesia NHL MMC, at present Associate Professor of Anaesthesia, AMCMET Medical college Ahmedabad).
Dr. Uma Santoki (2nd year Resident of Anaesthesia, Department of Anaesthesiology, LG hospital, AMCMET college, Mani Nagar, Ahmedabad.)

Corresponding author: **Dr. Manisha Kapdi**: manisha_kapdi@yahoo.com

Abstract
Background: Endotracheal intubation is gold standard of general anaesthesia. But it has disadvantages of initiation of stress response to laryngoscopy and intubation. To alleviate it we have used Dexmedetomidine & Esmolol.
Methods
Group E - Inj. Esmolol (1.0 mg/kg) in 10 ml normal saline two minutes before induction
Group D – Inj. Dexmedetomidine (1µg/kg) in 10 ml normal saline over 10 minutes prior to induction.
Results and conclusion : both the drugs effectively supress stress response but Dexmedetomidine is better than Esmolol

Keywords: Dexmedetomidine, Esmolol, Stress response.

Introduction

Laryngoscopy is a method to visualise the vocal folds and the glottis.
Endotracheal intubation is mandatory in most surgical patients requiring general anaesthesia and critically ill patients requiring mechanical ventilation. Direct laryngoscopy and endotracheal intubation induce a transient circulatory reflex response characterized by tachycardia, hypertension and arrhythmias. This fluctuation of hemodynamic parameters is noted due to an increase in plasma catecholamine levels in response to this stimulus. This reflex lasts for 5-10 minutes after intubation. This momentary response is well tolerated in healthy individuals but is considered potentially dangerous in patients with cardiovascular or intracranial diseases. Alleviating stress response of laryngoscopy and endotracheal intubation is critical in management of general anaesthesia patients undergoing surgical intervention.
Several drugs and manoeuvres have been tried and there is a constant search for an ideal drug to mitigate this stress response. Newer drugs like Esmolol and Dexmedetomidine have been recently used for this purpose. Esmolol is an ultra-short acting beta-adrenergic receptor antagonist. It minimizes the increase in heart rate and myocardial contractility which is the primary determinant of myocardial oxygen consumption, by attenuating the positive chronotropic and inotropic effects of increased adrenergic activity. Dexmedetomidines an imidazole derivative and a highly selective alpha-2 adrenergic receptor agonist, and it produces sympatholytic. This study was undertaken to compare the efficacy of esmolol and dexmedetomidine for attenuation of stress response to laryngoscopy and endotracheal intubation in patients posted for elective surgeries under general anaesthesia.

AIMS AND OBJECTIVES

The main aim is to compare the efficacy and safety of intravenous Dexmedetomidine and Esmolol in attenuating hemodynamic response to laryngoscopy and intubation in normotensive patients undergoing elective surgeries under general anaesthesia.

Primary objective: To assess the hemodynamic changes due to intubation and direct laryngoscopy after study drug.

Secondary objective: To encounter the adverse effects of study drug or complications.

MATERIAL AND METHOD

After obtaining written and informed consent, we conducted a randomised study in 52 patients and compared the efficacy of Esmolol and Dexmedetomidine for attenuation of stress response to laryngoscopy and endotracheal intubation. Patients were divided randomly in two groups with 26 patients in each group.

Group E - Inj. Esmolol (1.0 mg/kg) in 10 ml normal saline two minutes before induction

Group D – Inj. Dexmedetomidine (1µg/kg) in 10 ml normal saline over 10 minutes prior to induction.

A. Patient selection and exclusion criteria

Inclusion criteria

Age: Between 18-60 years

Sex: Either sex

Physical status: ASA grading I or II

Type of surgeries: Surgeries conducted under general anaesthesia Exclusion criteria

Patient's refusal

Age below 18 years

Patients with Mallam Patti grade III and IV

Patients having chronic hypertension, sinus bradycardia, hypotension, co-existing cardiorespiratory diseases, hepatorenal diseases and on long term opioids.

Patients who could not be intubated within 2 minutes of administration of study drugs.

Known hypersensitivity to study drugs.

Patients having specific Electrocardiogram changes like conduction block, cardiac failure.

B. Preanesthetic Evaluation

• Pre anaesthetic evaluation of all patients consisted of detailed history, physical examination and routine investigations. A written informed consent was taken after proper counselling

C. Anaesthetic protocol

1. Preoperative preparation

All patients were fasted overnight

No sedatives or anxiolytics were given on the previous night

Vital parameters (Heart rate, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, Spo2) noted in preoperative room considered as baseline.

2. Pre-medication

a.Inj. Glycopyrrolate 0.01 mg/kg iv

b.Inj. Ondansetron 0.05 mg/kg iv

c.Inj. Fentanyl 2µg/kg iv

3.Study groups

Patients were randomly divided into two groups and each group consisted of 26 patients.

Group E - Inj. Esmolol (1.0 mg/kg) in 10 ml normal saline two minutes before induction

Group D – Inj. Dexmedetomidine (1µg/kg) in 10 ml normal saline over 10 minutes prior to induction.

4. Anaesthesia technique

Patient pre-oxygenated with 100% oxygen for 3 minutes

Induction done with Inj. Thiopentone sodium (5-7 mg/kg) iv + Inj. Succinylcholine (1.5 mg/kg) iv+ IPPV

Intubation done with appropriate sized cuffed endotracheal tube and received oxygen nitrous mixture (50:50)

Intubation done smoothly and gently within 30 seconds.

Anaesthesia maintained with Oxygen + Nitrous 2i Oxide + sevoflurane.1.5%to 2.5%

Muscle relaxation done with Inj. Atracurium with a loading dose of 0.5mg/kg iv and maintenance of 0.01mg/kg iv

After completion of surgery, patients were extubated following reversal of residual muscle paralysis with Inj. Neostigmine 0.05mg/kg iv and Inj. Glycopyrrolate8µg/kg iv

5. Hemodynamic parameters monitoring at various intervals

Baseline (T0)

Vitals after premedication (T1)

Immediately after giving the study drug (T2)

During Intubation (T3)

Immediately after intubation (T4)

3 minutes after intubation (T5)

5 minutes after intubation but prior to surgical incision (T6)

6. Complications and side effects, if noted

Bradycardia was defined as heart rate < 60/ min

If bradycardia occurred, it was treated with Inj. Atropine 0.6 mg IV

Hypotension defined as low blood pressure, typically less than 20% of baseline.

If hypotension occurred, it was managed with 100ml crystalloid bolus and Inj. Me phentermine 6 mg IV.

Respiratory depression was defined as Spo2 < 90% on room air and/or respiratory rate of <8/ min.

Statistical analysis

Statistical analysis was done using suitable statistical software. Interpretations of observations and results was done using unpaired Student t- test.

A P-value of:

<0.001: Highly significant

<0.05: Significant

>0.05: Not significant

OBSERVATIONS AND RESULTS

TABLE 1. DEMOGRAPHICAL PROFILE OF THE PATIENTS OF BOTH THE GROUPS

PARAMETERS	GROUP E (n=26)	GROUP D (n=26)	P-VALUE	INFERENCE
AGE in years (Mean ± SD)	34.7 ±2.83	35±2.40	0.40	NS
SEX (male/female)	12/14	14/12		
HEIGHT (cm)	165.1±6.60	164.6±7.12	0.45	NS
BODY WEIGHT (kg)	71.4±5.75	70.3±6.25	0.35	NS
ASA GRADE I/II	13/13	13/13		

No significant difference was found in Age, Sex, Height, Body weight and ASA grade.

TABLE 2. HEART RATE AT DIFFERENT TIME INTERVALS IN THE TWO GROUPS

	GROUP E (n=26)	GROUP D (n=26)	P-VALUE	INFERENCE
BASELINE (T0)	82.9±3.60	82.6±4.11	0.42 (>0.05)	NS
AFTER PREMEDICATION (T1)	86±2.98	86.2±3.70	0.43 (>0.05)	NS
IMMEDIATELY AFTER STUDY DRUG (T2)	80.2±3.58	76.8±4.44	0.01 (<0.05)	S
DURING INTUBATION (T3)	103.8±6.49	91.8±4.26	<0.001	HIGHLY SIGNIFICANT
IMMEDIATELY AFTER INTUBATION (T4)	102.2±5.20	89.6±4.50	<0.001	HIGHLY SIGNIFICANT
3 MINUTES AFTER INTUBATION (T5)	98.6±4.78	84±5.49	<0.001	HIGHLY SIGNIFICANT
5 MINUTES AFTER INTUBATION BUT PRIOR TO SURGICAL INCISION (T)	92.4±4.42	79.1±5.85	<0.001	HIGHLY SIGNIFICANT

6 No statistical difference was found between both the groups at T0 and T1.
Significant difference was found in Heart rate between the two groups at T2.
The heart rate of patients in Group D was found to be lower than that of Group E and this difference was found to be statistically highly significant (P<0.001) at T3, T4, T5, T6.
Hence, dexmedetomidine decreases heart rate more than Esmolol.

TABLE 3. SYSTOLIC BLOOD PRESSURE OF TWO GROUPS AT DIFFERENT TIME INTERVALS

	GROUP E (n=26)	GROUP D (n=26)	P-VALUE	INFERENCE
BASELINE (T0)	132.8±4.63	134.6±4.71	0.23	NS
AFTER PREMEDICATION (T1)	134.4±7.98	136.7±5.96	0.20	NS
IMMEDIATELY AFTER STUDY DRUG (T2)	131±6.48	128±5.57	0.066	NS
DURING INTUBATION (T3)	144.1±4.59	136.9±2.02	<0.001	HIGHLY SIGNIFICANT

IMMEDIATELY AFTER INTUBATION (T4)	141.4±4.11	133.2±3.58	<0.001	HIGHLY SIGNIFICANT
3 MINUTES AFTER INTUBATION (T5)	140.2±4.26	129.6±4.40	<0.001	HIGHLY SIGNIFICANT
5 MINUTES AFTER INTUBATION BUT PRIOR TO SURGICAL INCISION (T6)	137.6±4.94	127±4.73	<0.001	HIGHLY SIGNIFICANT

The Mean Systolic blood pressure were statistically comparable at T0 and T1.The systolic pressure was found to be lower in Group D as compared to Group E at T2, T3 , T4,T5 and T6.

Statistical difference was found to be highly significant at T3, T4, T5, and T6 Hence , dexmedetomidine decreases systolic blood pressure more than Esmolol.

TABLE 4. DIASTOLIC BLOOD PRESSURE OF TWO GROUPS AT DIFFERENT TIME INTERVALS

	GROUP E (n=26)	GROUP D (n=26)	P-VALUE	INFERENCE
BASELINE (T0)	82.2±6.28	83±5.43	0.39	NS
AFTER PREMEDICATION (T1)	83.6±5.94	83.2±5.82	0.44	NS
IMMEDIATELY AFTER STUDY DRUG (T2)	80.8±6.05	76.2±5.47	0.06	NS
DURING INTUBATION (T3)	92.3±6.49	86.7±4.83	<0.05	S
IMMEDIATELY AFTER INTUBATION (T4)	91.1±4.33	85.3±5.14	<0.05	S
3 MINUTES AFTER INTUBATION (T5)	88.6±3.74	82.6±5.58	<0.05	S
5 MINUTES AFTER INTUBATION BUT PRIOR TO SURGICAL INCISION (T6)	86.4±4.00	78.4±5.37	<0.05	S

Comparison of Diastolic blood pressure between both the groups was found to be statistically insignificant at T0 , T1 , T2. Statistical difference was found at T3 , T4 , T5 and T6 (P<0.05) . The diastolic pressure was lower in Group D as compared to Group E. Hence, dexmedetomidine decreases Diastolic blood pressure more than Esmolo

TABLE 5. MEAN ARTERIAL PRESSURE OF TWO GROUPS AT DIFFERENT TIME INTERVALS

	GROUP E (n=26)	GROUP D (n=26)	P-VALUE	INFERENCE
BASELINE (T0)	97.9±6.69	99±7.42	0.14	NS
AFTER PREMEDICATION (T1)	98.8±8.54	99.5±5.08	0.41	NS
IMMEDIATELY AFTER STUDY DRUG (T2)	97.5±8.31	91.5±2.87	<0.05	S
DURING INTUBATION (T3)	110.9±6.78	103.4±2.75	<0.05	S
IMMEDIATELY AFTER INTUBATION (T4)	108.1±6.52	99.9±4.62	<0.05	S
3 MINUTES AFTER INTUBATION (T5)	105.1±5.80	97.1±3.41	<0.05	S
5 MINUTES AFTER INTUBATION BUT PRIOR TO SURGICAL INCISION (T)	101.8±4.51	91.8±2.34	<0.001	HIGHLY SIGNIFICANT

6 Statistical difference was noted between both the groups in MAP immediately after administering the study drug, during intubation immediately after intubation and 3 minutes after intubation. ($p<0.05$) A highly significant difference was noted between both groups at 5 minutes after intubation($p<0.001$). Dexmedetomidine proved to be a better drug in comparison to esmolol for Mean Arterial Pressure.

TABLE 6. COMPLICATIONS IN BOTH GROUPS

COMPLICATIONS	GROUP E (N=26)		GROUP D (N=26)	
	NO. OF PATIENTS	%	NO. OF PATIENTS	%
NAUSEA	1	3.8	0	0
VOMITING	0	0	0	0
BRADYCARDIA	1	3.8	1	3.8
HYPOTENSION	5	19	5	19
RESPIRATORY DEPRESSION	0	0	0	0

Incidence of complications were not significant in any group.

DISCUSSION

Direct laryngoscopy and endotracheal intubation are inevitable traumatic procedures for initiation of general anaesthesia for prolonged elective surgeries as well as cardiopulmonary resuscitation. It leads to a temporary, yet prompt sympathoadrenal reflex resulting in hypertension and tachycardia. In healthy individuals, this momentary reflex is not significant whereas it can be detrimental in patients with hypertension, coronary vascular disease and cerebrovascular diseases Such patients need prophylaxis in the form of antihypertensive agents, beta-blockers, narcotics and other drugs. In this study, we have used two agents (Esmolol and Dexmedetomidine) to study its efficacy in attenuating hemodynamic stress responses to laryngoscopy and endotracheal intubation. Dexmedetomidine is an imidazole derivative, which acts on α-2 adrenergic receptors in the brain and spinal cord inhibiting neuronal firing, thereby resulting in hypotension, bradycardia , sedation and analgesia

Its effects are mediated by inhibition of central sympathetic outflow. Esmolol is an ultra-short acting cardio selective beta blocker with a transient effect and short half-life.

It prevents the action of epinephrine and nor-epinephrine. It decreases the force and rate of heart contractions by blocking the beta-adrenergic receptors of the sympathetic nervous system and heart.

Chung F and McCammon R. L. Proved that laryngoscopy and tracheal manipulation were responsible for rise in hemodynamic parameters. This is consistent with our study as the peak rise in blood pressure was noted during intubation. Most of the previous studies have compared blood pressure and Heart rate before and after laryngoscopy. In our study, we also compared the parameters during intubation. Various studies have used dexmedetomidine in the dose ranging from 0.5 to 10µg/kg and observed that notable hypotension and bradycardia occurred at higher doses. We, therefore, used dexmedetomidine in the dose of 1µg/kg over 10 minutes prior to intubation and observed a consistent protective effect on Heart rate.

Studies have used Esmolol as bolus and infusion in the dose ranging from 0.42mg/kg. The results observed have been variable and no agreement has been reached regarding the optimum dose and timing of delivery. A study Saurabh Varshney et al ,2019(1) used Dexmedetomidine(0.5µg/kg) and Esmolol (0.5mg/kg) in lower doses than our study and found similar results. (1) In study of Mavri etal (3) Dexmedetomidine(1µg/kg), Esmolol (2mg/kg) and Fentanyl (2µg/kg) and observed their effects on heart rate, Blood pressure due to tracheal manipulation. They concluded that Dexmedetomidine blunted tachycardia better than esmolol and the converse was true for blood pressure. , (3).In study of Reddy etal (4),Li Z etal(5),& Selvaraj etal(6) comparison of Dexmedetomidine or Esmolol was done & they concluded that Dexmedetomidine is better in terms of SBP,DBP,HR attenuation periodically after intubation.

In our study all stages after premedication at time of intubation,1,3,5 min after intubation SBP, DBP, MAP, HR were more attenuated in group D than group E(table2,3,4,5) $p<0.05$

Shamim etal (7) showed that Dexmedetomidine in lower doses also attenuate pressure response to laryngoscopy and intubation & it attenuate response dose dependently.

Gogus etal(8)have also compare Dexmedetomidine,esmolol,& Fentanyl for attenuation of stress response & concluded that Dexmedetomidine is superior than other 2.In the present study , no side effects of either two drugs were significant. Both drugs provided a good attenuating response. However, dexmedetomidine provided superior control over pressor response. Studies of Sulaiman et al, 2015 (9) with use of Dexmedetomidine in the range of 0.5-2µg/kg have resulted in effective control of hemodynamic responses during tracheal manipulation. Keniya VM etal (10) notice hypertension and bradycardia with higher doses of Dexmedetomidine In present study hypotension and bradycardia incidence was comparable & similar.

LIMITATIONS:

1.we have not estimated epinephrine levels in each group.
2.We have no control group as we want to attenuate pressure response to laryngoscopy& endotracheal intubation in each patient.

Future recommendations:

To access large scale study with overcoming limitations

CONCLUSION

In nutshell we conclude on the basis of the findings of this study, that Dexmedetomidine (1.0 µg/kg) is better than Esmolol (1mg/kg) in attenuating the sympathomimetic response to laryngoscopy and intubation.

REFERENCES

1.VarshneyS, Shahi V, Bhardwaj M. To compare the efficacy of dexmedetomidine and esmololin attenuation of pressor response to laryngoscopy and intubation in patients undergoing general anaesthesia for elective laparoscopic cholecystectomy. Indian J Clin Anaesth 2019;6(4):576-580.

2. Singh D, Jagannath S, Priye S, Mudassar AS. The comparison of dexmedetomidine, esmolol, and the combination of dexmedetomidine with esmolol for attenuation of sympathomimetic response to laryngoscopy and intubation in patients undergoing coronary artery bypass grafting. Ann Card Anaesth 2019; 22:353-7

3. Mavri et al: Dexmedetomidine, fentanyl and semicolon prevention of the hemodynamic effects of laryngoscopy and endotracheal intubation. A prospective, randomized, double blind study. Intensive Care Medicine Experimental 2015 3(Suppl 1): A210

4. Reddy SV, Balaji D, Ahmed SN. Dexmedetomidine versus esmolol to attenuate the hemodynamic response to laryngoscopy and tracheal intubation: A randomized double blind clinical study. Int J Appl Basic Med Res. 2014;4(2):95-100

5.Li Z, Xu L, Zheng J, Wang Q. Comparison of intravenous dexmedetomidine versus esmolol for attenuation of Hemodynamic response to tracheal intubation after rapid sequence induction: A systematic review and meta-analysis. Biomed Res Int. 2019;2019:6791971.Published 2019 Apr 17.

6.Selvaraj V, Manoharan KR. Prospective randomized study to compare between intravenous dexmedetomidine and esmolol for attenuation of hemodynamic response to endotracheal intubation. Anaesth Essays Res. 2016; 10(2):343-348

7.Shammim R, Srivastava S, Rastogi A, Kishore K, Srivastava A. Effect of two different doses of Dexmedetomidine on stress response in laparoscopic pyeloplasty: A randomized prospective Controlled study. Anesth Essays Res. 2017; 11(4):1030-1034.

8. Gogus N, Akan B, Serger N, Baydar M. The comparison of the effects of dexmedetomidine, fentanyl and esmolol on prevention of hemodynamic response to intubation. Braz J Anaesthesiol. 2014 ;64(5):314-319.

9. Sulaiman S et al. The effects of Dexmedetomidine on attenuation of stress response to endotracheal intubation in patients undergoing elective off-pump coronary artery by-pass grafting. Ann CardAnaesth 2012;15:39-43

10.Keniya VM et al. Dexmedetomidine attenuates sympathoadrenal response totracheal intubation and rescues perioperative anaesthetic requirement. Indina J Anaesth 2011;55:352-7.

CONFLICT OF INTEREST: Nil

FUNDING: Nil

ACKNOWLEDGEMENT: Nil