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ORIGINAL ARTICLE

ALPHA 2 AGONIST DEXMEDETOMIDINE ATTENUATES PRESSOR RESPONSE DURING LARYNGOSCOPY AND INTUBATION: A CLINICAL STUDY

Anish Sharma N. G[1], Shanakarnarayana P[2]

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ABSTRACT: AIM AND OBJECTIVE: This randomized prospective study was done to evaluate the effects of single premedication dose of I.V dexmedetomidine in attenuating pressor response to laryngoscopy and endotracheal intubation. **METHODOLOGY:** In this study, 60 patients in the age group 20-40yrs, belonging to ASA grade I and II scheduled for elective surgical procedures under general anaesthesia were included. The patients were randomly divided into 2 groups of 30 each. Group I patients received 100ml NS 15min before induction and Group II patients received Dexmedetomidine 1microgm/kg in 100ml NS 15mins before induction. HR, SBP, DBP, MAP were monitored at $T_0, T_1, T_2, T_3, T_4, T_5, T_6$ respectively. Patients were maintained with O_2, N_2O, Isoflurane and vecuronium at titrated doses. ECG, NIBP, HR were monitored throughout the procedure. All patients were monitored for 24 hours post operatively. **RESULTS:** In Group II patients had attenuation of sympathetic response with decrease in HR, SBP, DBP and MAP where as in Group I there was increase in HR, SBP, DBP and MAP throughout the study period. Maximum changes in HR, SBP, DBP and MAP were observed at 1 min after intubation in both the Groups. In Group II there was a constant decrease in HR, SBP, DBP and MAP from the time of pre induction until 10^{th} min of intubation which when compared to that of Group I was statistically highly significant($p=0.000$). There were no significant changes in ECG and SPO_2 in both the Groups. Recovery was satisfactory without any side effects. **CONCLUSION:** Dexmedetomidine in the dose of 1µg/kg as IV infusion, given 15 minutes before induction can be used safely to attenuate the pressor response to laryngoscopy and intubation without any side effects. HR-Heart rate, SBP- Systolic blood pressure, DBP- Diastolic blood pressure, MAP- Mean arterial pressure, IV- Intravenous, T_0- Basal reading when the patient is shifted to OR, T_1- At 5mins after infusion of dexmedetomidine/saline, T_2- At Induction (2mins after Thiopentone sodium+ vecuronium), T_3- At 1 min after intubation, T_4- At 3mins after intubation, T_5- At 5mins after intubation, T_6- At 10mins after intubation.

KEYWORDS: Dexmedetomidine; Endotracheal intubation; Pressor response.

INTRODUCTION: Since the time of introduction of Endotracheal anaesthesia in the last quarter of 19^{th} century endotracheal intubation has become one of the frequently performed procedures in the practice of anaesthesia.

Endotracheal intubation is the translaryngeal placement of a tube into the trachea via the nose or mouth. Endotracheal intubation includes laryngoscopy and intubation. The process of laryngoscopy and intubation are noxious stimuli and therefore constitute a period of extreme haemodynamic stress and is associated with intense sympathetic activity marked by tachycardia and hypertension.[1]

The cardiovascular response is a reflex phenomenon. This is mediated by Vagus (X) and Glossopharyngeal (IX) cranial nerves. Vagus and Glossopharyngeal nerves carry the afferent stimulus

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from epiglottis and infraglottic region and activate the vasomotor centre to cause a peripheral sympathetic adrenal response to release adrenaline and noradrenaline.[2]

The increase in Pulse rate, blood pressure is usually transitory, variable and unpredictable. Normal, healthy persons tolerate this response, but in susceptible individuals, this transient sympathetic response can evoke life – threatening conditions.[3]

Herein lays the rationale to continue the quest for an anaesthetic technique where the cardiovascular response can be attenuated. This has drawn the attention of many anaesthetists over the last forty years.

Various pharmacological and non–pharmacological methods have been used to attenuate the haemodynamic response to laryngoscopy and endotracheal intubation but none of them have proved to be ideal. Hence the search for an ideal agent to attenuate the hemodynamic responses is still continuing.

Alpha-2 agonists have been used for attenuating the sympathetic response[4] and among α-2 agonists both clonidine and dexmedetomidine appear to fulfil all the above criteria. Both Clonidine and dexmedetomidine have actions on both α-1 and α-2 receptors but Dexmedetomidine is highly specific and selective α-2 adrenoceptor agonist with α2:α1 binding selectivity ratio of 1620:1 compared to 220:1 for clonidine.[5]

Various studies have also found that dexmedetomidine can decrease the hemodynamic response to laryngoscopy and intubation.[6, 7, 8, 9, 10, 11, 12 and 13]

The study was undertaken to evaluate the effects of recently introduced alpha-2 agonist, dexmedetomidine as premedication in attenuating pressor response during Laryngoscopy and Endotracheal intubation.

AIMS AND OBJECTIVES:

AIM: This randomized prospective study was done to evaluate the efficacy of single premedication dose of I.V dexmedetomidine in attenuating pressor response to laryngoscopy and endotracheal intubation.

OBJECTIVE: To evaluate the efficacy of single premedication dose of intravenous dexmedetomidine 1μg/kg body weight in 1) Attenuating the pressor response to laryngoscopy and endotracheal intubation 2) Post anaesthesia recovery characteristics 3) Side effects if any.

MATERIALS AND METHODS: In this study, 60 patients in the age group 20-40yrs, of either sex belonging to ASA grade I and II scheduled for elective procedures under GA was included. The study was done in KVG medical college, Sullia from December 2013 to May 2014.

Patients with anticipated difficult airway, Hiatus hernia, GERD, BMI>30, patients on antihypertensive drugs, Patients on sedatives, hypnotics and antidepressants, H/o cardiovascular, respiratory, hepatic, renal diseases, Laryngoscopy time > 30 sec, Patients with ASA grade III and above, endocrine diseases, malnourished were excluded.

Pre-Anaesthetic Evaluation: All patients were evaluated for fitness for anaesthesia on the day prior to surgery. Clinical examination of the patient was performed including general physical examination and systemic examination.

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All patients were explained about the anaestheia technique and informed consent taken. Patients were kept NPO for 8hrs prior to surgery.

Routine investigations were done. { Hb%, BT, CT, Blood grouping, Urine analysis, ECG, BUN, Serum creatinine, and Fasting blood sugar}. No specific investigations were required pertaining to the study.

Pre - Medication: All patients were given tablet Diazepam 5mgs orally at bed time on the previous night of surgery.

Technique of Anaesthesia/Procedure: 60 patients aged between 20 to 40yrs belonging to ASA grade I and II were randomly divided into 2 groups, each group consists of 30 patients Group I [Saline group], Group II [Dexmedetomidine group] On the day of surgery, Anaesthesia machine and circuits were checked, resuscitation equipment's were kept ready.

After confirmation of NPO status patients were shifted to the operating room and connected to multi-channel monitor. Basal systolic blood pressure (SBP), diastolic blood pressure (DBP), Mean arterial pressure (MAP), heart rate and SpO_2 (T_0) were recorded after 5mins of settling in the OR. Rhythm monitoring from a continuous visual display of ECG along with continuous monitoring of the vital parameters were done.

An Intravenous line was secured with 18G cannula and preloading with 500ml of Ringer lactate done over 30 mins for all patients. Following this,

Group I [Saline group] patients received 100ml normal saline infused over 15mins.

Group II [Dexmedetomidine group] patients received Intravenous dexmedetomidine 1µg per kg in 100ml normal saline infused over 15mins.

After 5mins of stabilizing period SBP, DBP, MAP, Heart rate, SpO_2 (T_1) was recorded. Prior to induction, Inj Glycopyrrolate 0.2mg, Inj Ondansetron 4mg and Inj Esomeprazole 40mg administered IV.

All patients were pre- Oxygenated for 3mins and Anaesthesia induced with 5mg/kg Thiopentone sodium (2.5%). After successful trial, ventilation with 100% oxygen, Vecuronium0.1mg/kg was given to facilitate laryngoscopy and intubation. Oxygenation continued by positive pressure mask ventilation using Bains circuit and was maintained with 50% O_2 and 50% N_2O. At 2mins after induction, SBP, DBP, MAP, Heart rate and SpO_2 was recorded (T_2).

At 3mins after induction, using laryngoscope with a Macintosh blade intubation was done with well lubricated, appropriate sized cuffed, disposable oral endotracheal tube by an experienced anaesthesiologist and accomplished within 20sec. SBP, DBP, MAP, Heart rate and SpO_2 were recorded.

After confirmation of the tube position by bilateral auscultation for air entry, cuff inflated and tube fixed, connected to Boyle's machine through Bain's circuit. Anaesthesia maintained with N_2O, O_2, Isoflurane, controlled ventilation with appropriate fresh gas flow.

Isoflurane was used in the lower possible concentration necessary to keep the BP and HR within 20% of the patient's pre-operative baseline values. SBP, DBP, MAP, Heart rate and SpO_2 were recorded at 1 (T_3), 3 (T_4), 5 (T_5), and 10min (T_6) after laryngoscopy and intubation.

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Sequence	SBP, DBP, MAP, Heart rate, SpO_2 recording
Basal reading when the patient is shifted to OT	T_0
At 5 min after infusion of Dexmedetomidine /saline	T_1
At Induction (2min after Thiopentone-sodium+ Vecuronium)	T_2
At 1 min after intubation	T_3
At 3min after intubation	T_4
At 5min after intubation	T_5
At 10min after intubation	T_6

Surgery commenced at the end of 10min after laryngoscopy and intubation. No form of stimulus was applied during this period.

Anaesthesia continued with N_2O, O_2 and Isoflurane. Vecuronium top up doses, analgesics and IV fluids administered based on the requirements.

At the end of surgery, Isoflurane and N_2O were discontinued and when respiratory attempts were present, residual neuromuscular blockade was reversed with Inj. Neostigmine (0.05mg/kg) and Glycopyrrolate(0.01mg/kg). Recovery assessed and extubation done after thorough throat suction. After adequate clinical recovery patient was shifted to post anaesthesia care unit and observed for 2 hrs for nausea vomiting, bradycardia, Hypotension and Sedation.

STATISTICAL METHOD EMPLOYED: All data are presented as mean±SD (standard deviation). Demographic data were analyzed by student's t test. Analysis of variance for repeated measures (ANOVA) was used to analyses changes over time:

$p<0.01$- Statistically highly significant (HS)

$p<0.05$- Statistically significant (S)

$p>0.05$- Statistically not significant (NS)

STATISTICAL SOFTWARE: The statistical software SPSS version 16.0 was used for the analysis of the data and Microsoft Word and Excel have been used to generate graphs, tables etc.

OBSERVATION AND RESULTS: Total of 60 patients were randomly assigned to receive either dexmedetomidine or Saline. Patients in the 2 groups had similar demographic profile. None of the patients were excluded from the study. Baseline hemodynamic data were also similar in both the groups.

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HEART RATE: Statistical evaluation between the groups showed that the basal mean HR between Group I and Group II was statistically not significant(p=0.73) at pre- induction, induction, 1, 3, 5 and 10 minutes after intubation the HR changes were statistically highly significant (p=0.000).

Maximum HR changes were observed at 1 min after intubation in both the Groups. In Group II there was 9% decrease in HR compared to basal. In Group I there was 13.6% increase in mean HR compared to basal. In Group II there was a constant decrease in HR from the time of pre induction until 10th min of intubation which when compared to that of Group I was statistically highly significant (p=0.000).

SYSTOLIC BLOOD PRESSURE: Statistical evaluation between the groups showed that the basal mean SBP between Group I and Group II was statistically not significant (p=0.60) but the comparison of SBP changes between the 2 Groups at pre-induction and induction was statistically significant (p=0.03, p=0.01) and at 1, 3, 5 and 10 minutes after intubation it was statistically highly significant (p=0.000, p=0.000, p=0.0001, p=0.0003 respectively). In Group II SBP continued to remain below the basal value from the time of pre induction until 10th min after intubation which was statistically significant.

DIASTOLIC BLOOD PRESSURE: Statistical evaluation between the groups showed that the basal mean DBP between Group I and Group II was statistically not significant(p=0.71). The comparison between the 2 groups at pre-induction, induction, 1, 3, 5 and 10 minutes after intubation was statistically highly significant (p=0.000). Maximum DBP changes were observed at 1 min after intubation in both the Groups, compared to basal there was a 9.4% decrease in Group II in DBP and in Group I there was 7% increase in DBP. In Group II there was a steady decrease in DBP from the time of pre induction until 10th min of intubation which when compared to that of Group I was statistically highly significant.

MEAN ARTERIAL PRESSURE: Statistical evaluation between the groups showed that the basal mean MAP between Group I and Group II was statistically not significant(p=0.96) but the changes observed at pre-induction, induction, 1, 3, 5 and 10 minutes after intubation was statistically highly significant (p=0.002, p=0.0001, p=0.000, p=0.000, p=0.000, p=0.000 respectively). Maximum MAP changes were observed at 1 min after intubation in both the Groups, compared to basal there was 8% decrease in MAP in Group II and 5% increase in MAP in Group I. In Group II there was a constant decrease in MAP from the time of pre induction until 10th min of intubation which when compared to that of Group I was statistically highly significant.

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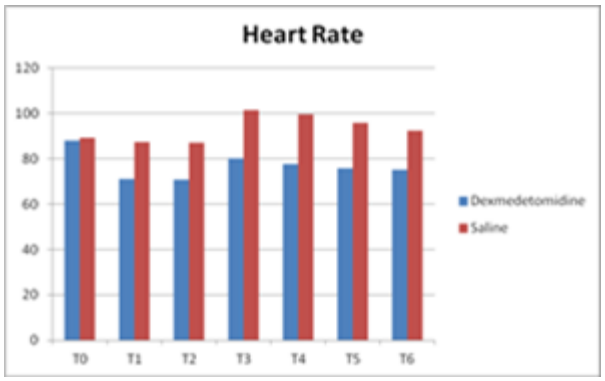

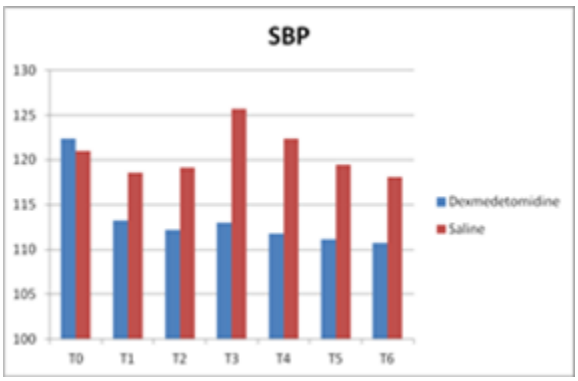

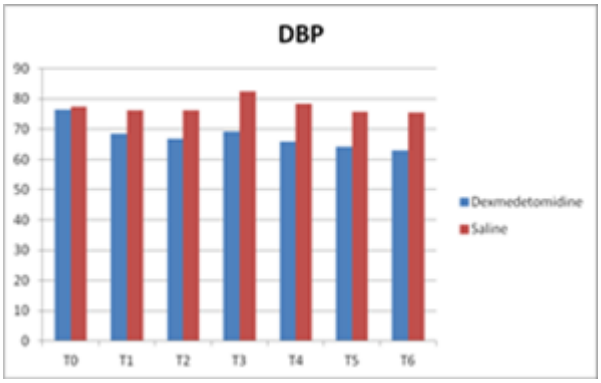

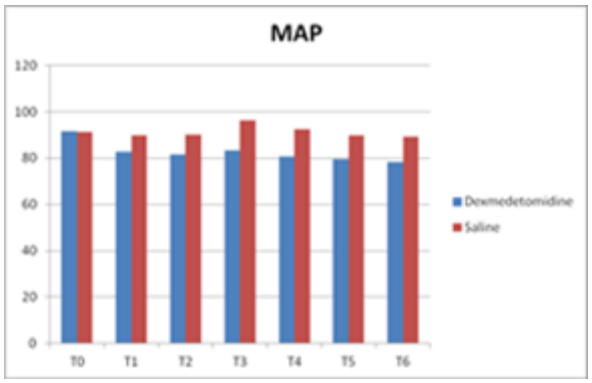

No significant ECG and SPO_2 changes were observed in both the groups throughout the study period.

SIDE EFFECTS: All patients were followed up for 24hours post operatively. Side effects attributed to the study drug (Dexmedetomidine) like nausea, vomiting, dryness of mouth, sedation were not observed.

DISCUSSION: Most of the general anaesthetic procedures in the modern anaesthetic practice are carried out with endotracheal intubation. Laryngoscopy and tracheal intubation are considered as the most critical events during administration of general anaesthesia as they provoke transient but marked sympatho-adrenal response manifesting as hypertension and tachycardia.[1]

These responses are transitory, variable and may not be significant in otherwise normal individuals, but in patients with cardiovascular compromise like hypertension, Ischemic heart disease, Cerebrovascular disease and in patients with intracranial aneurysms even these transient changes in haemodynamics can result in potentially harmful effects like left ventricular failure, pulmonary edema, myocardial ischemia, ventricular dysrhythmias and cerebral haemorrhage[3].This is by far the most important indication for attenuation of haemodynamic response to laryngoscopy and tracheal intubation.[6]

Many drugs and techniques have been used to reduce these stressful stimuli. Alpha 2 agonist clonidine and dexmedetomidine are such drugs that are being frequently used to modify this cardiovascular response.

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The present study was undertaken to evaluate the effects of single premedication dose of IV dexmedetomidine in attenuating the pressor response to laryngoscopy and endotracheal intubation.

The study population consisted of 60 patients in the age group of 20- 40 belonging to ASA grade I were randomly divided into 2 groups. Each group consisting of 30 patients.

Group I (Saline) patients received 100 ml normal saline infused over 15 min before induction. Group II (Dexmedetomidine) patients received IV Dexmedetomidine 1 microgram/kg[13, 14 and 15] in 100ml normal saline infused over 15 min before induction.

Various authors Kunisawa et al,[12] Ferdi et al[13] have administered dexmedetomidine in 100ml NS 15 minutes before induction and found better haemodynamic stability.

Hence in the present study dexmedetomidine was administered 15 minutes before induction to blunt the haemodynamic response to laryngoscopy and intubation.

The basal mean HR in the present study in Group II and Group I were 88.1bpm and 89.1bpm respectively. 1 min after intubation in Group II there was 8bpm decrease in mean HR compared to basal, whereas in Group I there was 12.2bpm increase in mean HR which was statistically significant. At 3, 5 and 10 min there was further decrease in mean HR in dexmedetomidine group compared to saline group where there was an increase and is comparable to the results of Basar et al,[11] kunisawa et al[12] and Ferdi et al.[13]

In the present study, the basal mean SBP in Group II and Group I were 122.36 mmHg and 121 mmHg respectively. 1 min after intubation in Group II there was 9.36 mmHg decrease in SBP compared to basal whereas in Group I there was 4.7 mmHg increase in SBP which was statistically significant. At 3, 5 and 10 min after intubation in Group II the decrease in SBP when compared to basal were 10.56mmHg, 11.26 mmHg and 11.66mmHg respectively. In group I there was increase in SBP at 1 and 3min but returned to basal at 5min after intubation. Scheinin et al.[6] Jaakola et al[7] and Aho et al[8] also observed similar results.

The basal mean DBP in the present study in Group II and Group I were 76.5 mmHg and 77.4 mmHg respectively. There was a steady decrease in DBP from pre induction in Group II. At 1 min after intubation the DBP was 7.2mmHg less compared to that of the basal value whereas in Group I there was 5 mmHg increase in DBP which was statistically significant. At 3 min, 5 min and 10 min after intubation the fall in DBP in Group II compared to basal value was 10.7mmHg, 12.3 mmHg and 13.5 mmHg respectively. Jaakola et al[7], kunisawa et al[12] and Ferdi et al[13] also observed similar results.

In the present study basal mean MAP in Group II and Group I were 91.46 mmHg and 91.36 mmHg respectively. There was a steady decrease in MAP from pre-induction in Group II. At 1 min after intubation the MAP was 8mmHg less compared to basal value whereas in Group I there was 5mmHg increase in MAP which was statistically significant. At 3, 5 and 10 mins the fall in MAP in Group II was 10.9mmHg, 12mmHg and 13.13mmHg respectively. Mowafi et al[9] observed similar results.

SIDE EFFECTS: All the patients in the study were adequately hydrated, hence no side effects were observed.

CONCLUSION: From the present study it can be concluded that. In control group, where no drug was administered to attenuate the pressor response patients had significant rise in the mean heart rate

(HR), systolic Blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) throughout the study period with maximum changes observed at 1 min after intubation.

In Dexmedetomidine group, patients received dexmedetomidine in the dose of 1μg/kg as IV infusion, given 15 minutes before induction, showed significant decrease in HR, SBP, DBP and MAP throughout the study period.

Side effects like bradycardia, hypotension, nausea, vomiting, dryness of mouth, sedation were not observed in all the patients and recovery was satisfactory.

Hence dexmedetomidine in the dose of 1μg/kg as IV infusion, given 15 minutes before induction can be used safely to attenuate the pressor response to laryngoscopy and intubation without significant side effects. However the study has to be done on a larger population and in high risk patients for further evaluation.

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AUTHORS:

1. Anish Sharma N. G.
2. Shanakarnarayana P.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Anaesthesiology, KVG Medical College & Hospital, Kurunjibab, Sullia, Karnataka, India.
2. Associate Professor, Department of Anaesthesiology, KVG Medical College & Hospital, Kurunjibab, Sullia, Karnataka, India.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Anish Sharma N. G,
Assistant Professor,
Department of Anesthesiology,
KVG Medical College & Hospital,
Kurunjibag, Sullia-574327,
Karnataka, India.
Email: anish84guthu@gmail.com

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