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A STUDY OF "DEXMEDETOMIDINE FOR ATTENUATING STRESS RESPONSE AFTER LARYNGOSCOPE AND INTUBATION"

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KEYWORDS :

Endotracheal intubation has become one of the frequently performed procedure in the practice of Anesthesia since the time of Introduction of Endotracheal Anesthesia in the last quarter of 19th century. The process of Laryngoscopy & Intubation are noxious stimuli & therefore constitute period of extreme Haemodynamic stress and associated with intense sympathetic activity mediated by Hypertension & Tachycardia1.The increase in Pulse rate, Blood pressure are usually unpredictable, variable & transistory.Pharmac ological methods like use of β-blockers, Vasodilator, Inhalation agents , Topical & Intravenous Lidocaine, Narcotics, Calcium channel blockers has been tried. For attenuating the stress response,Dexme detomidine is highly specific and selective α-2 adrenoreceptor agonist with α2:α1 binding selectivity ratio of 1620:1 compare to 220:1 for Clonidine.Various studies have also found that Dexmedetomidine can decrease the Hemodynamic response to laryngoscopy and Intubation [3,4,5,6,7,8,9].

AIM

This randomized prospective study was done to evaluate the efficacy of a single premedication dose of I.V.Dexmedetomidine in attenuating stress response to laryngoscopy and intubation.

OBJECTIVE:

To evaluate the efficacy of single premedication dose of intravenous Dexmedetomidine .5µg/kg body weight in

- Attenuating the stress response to laryngoscopy and endotracheal intubation.

Dexmedetomidine

Mechanism of actions Receptor Pharmacology

Specific *alpha-2* receptor subtypes mediate the various pharm acodynamics effects of Dexmedetomidine. Agonism at the Aipha-2Areceptor appears to promote sedation, hypnosis, analgesia, Symphatholysis, Neuro protection, and inhibition of insulin secretion. Agonism at the Alpha-2_B, receptor suppresses shivering centrally, promotes analgesia at spinal cord sites, and induces vasoconstriction in peripheral arteries. The Alpha-2,receptor is associated with modulation of cognition, sensory processing, mood and stimulant-induced locomotor activity, and regulation of Epinephrine outflow from the Adrenal medulla. Inhibition of Norepinephrine release appears to be equally affected by all three aipha-$_2$ receptor subtypes. Dexmedetomidine also binds to Imidazoline receptors, which recognize the Imidazoline or Oxaziline structure of alpha-$_2$ agonist agents.This activity may explain some of the non-alpha-$_2$ receptor -related effects of this drug class. Imidazoline receptor subtypes have also been identified. Imidazoline-I receptors modulate blood pressure regulation and have anti-arrhythmic effects. They are found in the Ventro lateral medulla and are lined to G-proteins. Imidazoline-$_2$ receptors have been implicated in Neuro-protection in cerebral ischemia model in animals and in generation of memory. They are typically located on the mitochondrial outer membrane and are not G-protein coupled, but may exert their effects by decreasing tissue Norepinephrine levels.A Specific Alpha-$_2$ adrenoceptor agonist, its action is unique and different. Alpha-$_2$ adrenoreceptors are membrane-spanning G proteins, and Mechanism of action is through activation of G_1proteins, which signals activation of second messenger system, which inhibits Adenylate cyclase thus decreasing cAMP production.As a result cAMP kinases act at target proteins, leading to modulation of ion channels causing hyperpolarization of cell membrane, by the inward movement of excessive K ions through ionic channels and suppression of entry of calcium ions at nerve terminals. These mechanisms, effectively suppress, both neuronal firing as well as, release of neurotransmitter, Nor-adrenaline at the nerve terminals. Both of these are the most essential and very useful mechanisms of action of the drugs which act as Alpha-$_2$ adrenergic agonist. Analgesia is provided through binding of Dexmedetom idine to Alpha-$_2$ adrenoceptors in the spinal cord. The overall response to Alpha-$_2$ adrenoceptor agonists is related to the stimulation of Alpha-$_2$ adrenoreceptors located in the CNS and spinal cord.The Alpha-$_2$ agonists produce their sedative-hypnotic effect by an action on Alpha-$_2$ receptors in the Locus caeruleus and an analgesic action at Alpha-$_2$ receptors within the Locus caeruleus and within the spinal cord.

MATERIALS AND METHODS

Design

This study "Dexmedetomidine for attenuating stress response after laryngoscope and intubation" was carried out at Meenakshi medical college and research institution, kancheepuram, Enathur between December 2013 to march 2015. This study was undertaken after obtaining Ethical committee as well as written informed consent for all 60 patients. 60 patients in different age group, either sex, belonging to ASA I and ASA II scheduled for elective surgical procedures under General Anesthesia were included.

Materials

Dexmedetomidine (DEXTOMID - 100µg/ml -2ml ampule)
Normal saline

Inclusion criteria:

1. Patients of either sex
2. Patient with ASA grade I and II
3. Patients scheduled for Elective surgical procedures under General Anesthesia.

Exclusion criteria:

1. Patient with anticipated difficult Airway
2. Hiatus Hernia
3. GERD
4. BMI>30
5. Patients on sedative,Hypnotics,Anti-hypertensive.

Pre-anesthetic evaluation:

On the day prior to surgery pre anesthetic evaluation was done. A through clinical examination of the patient was performed

including General examination and Systemic examination. Airway assessment was done by Mallampati grading to anticipate difficult intubation.All patients were explained about the Anesthetic technique and written informed consent taken. Patients were kept NPO for 8 hours prior to surgery. Routine investigation done [Hb, RBS, Urea, Creatinine, BT, CT, HIV, HbsAg, Chest X-ray,ECG]. No specific were required pertaining to the study.

Technique of Anesthesia/procedure:

60 patients belonging to ASA grade I & II were randomly divided into 2 groups, each group consist of 30 patients

GROUP I [SALINE group]

GROUP II [DEXMEDETOMIDINE group]

On the day of surgery, Anesthesia machines and circuits were checked, resuscitation equipments were kept ready. After confirmation of NPO status patient were shifted to the operation theatre & connected to monitor, Basal Systolic pressure(SBP), Diastolic blood pressure(DBP),Mean Arterial pressu re(MAP),Heart rate and SPO2(To) were recorded after 5 min of settling in the OT. An Intravenous line is secured of different size according to patient age. Following this,

- GROUP I [Saline group] patients receive 100 ml saline infused over 20 minutes.
- GROUP II [Dexmedetomidine group] patient receive Intravenous Dexmedetomidine .5µg per Kg in 100 ml normal saline infused over 20 minutes.

After 5 minutes of stabilization period SBP, DBP, MAP, Heart rate, SpO_2 (T_1) was recorded. Prior to Induction, Inj.Glycopyrrolate 0.2mg, Inj.Ondensatron 4mg administered IV. All patients were preo xygenated for 3 minutes and Anesthesia induced with 2mg/kg Propofol. After successful trial ventilation with 100% oxygen, Vecuronium 0.1mg/Kg to facilitate laryngoscopy and intubation. Oxygenation continued by positive pressure mask ventilation using Bain's circuit. Maintained with 50%O_2 and 50%N_2O. At 2 minutes after induction SBP, DBP, MAP,Heart rate, $SpO_2$was recorded (T_2). At 3 minutes after induction, using laryngoscope with a Macintosh blade intubation was done with well lubricated, appropriate sized cuffed, disposable oral Endotracheal Tube. After confirmation of the tube position by bilateral Auscultation for air entry, cuff inflated, and tube fixed, connected to Boyle's machine via Bains circuit. Anesthesia maintained with O_2,N_2O, Sevoflurane, controlled ventilation with appropriate fresh gas flow. SBP, DBP, MAP, Heart rate, SpO_2were recorded at 1(T_3),3(T_4),5(T_5),10 min(T_6) after laryngoscopy and Intubation.

Statistics and analysis :

Sample size of 30 per group was taken for this study data was expressed as mean +_ SD or absolute values quqlitative data were compared with chi square test and fisher's exact test.

Quantitative variables were compared with the student t test .The level of statistical significance was set at p<0.05.

Table 1. Showing the intergroup comparision of mean heart rate (bpm) changes in response to laryngoscope and intubation between saline group and Dexmedetomidine group

TIME	SALINE	DEXMEDE TOMIDINE	P VALUE	REMARKS
To(Basal)	89.13±11.40	87.50±11.02	0.575	NS
T1(Preinduction)	87.37±11.10	70.47±11.09	0.000	HS
T2(Induction)	87.10±10.78	69.93±10.26	0.000	HS
T3(1 min)	101.33±11.55	80.13±10.05	0.000	HS
T4(3 min)	99.53±11.64	77.47±9.74	0.000	HS
T5(5 min)	95.63±10.74	73.90±9.30	0.000	HS
T6(10 min)	92.47±10.23	73.17±9.68	0.000	HS

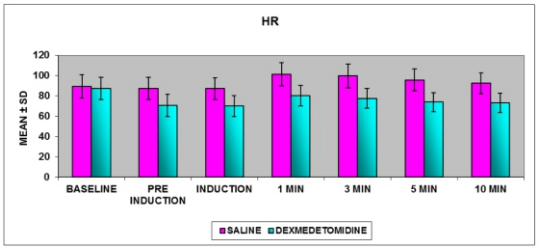

Figure 1: intergroup comparision of mean heart rate (bpm) changes in response to laryngoscopy and intubation between saline and dexmedetomidine group

Statistical evaluation between the group showed that the basal mean HR between Group I and Group II was Statistically not significant (p=.575), as pre-induction, Induction, 1, 3, 5 & 10 minutes after Intubation the HR changes were statistically Highly Significant (P=.000). In Group II there was a constant Decrease in HRfrom the time of pre-induction until 10th minute ofIntubation which when compared to that of Group I was Statistically Highly Significant.

Table 2. Showing inter group comparision of mean systolic blood pressure (SBP in mmHg) changes in response to laryngoscope and intubation between saline group and Dexmedetomidine group

TIME	SALINE	DEXMEDE TOMIDINE	P VALUE	REMARKS
To(Basal)	121.07±9.47	125.37±11.68	.123	NS
T1(Preinduction)	118.63±8.47	114.87±9.17	.104	NS
T2(Induction)	119.10±8.46	107.47±9.06	0.000	HS
T3(1 min)	125.77±7.90	114.33±8.70	0.000	HS
T4(3 min)	122.43±7.57	111.63±7.54	0.000	HS
T5(5 min)	119.47±6.99	110.00±8.09	0.000	HS
T6(10 min)	118.03±7.12	108.53±8.45	0.000	HS

Statistical evaluation between the group showed that the basal mean SBP between Group I and Group II was Statistically not significant (p=.123). Comparision of SBP between the 2 Groups at Pre-Induction was also Statistically not significanit (p=.104), at Induction, 1, 3, 5 & 10 minutes after Intubation the SBP changes were statistically Highly Significant (P=.000). In Group II SBP continued to remain below the base value from the Time of Pre-induction until 10th minute after Intubation which was Statistically Significant.

Figure 2: Intergroup comparision of mean systolic blood pressure (SBP in mm Hg) changes in response to laryngoscopy and intubation between saline and dexmedetomidine group

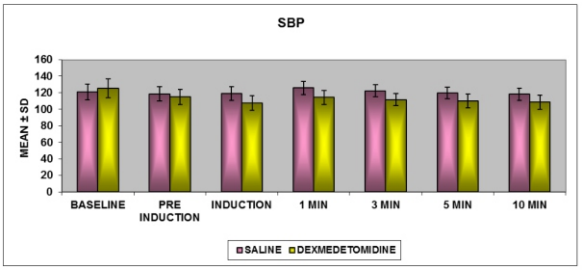

Table 3. Showing inter group comparision of mean diastolic blood pressure (DBP in mmHg) changes in response to laryngoscope and intubation between saline group and Dexmedetomidine group

TIME	SALINE	DEXMEDE TOMIDINE	P VALUE	REMARKS
To(Basal)	77.33±8.02	77.47±10.36	.956	NS
T1(Preinduction)	76.00±7.83	69.57±8.14	.003	S

T2(Induction)	76.10±7.19	65.60±7.26	0.000	HS
T3(1 min)	82.43±5.90	72.83±7.12	0.000	HS
T4(3 min)	78.40±7.15	67.90±6.38	0.000	HS
T5(5 min)	75.77±7.03	66.70±5.84	0.000	HS
T6(10 min)	75.77±7.26	64.50±5.20	0.000	HS

Statistical evaluation between the group showed that the basal mean DBP between Group I and Group II was Statistically not significant (p=.956), Comparision of DBP between the 2 Groups at Pre-Induction was also Statistically significant (p=.104). The comparision between the 2 Groups at Induction, 1, 3, 5 & 10 minutes after Intubation the DBP changes were statistically Highly Significant (P=.000). In Group II there was a constant Decrease in DBP from the time of pre-induction until 10th minute of Intubation which when compared to that of Group I was Statistically Significan .

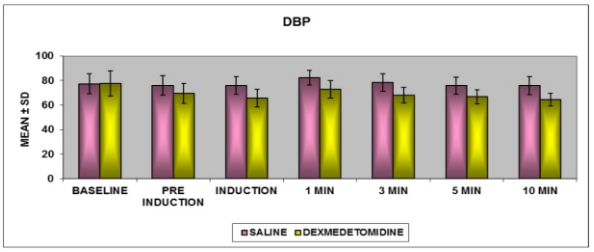

Figure 3: Intergroup comparision of mean diastolic blood pressure (DBP in mm Hg) changes in response to laryngoscopy and intubation between saline and dexmedetomidine group

Table 4. Showing inter group comparisionof mean mean arterial pressure (MAP in mmHg) changes in response to laryngoscope and intubation between saline group and Dexmedetomidine group

TIME	SALINE	DEXMEDE TOMIDINE	P VALUE	REMARKS
To(Basal)	91.40±8.05	93.20±10.58	.956	NS
T1(Preinduction)	89.83±7.65	84.80±8.61	.003	S
T2(Induction)	89.77±7.50	79.60±7.38	0.000	HS
T3(1 min)	96.33±6.15	86.53±7.12	0.000	HS
T4(3 min)	92.43±6.73	82.43±5.95	0.000	HS
T5(5 min)	89.50±6.52	80.97±6.06	0.000	HS
T6(10 min)	88.90±7.18	79.13±5.61	0.000	HS

Statistical evaluation between the group showed that the basal mean MAP between Group I and Group II was Statistically not significant (p=.956), Comparision of DBP between the 2 Groups at Pre-Induction was also Statistically significant (p=.003). The comparision between the 2 Groups at Induction, 1, 3, 5 & 10 minutes after Intubation the DBP changes were statistically Highly Significant (P=.000). In Group II there was a constant Decrease in MBP from the time of pre-induction until 10th minute of Intubation which when compared to that of Group I was Statistically Significant

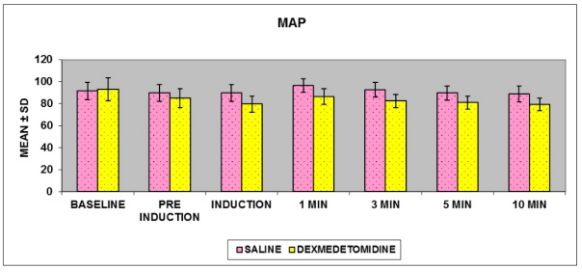

Figure 4: Intergroup comparision of mean mean arterial pressure (MAP in mm Hg) changes in response to laryngoscopy and intubation between saline and Dexmedetomidine group

DISCUSSION

The hemodynamic responses to laryngoscopy and endotracheal intubation have been recognized since 1951. Though these pressor responses have been observed frequently they have been interpreted differently by many authors. The induction of anaesthesia, laryngoscopy, endotracheal intubation and surgical stimulation often evoke cardiovascular responses characterized by alterations in systemic blood pressure, heart rate and cardiac rhythm. The response following laryngoscopy and intubation peaks at 1-2 min and returns to baseline within 5-10 mins

Pry's Roberts[10] et alstudied the laryngoscopy and intubation response in treated and untreated hypertensive patients, he observed tachycardia, hypertension and cardiac arrhythmias in both groups but it was more pronounced in untreated group. On discussion he has mentioned sympathoadrenal stress response to laryngoscopy results in an increase in myocardial oxygen demand leading to myocardial ischemia and acute heart failure in susceptible individuals. This reflex sympathetic response may be diminished or modified locally, centrally and peripherally, attempts have been made to accomplish this with varying success. In an attempt to blunt these potentially adverse hemodynamic responses, different techniques and agents were used by many authors with varying success.In this study, laryngoscopy response to intravenous Dexmedetomidine and saline groups are compared . The results obtained showed a stable haemodynamic profile with patients who received Dexmedetomidine when compared to saline groups.The indirect methods of determining anxiety or stress reduction are to examine changes in heart rate and blood pressure. With increasing anxiety or stress, a subject's heart rate and blood pressure (especially systolic) tend to increase as well, and vice versa. This is because fear and anxiety elicits the sympathetic nervous system, or the so-called "fight or flight" system response. One of the effects of sympathetic nervous system is to increase heart rate and systolic blood pressure. In fact, increase in heart rate and blood pressures are among the signs used to detect inadequate depth of Anesthesia by Anaesthesiologists. Therefore, the difference in heart rate, systolic & diastolic blood pressure and mean arterial pressure at different time intervals of the study when compared with baseline values prior to induction would indicate subject's level of stress.So this study was done to compare the effects of Dexmedetomidine in attenuating the haemodynamic response to laryngoscopy and intubation. Dexmedetomidine injection (5µg/kg) in 100ml normal saline infused over 20 minutes prior to intubation provided consistent and reliable protection against increases in mean heart rate ,systolic pressure, diastolic pressure, and mean arterial pressure during laryngoscopy and endotracheal intubation. In Dexmedetomidine group, HR, SBP, DBP, MAP showed significant decrease through the study period.Hence Intravenous Dexmedetomidine given 20 min before in the dose of .5 µg/kg body weight as infusion effectively attenuate the stress response after laryngoscope and intubation.

SUMMARY

A Prospective randomized study **"DEXMEDITOMIDINE FOR ATTENUATING THE STRESS RESPONSE AFTER LARYNGOSCOPE AND INTUBATION"**was carried out at Meenakshi medical college and research institution, Kancheepuram between December 2014 to March 2016.60 patients in different age group, either sex, belonging to ASA I and ASA II scheduled for elective surgical procedures under General anesthesia were included in the study. The patients with Hypertension, Difficult Airway, Obesitywere Excluded in the study. The study population was randomly divided in to twe groups of 30 each. GROUP I [Saline group] patients receive 100 ml saline infused over 20 minutes. GROUP II [Dexmedetomidine group] patient receive Intravenous Dexmedetomidine .5µg per Kg in 100 ml normal saline infused over 20 minutes. All patiets were premedicated with Inj.Glycopyrrolate 0.2mg, Inj.Ondensatron 4mg administered IV. Anesthesia was induced 20 minutes after the study drug with Inj. Propofol 2 mg/kg and Inj.Vecuronium .1 mg/kg was given to facilitate Laryngoscopy and intubation. Laryng oscopy and intubation was done after 3 min. The HR, SBP, DBP, MAP were recorded at 1, 3, 5 & 10 min after intubation.In Dexmedetomidine group, HR, SBP, DBP, MAP showed significant decrease through the study period. Hence Intravenous Dexmedetomidine given 20 min

before in the dose of .5 µg/kg body weight as infusion effectively attenuate the stress response after laryngoscope and intubation.

CONCLUSION

From the present study it has been concluded that

- Rather it produce stable heart rate than hypotension or hypertension.
- Produces greater cardiovascular stability on for as HR.MAP concern.
- Eventually BP varies in some individuals, it definetly attenuates pressor response as well as tachycardia.

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