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Intubation response suppression with dexmeditomidine and clonidine and a control- comparative study

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Abstract: *Endotracheal intubation includes laryngoscopy & intubation. The process of laryngoscopy & intubation are noxious stimuli & therefore constitute a period of extreme haemodynamic stress and is associated with intense sympathetic activity marked by tachycardia & hypertension[1].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[21] and among α-2 agonists both Clonidine and Dexmedetomidine appear to fulfil all the criteria of ideal agent.The study was undertaken to compare the effects of Dexmedetomidine and Clonidine in attenuating hemodynamic response to laryngoscopy and intubation. This study was done in 90 patients divided into 3 groups, in operation theatre in the department of anaesthesiology, smc. This study showed that IV bolus dose of Dexmedetomidine 1 mcg/kg administered 10 minutes before laryngoscopy and intubation can be recommended to attenuate the sympathetic response to laryngoscopy and intubation without any side effects than clonidine.*

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I. Introduction

Endotracheal intubation is the Trans laryngeal placement of a tube into the trachea via the nose or mouth. Endotracheal intubation includes laryngoscopy & intubation. The process of laryngoscopy & intubation are noxious stimuli & therefore constitute a period of extreme haemodynamic stress and is associated with intense sympathetic activity marked by tachycardia & hypertension[1]. Various pharmacological & non – pharmacological methods have been used to attenuate the haemodynamic response to laryngoscopy & endotracheal intubation.The non - pharmacological methods like smooth & gentle intubation with a shorter duration of laryngoscopy, insertion of LMA in place of endotracheal intubation[4]& blocking Glossopharyngeal & superior laryngeal nerves have been used to attenuate the cardiovascular response to laryngoscopy & endotracheal intubation[5]. Pharmacological methods like use of Inhalational anesthetics[6],Topical and Intravenous lidocaine[7,8,9], narcotics[10,11,12], β-Blockers[13,14,15], calcium channel Blockers[16,17,18], vasodilators[19,20],have been tried.None of the above approaches or agents 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[21] and among α-2 agonists both Clonidine and Dexmedetomidine appear to fulfil all the criteria of ideal agent. 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[22].

II. Material And Methods

The study was undertaken to compare the effects of Dexmedetomidine and Clonidine in attenuating hemodynamic response to laryngoscopy and intubation. This study was done in 90 patients divided into 3 groups

- To observe the variations in sympathetic response to laryngoscopy and intubation.
- To study effectiveness of

a) Dexmedetomidine 1mcg /kg bolus administration 10 minutes before laryngoscopy and intubation and
b) Clonidine 0.5mcg/kg administered 10 minutes before laryngoscopy and intubation in attenuating the sympathetic response.
c) And comparison of Dexmedetomidine and Clonidine in suppressing pressor response to intubation.

Inclusion criteria:

1. Patients aged between 20-50yrs
2. Patients of either sex
3. Patients with ASA grade I & II
4. Patients scheduled for elective surgical procedure under generalanaesthesia.

Exclusion criteria:
1. Unwilling patients,
2. Emergency surgeries,
3. Anticipated difficult intubation,
4. Patients SBP >140 mm of Hg and DBP <90mm of Hg,
5. Patients with ASA grading of 3 and 4.

Technique of anaesthesia/Procedure:
90 patients aged between 20 to 50 yrs. belonging to ASA grade I & II were randomly divided into 3 groups in a double blind manner, each group consists of 30 patients

1. **GROUP NS**- received plain normal saline
2. **GROUP D**- received 1mcg/kg of IV Dexmedetomidine 10 min before laryngoscopy and intubation
3. **GROUP C**-received 0.5mcg/kg of Clonidine 10 min before laryngoscopy and intubation

On the day of surgery, Anaesthesia machine and circuits were checked, resuscitation equipments were kept ready. After confirmation of NPO status patients were shifted to the operating room & connected to multichannel monitor Basal systolic blood pressure (SBP), diastolic blood pressure (DBP), Mean arterial pressure (MAP), heart rate and SpO2 (T0) were recorded after 5 min 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 & preloading with 500ml of Ringer lactate done over 30 min for all patients. Following this, Group NS [Saline group] patients received 100ml normal saline infused over 10 mins. Group D [Dexmedetomidine group] patients received Intravenous Dexmedetomidine 1µg per kg in 100ml normal saline infused over 10 mins. Group C [Clonidine group] patients received Intravenous Clonidine 0.5 µg per kg in 100ml normal saline infused over 10 mins. Prior to induction, Inj Glycopyrrolate 0.2mg, Inj Ondansetron 4mg, & Inj. Ranitidine 50mg were administered IV.

All patients were pre- Oxygenated for 3 mins& Anaesthesia induced with 5mg/kg Thiopentone sodium (2.5%).After successful trial ventilation with 100% oxygen, Succinyl choline 2 mg / kg given to facilitate laryngoscopy & intubation. Oxygenation continued by positive pressure mask ventilation using Dragger anaesthesia work station. Maintained with 50% O2 and 50% N2O.

After conforming relaxation, using laryngoscope with a Macintosh blade intubation was done with well lubricated, appropriate sized cuffed, disposable oral endotracheal tube by an experienced anaesthesiologist.

After confirmation of the tube position by bilateral auscultation for air entry, cuff inflated, and tube fixed, connected to anaesthesia work station. Anaesthesia maintained with N2O, O2, Isoflurane, controlled ventilation with appropriate fresh gas flow. SBP, DBP, MAP, Heart rate, SpO2 were recorded at 1 (T1), 3 (T2), 5 (T3) after laryngoscopy & intubation.

Sequence	SBP, DBP, MAP, Heart rate, SpO2 Recording
Basal reading when the patient is shifted to OT	T0
At 1 min after intubation	T1
At 3min after intubation	T2
At 5min after intubation	T3

Surgery commenced at the end of 5 min after laryngoscopy & intubation. No form of stimulus was applied during this period. Anaesthesia continued with N2O, O2, Isoflurane, Vecuronium loading dose given &top up doses, analgesics & IV fluids administered based on the requirements.

At the end of surgery, Isoflurane and N2O were discontinued and when respiratory attempts were present, residual neuromuscular blockade was reversed with Inj Neostigmine (0.05mg/kg) & Glycopyrrolate (0.01mg/kg). Recovery assessed &extubation done after thorough throat suction. After adequate clinical recovery patients shifted to post anaesthesia care unit, observed for 2 hrs. for Nausea vomiting, Bradycardia, Hypotension, & Sedation. Post-operative follow up for 24hrs was done; side effects if any were treated & recorded.

III. Observations & Results

Statistical analysis:
Descriptive data is presented as Mean ±SD and in percentage. Multiple group comparisons were made by one way ANOVA followed by unpaired t test for pair wise comparison for all the tests a p value of <0.05 was considered for statistical significance.

Table 1- Age Distribution
Case summaries

GROUP	N=no of patients	MEAN	STANARD DEVIATION	MINIMUM Age in years	MAXIMUM Age in years
Normal saline	30	32.1	8.8	20	50
Dexmedetomidine	30	35.8	9.6	20	50
Clonidine	30	33.4	9.2	20	50

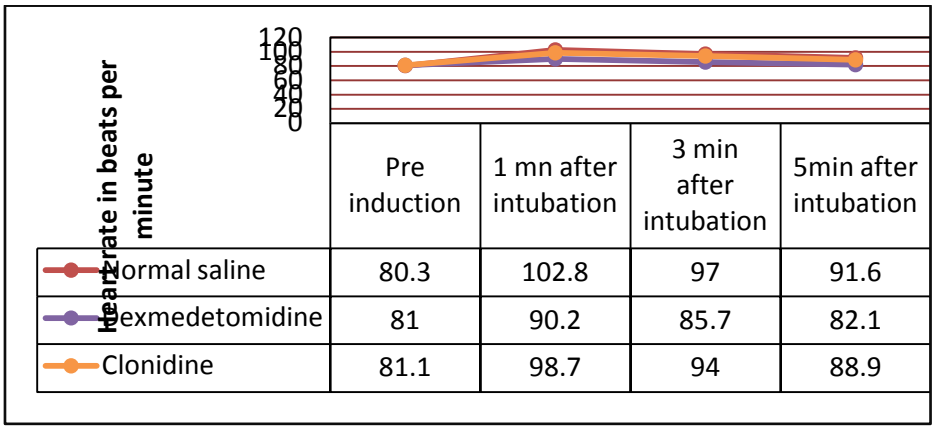
The above table shows age distribution in control study groups. The mean values of age with standard deviations are 32.1±8.8, 35.8±9.6, and 33.4±9.2 for normal saline, Dexmedetomidine and Clonidine groups respectively. There are no statistically significant difference between three groups. (P=0.28)

Table 3: Comparision Of Changes In Heart Rate

TIME OF ASSESSMENT	CONTROL(NS)		DEXMEDITOMIDINE(D)		CLONIDINE (C)		ANOVA "F"&*P VALUES	Difference between groups**		
	Mean +S.D	%diff	Mean +S.D	%diff	Mean +S.D	%diff		1-2	1-3	2-3
Pre induction	80.3+17.9	-	81 +20.3	-	81.1+13.1	-	0.94 >0.05	>0.05	>0.05	>0.05
1 min after intubation	102.8±19.6	28	90.2±18.4	11.3	98.7±14.5	21.7	3.34 <0.01	<0.01	>0.05	<0.05
3 min after intubation	97±12.2	20.8	85.7±16.2	5.8	94±12.8	15.9	5.27 <0.01	<0.01	>0.05	<0.05
5 min after intubation	91.6±11.7	14	82.1±15.4	1.3	88.9±14.1	9.6	3.81 <0.01	<0.01	>0.05	<0.05

-ve sign indicate decrease,*
P<0.05, P<0.01 are significant,
P<0.001 is highly significant,
P>0.05 is not significant (NS).

GRAPH 3: COMPARISION OF CHANGES IN HEART RATE



Changes in heart rate assessed at pre induction and at different time intervals from the onset of laryngoscopy and intubation in control & study groups and their comparative statistics are presented in the table.
There is no statistically significant difference between the pre induction heart rate between three groups.

Normal saline group:

The mean heart rate in this group before induction of anaesthesia was 80.3+17.9. At one minute from the onset of laryngoscopy and intubation heart rate increased by 28% with mean of 102.8±19.6 and remained at same significantly higher level with 20.8% rise with mean heart rate of 97±12.2 at the end of 3 minutes. A decreasing trend noticed from 5 minutes with mean heart rate of 91.6±11.7 which is 14% higher than pre induction value.

Dexmedetomidine group:

This study group shows the mean heart rate of 81 +20.3 before induction of anaesthesia. An increase of 11.3%in heart rate was observed at 1 minute from onset of laryngoscopy and intubation, having a mean value ± standard deviation 90.2±18.4.At 3minutes it decreased to 5.8%(85.7±16.2), Increase was only 1.3%(82.1±15.4) of pre induction level at the end of 5 minutes.

Clonidine group:

The mean pre induction heart rate in this group of patient`s was 81.1+13.1 .there was 21.7% increase in heart rate (98.7±14.5) noticed at the end of 1 minute from the onset of laryngoscopy and intubation. An increase in heart rate was 15.9% (94±12.8) observed at 3 minutes. Increase at the end of 5 minutes was 9.6% (88.9±14.1) of pre induction level.

One way ANOVA study showed significant variations in heart rate before and after induction and at the intervals if 1, 3,5 minutes from the onset of laryngoscopy and intubation(P<0.01).

The difference in heart rate between normal saline and Dexmedetomidine group remain statistically significant at all times of assessment (P<0.01).

There is no significant difference between normal saline and Clonidine groups (P>0.05).

There is a significant difference between Dexmedetomidine and Clonidine groups (P<0.05).

The maximum increase in heart rate is 28% in normal saline and 21.7%in Clonidine group. Attenuation of heart rate by Clonidine when compared with control group is not significant (P>0.05).

Increase in heart rate remain clinically significant till the end of 5 minutes in normal saline and in Clonidine groups.

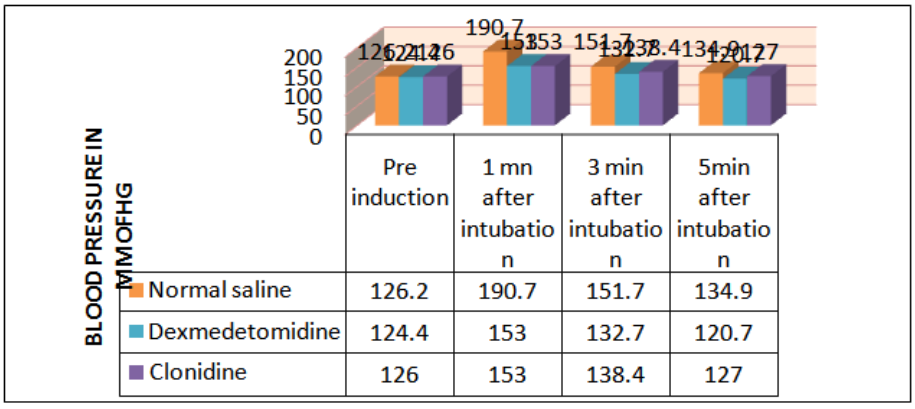
The heart rate response was clinically& statistically significantly attenuated with Dexmedetomidine group compared with normal saline and Clonidine groups at 1, 3, 5 minutes.

Table 4: Comparision of Changes In Systolic Blood Pressure

TIME OF ASSESSMENT	CONTROL(NS)		DEXMEDITOMIDINE(D)		CLONIDINE (C)		ANOVA "F"&*P VALUES	Difference between groups**		
	Mean +S.D	%diff	Mean +S.D	%diff	Mean +S.D	%diff		1-2	1-3	2-3
Pre induction	126.2±11	-	124.4±24.3	-	126±11.7	-	0.1 >0.05	>0.05	>0.05	>0.05
1min after intubation	190.7±30.4	51.1	153±21	22.9	153±29.3	21.4	3.7 <0.05	<0.05	<0.05	>0.05
3min after intubation	151.7±19.2	20.2	132.7±32.5	6.7	138.4±14.2	9.8	5.24 <0.01	<0.01	<0.01	>0.05
5min after intubation	134.9±14.7	6.8	120.7±15.1	-2.9	127±13	0.007	7.37 <0.005	<0.01	<0.05	>0.05

-ve sign indicate decrease than basal value,
P<0.05, P<0.01 are significant,
P<0.001 is highly significant,
P>0.05 is not significant (NS).

GRAPH 4: COMPARISION OF CHANGES IN SYSTOLIC BLOOD PRESSURE



The Changes in systolic blood pressure assessed at pre induction and at different time intervals from the onset of laryngoscopy and intubation in control & study groups and their comparative statistics are presented in the table. There was no statistically significant difference between the pre induction systolic blood pressures between three groups.

Normal saline group:

The mean systolic blood pressure in this group before induction of anaesthesia was 126.2±11. At one minute from the onset of laryngoscopy and intubation systolic blood pressure increased by 51.1% with mean systolic blood pressure of 190.7±30.4 and remained at same significantly higher level above basal value with 20.2%(mean of 151.7±19.2) at the end of 3 minutes. At 5 minutes mean systolic blood pressure was134.9±14.7 which is 6.8% higher than pre induction value.

Dexmedetomidine group:

This study group shows the mean systolic blood pressure of 124.4±24.3 before induction of anaesthesia. An increase of 22.9%in systolic blood pressure was observed at 1 minute from onset of laryngoscopy and intubation, having a mean value ± standard deviation 153±21 .At 3minutes increase was only 6.7%(132.7±32.5) It was further decreased to -2.9%(120.7±15.1) of pre induction level at the end of 5 minutes.

Clonidine group:

The mean systolic blood pressure before pre induction in this group of patients was126+11.7 .There was 21.4% increase in systolic blood pressure (153±29.3) noticed at the end of 1 minute from the onset of laryngoscopy and intubation. The increase was only 9.8% (138.4±14.2) observed at 3 minutes. It was 0.007% (127±13) at the end of 5 minutes compared to pre induction level. One way ANOVA study shows a statistically significant difference among all the groups at subsequent assessments (P<0.001 and P<0.01).

Attenuation of rise in systolic blood pressure is significant in Dexmedetomidine group with in 1 minute with P<0.05 and in 3& 5 minutes with P<0.01 in comparison to control group.

Also with Clonidine group statistically significant attenuation in comparison with control group seen in 1 minute P<0.05, in 3 minutes P<0.01 and in 5 minutes p<0.05.

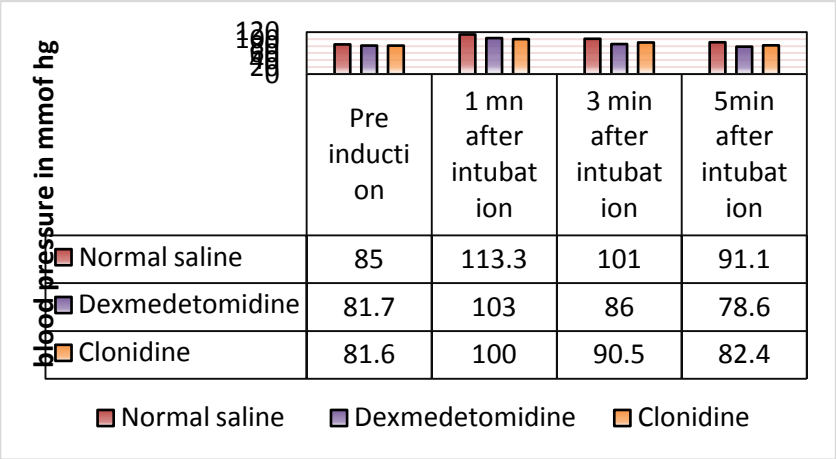
It returned to base line in both Dexmedetomidine and Clonidine groups in 5 minutes than normal saline group. But there is no statistically significant difference between Dexmedetomidine and Clonidine groups (P>0.05).

Table 5: Comparision Of Changes In Diastolic Blood Pressure

TIME OF ASSESSMENT	CONTROL(NS)		DEXMEDITOMIDINE(D)		CLONIDINE (C)		ANOVA "F"&*P VALUES	Difference between groups**		
	Mean +S.D	%diff	Mean +S.D	%diff	Mean +S.D	%diff		1-2	1-3	2-3
Pre induction	85±10.3	-	81.7±9	-	81.6±8.9	-	1.19 >0.05	>0.05	>0.05	>0.05
1 min after intubation	113.3±19	33.6	103±24.5	26	100±17.5	22.5	3.5 <0.05	<0.05	<0.01	>0.05
3 min after intubation	101±18.2	18.8	86±15.1	5.2	90.5±11.7	10.9	7.4 <0.001	<0.001	<0.01	>0.05
5 min after intubation	91.1±13.2	7.1	78.6±13.1	-3.7	82.4±9.2	0.9	8.4 <0.001	<0.001	<0.01	>0.05

-ve sign indicate decrease,
P<0.05, P<0.01 are significant,
P<0.001 is highly significant,
P>0.05 is not significant (NS).

Graph 5: Comparision Of Changes In Diastolic Blood Pressure



The Changes in Diastolic blood pressure assessed at pre induction and at different time intervals from the onset of laryngoscopy and intubation in control study groups and their comparative statistics are presented in the table. There was no statistically significant difference between the pre induction diastolic blood pressures between three groups

Normal saline group:

The mean Diastolic blood pressure in this group before induction of anaesthesia was 85±8.9. At one minute from the onset of laryngoscopy and intubation Diastolic blood pressure increased by 22.5% with mean diastolic blood pressure of 100±17.5 and increase was only with 18.8% rise with mean of 101±18.2 at the end of 3 minutes. At 5 minutes mean systolic blood pressure (91.1±13.2) which was 7.1% higher than pre induction value.

Dexmedetomidine group:

This study group shows the mean Diastolic blood pressure of 81.7±9 before induction of Anaesthesia. An increase of 26%in Diastolic blood pressure was observed at 1 minute from onset of laryngoscopy and intubation, having a mean value ± standard deviation 103±24.5 .At 3minutes it was only 5.2%(86±15.1) compared to pre induction value , It was further decreased to -3.7%(78.6±13.1) of pre induction level observed at the end of 5 minutes.

Clonidine group:

The mean Diastolic blood pressure before pre induction in this group of patients was 81.6+8.9 .There was 22.5% increase in diastolic blood pressure (100±17.5) at the end of 1 minute from the onset of laryngoscopy and intubation. It was 10.99% (90.5±11.7) at 3 minutes and it was 0.9% (82.4±9.2) at the end of 5 minutes compared to pre induction level. One way ANOVA test shows a statistically significant difference among all the groups (P<0.05 and P<0.001).

Attenuation of rise in diastolic blood pressure is significant in Dexmedetomidine group compared to normal saline group at 1 minute with P value of <0.05 and at 3& 5 minutes P<0.001. Also with Clonidine group significant attenuation compared to control group seen at 1 minute P<0.05 and at 3 &5 minutes P<0.01.

It returned to base line in both Dexmedetomidine and Clonidine groups at 5 minutes compared to normal saline group. But there is no statistically significant difference between Dexmedetomidine and Clonidine groups (P>0.05).

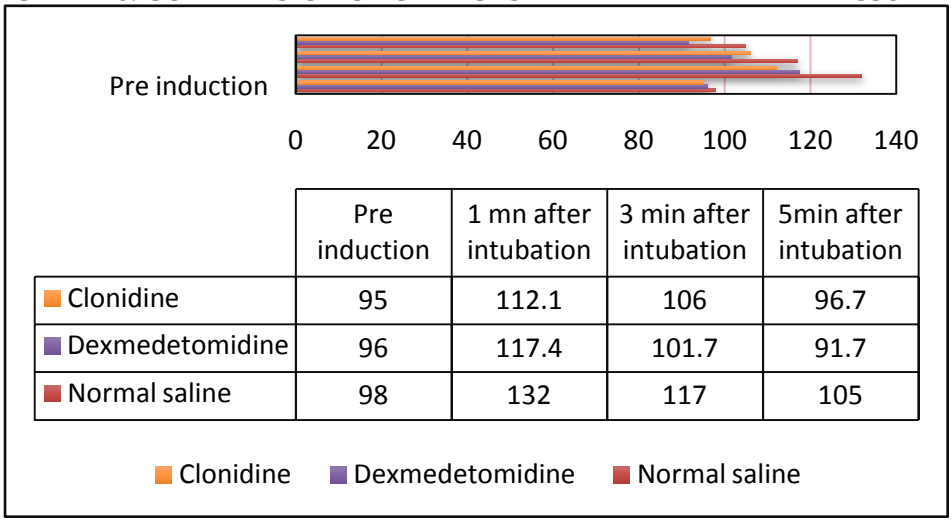
TABLE 6: Comparision of Changes in MeanArterial Blood Pressure

TIME OF ASSESSMENT	CONTROL(NS)		DEXMEDITOMIDINE(D)		CLONIDINE (C)		ANOVA "F"&*P VALUES	Difference between groups**		
	Mean +S.D	%diff	Mean +S.D	%diff	Mean +S.D	%diff		1-2	1-3	2-3
Pre induction	98±9.5	-	96±9.5	-	95±9.8	-	0.7 >0.05	>0.05	>0.05	>0.05
1 min after intubation	132±21	34.6	117.4±22	22.3	112.1±26.5	18	5.9 <0.005	<0.01	<0.01	>0.05
3 min after	117±18.	19.4	101.7±16.3	5.9	106±11.8	11.5	7.4	<0.01	<0.05	>0.05

intubation	5						<0.005			
5 min after intubation	105.2±12.3	7.1	91.7±14.1	-4.5	96.7±9.3	7.1	9.5 <0.005	<0.01	<0.01	>0.05

-ve sign indicate decrease,*
P<0.05, P<0.01 are significant,
P<0.001 is highly significant,
P>0.05 is not significant (NS).

GRAPH 6: COMPARISION OF CHANGES IN MEAN ARETRIAL PRESSURE



The Changes in mean arterial pressure assessed at pre induction and at different time intervals from the onset of laryngoscopy and intubation in control study and study groups and their comparative statistics are presented in the table. There was no statistically significant difference between the pre induction mean arterial pressures between three groups

Normal saline group:

The mean mean arterial pressure in this group before induction of anaesthesia was 98±9.5. At one minute from the onset of laryngoscopy and intubation mean arterial pressure increased by 34.6% with value of 132±21, 19.4% rise with value of 117±18.5 at 3 minutes, and at 5 minutes 7.1% rise with value of 105.2±12.3 which is above pre induction value.

Dexmedetomidine group:

This study group shows the mean mean arterial blood pressure of 81.7±9 before induction of anaesthesia. An increase of 22.3%in mean arterial pressure was observed at 1 minute from onset of laryngoscopy and intubation, having a mean value ± standard deviation 117.4±22 .At 3minutes it was 5.9%(101.7±16.3) Compared to pre induction value, It was decreased to -4.5%(91.7±14.1) of pre induction level at the end of 5 minutes.

Clonidine group:

The mean mean arterial pressure before pre induction in this group of patients was 95+9.8 .There was 18% increase in mean blood pressure(112.1±26.5) at the end of 1 minute from the onset of laryngoscopy and intubation. It was 11.5% (106±11.8) at 3 minutes. It was 7.1% (96.7±9.3) at the end of 5 minutes compared to pre induction level. One way ANOVA test shows a statistically significant difference among all the groups at subsequent assessments (P<0.01).

Attenuation of rise in mean arterial pressure is significant in Dexmedetomidine group and Clonidine group compared to normal saline group at all times with P<0.01. MAP returned to base line in both Dexmedetomidine and Clonidine groups at 5 minutes compared to normal saline group.
But there is no statistically significant difference between Dexmedetomidine and Clonidine groups. (P>0.05).

IV. Discussion

The sequence of induction in general anaesthesia, laryngoscopy and tracheal intubation are associated with marked haemodynamic changes and autonomic reflex activity which may be a cause of concern in many high risk patients. Laryngoscopy and intubation is associated with rise in heart rate, blood pressure and

incidence of cardiac arrhythmias[2].A powerful noxious stimulus like laryngoscopy and tracheal intubation induces hypothalamic activity and results in an increased outflow in the sympathetic tracts. Consequently norepinephrine is released by post ganglionic sympathetic fibers and increased secretion from adrenal medulla.

α-2 agonists like Clonidine and& Dexmedetomidine have been tried for suppressing the response to intubation and have been found to have better effects compared to all the drugs mentioned above, without any of the side effects like respiratory depression or increased incidence of PONV.

Dexmedetomidine does not appear to have any direct effects on the heart. A biphasic cardiovascular response has been described after the application of Dexmedetomidine. The administration of a bolus of 1 μg/kg body weight, initially results in a transient increase of the blood pressure and a reflex decrease in heart rate, especially in young healthy patients. The initial reaction can be explained by the peripheral alpha 2B adrenoceptors stimulation of vascular smooth muscles and can be attenuated by a slow infusion over 10 or more minutes. Even at slower infusion rate however the increase in mean arterial pressure over the first 10 minutes was shown to be in the range of 7% with a decrease in heart rate between 16% and 18%.The initial response lasts for 5-10 minutes and is followed by a decrease in blood pressure of approximately 10%-20% below baseline values; both these effects are caused by the inhibition of the central sympathetic outflow overriding the direct stimulant effects. Another possible explanation for the subsequent heart rate decrease is the stimulation of presynaptic alpha-2 adrenoceptors, leading to a decrease in norepinephrine release.

The affinity of Clonidine for these receptors is high, although the drug is a partial agonist with relatively low efficacy at these sites. The hypertensive response that follows parenteral administration of Clonidine generally is not seen when the drug is given orally. However, even after intravenous administration, the transient vasoconstriction is followed by a more prolonged hypotensive response that results from decreased sympathetic outflow from the CNS. The exact mechanism by which Clonidine lowers blood pressure is not completely understood. The effect appears to result, at least in part, from activation of α2 receptors in the lower brainstem region. This central action has been demonstrated by infusing small amounts of the drug into the vertebral arteries or by injecting it directly into the cisterna magna. The lack of an antihypertensive effect of Clonidine in knockout mice lacking α2A receptors supports a key role for these receptors in blood pressure regulations.

Clonidine being less potent (α-1: α-2=1:220) compared to Dexmedetomidine (α-1: α-2=1:1620) in its agonism to α-2 receptors. Dexmedetomidine may be a better drug among α-2 agonists for suppressing the haemodynamic responses to laryngoscopy and intubation.

Demographic criteria

Three groups were comparable and there was no statistically significant
Difference between the mean ages and sex. In this study optimal age range was 20 to 50 years.
The mean values of age with standard deviations are 32.1±8.8, 35.8±9.6, and 33.4±9.2 for normal saline, Dexmedetomidine and Clonidine groups respectively. There are no significant difference between three groups. (P=0.28)
In normal saline group 46%were males and 54% were females. Dexmedetomidine group had 56% males and 44% were females. Clonidine group contained 46%of male and 54% of female patients. No significant difference was observed in sex wise distribution of the cases between three groups (p>0.005).

Dose of Dexmedetomidine employed and administration

Various authors have employed IV Dexmedetomidine for blunting haemodynamic responses to laryngoscopy and intubation in different doses

Table 7: showing dose of Dexmedetomidine employed in various studies

Sl. No.	Authors and year	Dose of Dexmedetomidine employed
1	Kallio et al.[23]– 1989	12.5,25,50 and 75μg over 30 seconds
2	Aho et al.[24]- 1991	0.3 and 0.6μg/kg body weight over 60 sec 10 min prior to induction
3	Scheinin et al.[25]– 1992	0.6 μg/kg body weight in 10 ml saline over 1 min, 10 min before induction
4	Jaakola et al.[31]– 1992	0.6 μg/kg body weight over 1 min, 10 min before induction
5	Yildize et al.[26]– 2006	1μg/kg body weight infusion
6	Mowafi et al.[32]– 2008	0.6μg/kg body weight 50 ml saline 10 min before induction
7	Basar et al.[27]– 2008	0.5μg/kg body weight in 10 ml saline over 60 sec
8	Kunisawa et al.– 2009	1μg/kg body weight over 10 min, 15 min before induction followed by 0.7μg/kg/hr infusion

9	Ferdi et al.[28]– 2010	1µg/kg body weight in 100 ml saline over 15 min
10	Esra et al. [36]– 2010	0.5 and 1µg/kg body weight infusion 5 min and 10 min respectively before induction
11	Keniya et al [29].– 2011	1µg/kg body weight infusion 10 min before induction
12	SukhminderJit et al.[30]-2012	1µg/kg body weight in 100 ml saline over 20 min

Bijoy Kumar Panda et al In2012 conducted a study with groups of control, Clonidine and Dexmedetomidine. Of twenty patients each of ASA grade I & II category and >18 years of age. All the patients in the group C and D received injection Clonidine in the dose of 1 mcg/kg and Dexmedetomidine in the dose of 1 mcg/kg respectively over a period of 10 minutes prior to induction of anesthetic agents. During the infusion HR, systolic BP, diastolic BP, RR, oxygen saturation were recorded at 5 min interval and at 10 min.

They observed that Dexmedetomidine (Group D) showed a significant decrease in about 13% in DBP and HR compared to Clonidine (Group S) and Dexmedetomidine was well tolerated and no serious side effects or adverse reactions occurred in the present study.

They concluded that addition of Clonidine and Dexmedetomidine to the anesthetic regimen reduced the fluctuation of BP (DBP) and HR effectively during tracheal intubation. Dexmedetomidine compared to Clonidine to the anesthetic regimen, showed a significant reduction in myocardial contractility during tracheal intubation procedure. Even, during the intra-operative period the Dexmedetomidine compared to Clonidine showed a significant control of DBP and HR within a normal range.

Dishabanderi et al[25]in 2014 conducted a study to compare and evaluate the efficacy of the two alpha agonists Clonidine and Dexmedetomidine in prevention of hemodynamic stress response to laryngoscopy, intubation and carbon dioxide pneumoperitoneum. Forty five patients of ASA I & II posted for laparoscopic surgery were studied. Patients were randomly allocated into 3 groups. Group I (Placebo group; n=15) were given Inj Normal Saline i.v. Group II (Clonidine group; n=15) were given Inj Clonidine 1.5 mcg /kg i.v. 15 minutes before induction. Group III (Dexmed group; n=15) were given Inj Dexmedetomidine loading 1 mcg/kg over 10 minutes maintenance 0.4 mcg/ kg/ hr. iv infusion before induction. Heart rate, blood pressure, oxygen saturation, Etco2 were noted. Age, sex, weight and duration of surgery were comparable in all the three groups. The decrease in heart rate appeared more in Clonidine (group II) at all intervals when compared to Dexmedetomidine (group III) but the fall was found to be statistically significant only at end of pneumoperitoneum, and after reversal. The fall in mean blood pressure appeared more in Clonidine group at all intervals when compared to Dexmedetomidine group but the fall was not found to be statistically significant at any stage. Both Clonidine and Dexmedetomidine, maintained cardiovascular stability during laparoscopic surgery. But Clonidine was more effective in maintaining hemodynamic stability during the surgery.

In 2014 sharma et al [35] done a randomized prospective study to compare the effects of single premedication dose of I.V Dexmedetomidine with IV Clonidine in attenuating pressor response to laryngoscopy & endotracheal intubation. In this study Patients were randomly divided into 2 groups of 30 each. Group I patients received Clonidine 3 µg/kg and Group II patients received Dexmedetomidine 1microgm/kg in 100ml NS 10 min before induction. They observed in both the groups patients had attenuation of sympathetic response with decrease in HR and BP. At 1min and 3 min after Intubation rise in HR was more in Clonidine group which is statistically significant ($p < 0.01$). Fall in BP was comparable with both groups, after administering the study drug and at induction. At 1, 3, 5, 10 min after intubation both groups showed suppression of DBP, DBP, MAP ($p>0.05$) There was increase in HR in both the groups at 1, 3, 5, 10 min after intubation but increase in HR was more in Clonidine group which is statistically significant ($p<0.01$).From this study they concluded that both Clonidine and Dexmedetomidine attenuates the pressor response during laryngoscopy and Intubation but Dexmedetomidine is better in attenuating the tachycardia response.

V. Conclusion

- Dexmedetomidine significantly attenuates the sympathetic response to laryngoscopy and intubation.
- Clonidine also significantly attenuates the sympathetic response.
- Dexmedetomidine is more effective than Clonidine in attenuation in heart rate response to laryngoscopy and intubation.
- There is no statistically significant difference in attenuation of systolic blood pressure, diastolic blood pressure, and mean arterial blood pressure change during laryngoscopy and intubation between Dexmedetomidine and Clonidine groups, though clinical variability is observed.
- IV bolus dose of Dexmedetomidine 1 mcg/kg administered 10 minutes before laryngoscopy and intubation can be recommended to attenuate the sympathetic response to laryngoscopy and intubation without any side effects.

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