Original Research Paper

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COMPARING THE EFFECTS OF NEBULIZED DEXMEDETOMIDINE AND NEBULIZED NORMAL SALINE (0.9%) IN BLUNTING HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION

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ABSTRACT **BACKGROUND AND AIMS:** Laryngoscopy and tracheal intubation are considered as the most critical events during administration of general anaesthesia as they provoke transient but marked sympathoadrenal response manifesting as hypertension and tachycardia. In this study, we compared the effect of nebulized dexmedetomidine and nebulized normal saline (0.9%) in blunting haemodynamic response to laryngoscopy and intubation. **MATERIALS & METHOD:** This was a Prospective, double blinded randomized controlled study on 60 patients of 18 to 60 years of age and either sex with American society of Anaesthesiologists class I,II & III, who were posted for elective surgery requiring general Anaesthesia with endotracheal intubation. Patients are equally divided into two groups, Group D and Group S (30 patients each). Control group S (n = 30) received nebulisation with 5 ml of normal saline and group D (n = 30) received 1 µg/kg dexmedetomidine 5 ml 15 min before induction in sitting position. After intubation, the patient was undisturbed for a period of 10 minutes and cardiovascular parameters were recorded at different time. Statistical analysis was done by unpaired 't' test. P value of <0.05 is considered statistically Significant. **RESULTS:** Demographics were comparable. Following laryngoscopy and intubation, heart rate (HR) systolic (SBP), diastolic (DBP) and mean arterial pressure (MAP) were markedly increased in the control group whereas in group D there was a fall in Heart rate (P<0.001 at 0, 1 & 5 mins and P<0.05 at 10 min), SBP (P<0.001 at 0, 1, 5 & 10 mins interval), DBP (P<0.001 at 0, 1, 5 & 10 mins interval), MAP (P<0.001 at 0, 1, 5 & 10 mins interval). **CONCLUSION:** Nebulization of dexmedetomidine in a dose of 1 microgramg/kg is effective in blunting hemodynamic stress response to laryngoscopy and endotracheal intubation as compared to normal saline.

KEYWORDS : Dexmedetomidine, intubation, laryngoscopy.

INTRODUCTION:

Direct laryngoscopy and intubation are noxious stimuli and are associated with transient, unpredictable and variable haemodynamic changes. This response occurs within 30 sec after intubation and lasts less than 10 min.[1]

Many methods have been tried to blunt this haemodynamic response with variable success rate; including deep levels of general anaesthesia prior to endotracheal intubation, using topical anaesthesia of upper respiratory tract, administration of intravenous local anaesthetic agents (lignocaine), beta blocking agents (esmolol, metoprolol), vasodilators (sodium nitroglycerine), calcium channel blockers (nifedipine, nicardipine), narcotic analgesics (fentanyl, remifentanil) and some other agents including oral gabapentin, pregabalin and clonidine etc.

Dexmedetomidine a centrally acting α-2 agonist has sedative, analgesic, hypnotic actions in addition to reducing the anaesthetic drug requirements; has been found to blunt the haemodynamic response to laryngoscopy and endotracheal intubation.

Dexmedetomidine has the potential to produce bradycardia and hypotension when administered as a bolus; in a way to circumvent this problem, nebulisation route was chosen. Moreover, nebulised dexmedetomidine has a bioavailability of 65% through the nasal mucosa and 82% through the buccal mucosa.[2,3] Nebulised drug administration may be preferred over intranasal administration, as it avoids transient nasal irritation, cough, vocal cord irritation or laryngospasm.[4]

This study is planned to compare the efficacy of nebulized Dexmedetomidine and nebulized normal saline (0.9%) in attenuating this haemodynamic responses to laryngoscopy and endotracheal intubation. We hypothesized that Dexmedetomidine will blunt the haemodynamic response to laryngoscopy and tracheal intubation safely and more effectively.

METHODS:

After taking the Institutional Ethics Committee's approval (registration no. ECR/6/INST/GUJ/2013) and written informed consent of patient in their own vernacular language, This Prospective Randomized, double blinded study was conducted on 60 patients of 18 to 60 years of age, either sex, ASA grade I,II & III and BMI between 18.5 to 29.9 kg/m^2 who were posted for elective surgery requiring general Anaesthesia with endotracheal intubation. Patients having upper respiratory tract infection, coughing, cardiopulmonary disease, coagulopathies, raised intracranial tension, BMI more than 30kg/m^2, ASA grade IV & V, predicted difficult airway, head & neck pathology & patient undergoing emergency surgeries are excluded.

A day prior to the surgery, a preoperative visit was made and a detailed history and clinical examination of the patient was done. All patients were explained about the study protocol and the consent was obtained for the same.

The patients were kept fasting for 6 hours before surgery.

All patients received intravenous infusion of injection Ringer's lactate at rate of 100 ml/hr before beginning of induction of anaesthesia.

All patients in study group were divided equally in two groups by cheat method. Then the patients in group D were Nebulized with injection Dexmedetomidine 1µg/kg diluted with normal saline (0.9%) to a total volume of 5 ml with a nebulizer face mask before 15 minutes of induction in sitting position. Patients in group S were nebulized with injection normal saline (0.9%) 5ml with a portable electric nebulizer and face mask before 15 minutes of induction in sitting position.

Patients were premedicated with injection Ondansetron 80mcg/kg and injection Glycopyrrolate 4mcg/kg and injection midazolam 20mcg/kg intravenously before induction.

Then patients were preoxygenated for 5 minutes with 100% oxygen. Patients were induced with injection Propofol 2mg/kg iv slowly till the loss of eye lash reflex followed by injection Succinylcholine 2mg/kg iv stat. Laryngoscopy and intubation was performed using Macintosh curved blade and appropriate sized oral, portex, cuffed endotracheal tube. After confirmation of bilateral equal air entry, the endotracheal tube was fixed properly.

The patient was undisturbed for a period of 10 minutes after intubation and the following cardiovascular parameters were recorded in all patients at 0 min, 1 min, 5 min and 10 min.

- Heart rate [HR] in beats per minute
- Systolic blood pressure [SBP] in mm of H
- Diastolic blood pressure [DBP] in mm of Hg
- Mean arterial pressure [MAP] in mm of Hg
- Pulse oximetry(Spo2)

Neuromuscular blockade was done with loading Injection Atracurium

0.5mg/kg iv slow.

Anaesthesia was maintained using nitrous oxide (N2O) 60% and oxygen (O2) 40% with traces of inhalational anaesthetic agents and neuromuscular blockade maintain with injection Atracurium 0.1mg/kg iv slow as and when required.

All the patients were administered with Inj. paracetamol 15 mg/kg IV intraoperatively.

At the end of the surgery, reversal of anaesthesia was done with injection Neostigmine 80 mcg/kg and injection Glycopyrrolate 8 mcg/kg intravenously.

Patients were extubated smoothly in chest up position after adequate recovery of respiration, responses and reflexes.

After removal of endotracheal tube, patient was observed and was shifted to post Anaesthesia care unit with pulse oximetry monitoring.

Postoperatively patients were observed for complications like Bradycardia, Tachycardia, Hypertension, Hypotension, Drowsiness, Respiratory depression, Nausea, vomiting, Sore throat and Coughing. Statistical analysis was done using unpaired 't' Test to find P value. (p value >0.05 is considered Non significant, p value <0.05 is considered significant, p value <0.001 is considered Highly significant).

RESULTS:

Table 1 shows, In group D mean age was 51.50 years with SD 7.35, in group S mean age was 49.57 year and SD 3.66 which was statistically insignificant. In group D mean weight was 60.87 kgs with SD 5.43 in group S mean weight was 60 kgs and SD 4.91 which was statistically insignificant. In group D 14 were male and 16 were female, in Group S 14 were male and 16 were female.

Table 1 : Demographic Data

Demographic Data	Group D (%)	Group S (%)
Age (in years)	51.50 ±7.35	49.57 ± 3.66
Weight (in kg)	60.87 ± 5.43	60.00 ±4.91
Gender (Male:female)	14:16	14:16

Table - 2 shows comparison between both groups with regard to mean heart rate ± SD from baseline value, at various time intervals. P<0.0001 shows that there is highly significant difference in changes in mean pulse rate between both groups at all point of study except basal value.

Table 2: Showing The Intergroup Comparison Of Mean Heart Rate (bpm) Changes In All Groups

	Group D	Group S	P-value
Base Line	86.67 ± 7.51	85.60 ± 7.05	0.504
After Nebulization	80.93 ± 3.88	85.60 ± 7.05	0.002
Immediately after intubation (0 min)	85.80 ± 4.73	97.00 ± 6.78	0.00001
1 min after intubation	84.00 ± 4.36	91.87 ± 6.64	0.00001
5 min after intubation	82.20 ± 4.39	88.60 ± 7.01	0.00001
10 min after intubation	80.87 ± 4.22	84.73 ± 7.51	0.017

Table - 3 shows basal mean SBP were comparable in both groups (p=0.463). Statistical evaluation between the groups showed significant fall in SBP in group D after nebulization and before and after induction compared to group S. The decrease in mean SBP observed at 0, 1, 5 and 10 minutes after intubation in group D was statistically highly significant compared to the same in group S (p=0.0001).

Table 3: Showing The Intergroup Comparison Of Mean Systolic Blood Pressure (mm Hg) Changes In All Group

	Group D	Group S	p-value
Base Line	130.93 ± 5.34	132.00 ± 5.82	0.463
After Nebulization	123.80 ± 5.10	132.00 ± 5.82	0.0001
Immediately after intubation (0 min)	128.93 ± 5.52	141.67 ± 5.80	0.0001
1 min after intubation	127.06 ± 5.13	137.13 ± 5.84	0.0001
5 min after intubation	125.53 ± 5.39	133.53 ± 5.77	0.0001
10 min after intubation	124.06 ± 5.49	130.20 ± 5.59	0.0001

Table - 4 shows the basal mean DBP were comparable in both groups. The decrease in mean DBP observed at 0, 1, 5 and 10 minutes after intubation in group D was statistically highly significant compared to same in group S (p=0.0001).

Table 4 : Showing The Intergroup Comparison Of Mean Diastolic Blood Pressure (mmHg) Changes In All Group

	Group D	Group S	P-value
Base Line	84.33 ± 3.24	83.13 ± 4.15	0.218
After Nebulization	77.73 ± 3.05	83.13 ± 4.15	0.0001
Immediately after intubation (0 min)	82.46 ± 3.26	93.40 ± 4.36	0.0001
1 min after intubation	80.80 ± 2.99	89.20 ± 4.28	0.0001
5 min after intubation	79.67 ± 3.15	86.33 ± 4.20	0.0001
10 min after intubation	78.26 ± 3.09	83.06 ± 4.09	0.0001

Table - 5 shows the basal mean MAP values were comparable in both groups. Statistical evaluation between the groups showed a significant fall in MAP in group D after nebulization and before induction compared to group S. The decrease in mean MAP observed at 0, 1, 5 and 10 minutes after intubation in group D was statistically highly significant compared to same in group S (p=0.0001).

Table 5 : Showing The Intergroup Comparison Of Mean Arterial Pressure (mmHg) Changes In All Group

	Group D	Group S	P-value
Base Line	99.33 ± 3.24	98.13 ± 4.15	0.218
After Nebulization	92.73 ± 3.05	98.13 ± 4.15	0.0001
Immediately after intubation (0 min)	97.47 ± 3.26	108.06 ± 5.11	0.0001
1 min after intubation	95.80 ± 2.99	104.20 ± 4.28	0.0001
5 min after intubation	94.67 ± 3.15	101.33 ± 4.20	0.0001
10 min after intubation	93.27 ± 3.09	98.27 ± 3.98	0.0001

DISCUSSION:

The haemodynamic responses to laryngoscopy and intubation are elevation of heart rate, systolic and diastolic pressure which are well known. The potential for life threatening complications associated with these responses is also well documented. Traditionally used drugs like Lignocaine, Magnesium Sulfate, Opioids like Fentanyl, Sufentanil, Remifentanil, Alfentanil, Buprenorphine and blockers like Esmolol, labetalol etc. are either not fully effective or are associated with considerable side effects at doses required to attenuate these responses.

The drugs for controlling these haemodynamic responses aim to stabilize heart rate and blood pressure during laryngoscopy and endotracheal intubation in order to prevent any rise in myocardial work load and oxygen demand as well as to preserve the perfusion of vital organs.

Nebulisation is an alternate method of drug delivery with higher bioavailability, greater ease of administration[2,3] and less effect on haemodynamics as compared to the intravenous (IV) route. Various drugs have been tried through nebulisation for sedation and blunting haemodynamic response such as lignocaine by Laurito et al.[5] and midazolam by Kaabachi et al.[6] Nebulised dexmedetomidine[4,7] before induction of anaesthesia was contemplated as it has a very short distribution half-life of 6 min and elimination half-time of 2 h without the adverse haemodynamic effects of IV dexmedetomidine. Zanaty and El Metainy[4] compared nebulised dexmedetomidine, nebulised ketamine and their combination. They concluded that the combination resulted in better sedation, smoother induction and more rapid recovery. The present study aimed to study the effectiveness of nebulized dexmedetomidine (1µg/kg) in attenuating haemodynamic response to laryngoscopy and endotracheal intubation and to note any significant side effects caused by the drugs.

HAEMODYNAMIC CHANGES:

The mean basal heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were statistically similar in both groups.

Heart Rate :

In our study as shown in table no. 2, Mean basal heart rate was comparable in both the groups (p=0.504). So changes in mean basal pulse rate was statistically not significant (P>0.05). While at all other observations, the changes in mean pulse rate between group D and group S was statistically highly significant (P<0.0001).

A study conducted by Satyajeet Misra, Bikram Kishore Behera,

Jayanta Kumar Mitra, Alok Kumar Sahoo, Sritam Swarup Jena, Anand Srinivasan[8] on effect of preoperative dexmedetomidine nebulization on the hemodynamic response to laryngoscopy and intubation. They found significant effect of preoperative dexmedetomidine nebulization (1microgram/kg) versus saline treatment on the Heart Rate. After laryngoscopy, linear mixed effect modelling showed significantly lower trend of increase in HR in the dexmedetomidine group versus saline (P = 0.012).

A study conducted by Nimmagadda R R Kumar, Nirmala Jonnavithula, Shibani Padhy, Virinchi Sanapala, Vadithe Vasram Naik[9] on evaluation of nebulised dexmedetomidine in blunting haemodynamic response to intubation in which control group C (n = 50) received nebulisation with 5 ml of normal saline and group D (n = 50) received 1 µg/kg dexmedetomidine 5 ml 10 min before induction. In Heart Rate they found statistically significant result (p 0.03) when compared to baseline value within the group. The difference in HR between the two groups at various time intervals following laryngoscopy and intubation was comparable but not statistically significant with P 0.990 probably due to use of sedative and analgesic like fentanyl giving greater depth of sedation.

Mumtaz Hussain, Nidhi Arun, Sanjeev Kumar, Arvind Kumar, Rajnish Kumar, Saurav Shekhar[10] conducted a study on effect of Dexmedetomidine Nebulization on Attenuation of Haemodynamic Responses to Laryngoscopy. They patients in Group N had statistically higher values of Heart Rate after intubation at all time intervals in comparison to patients of Group D.

Findings of the above all studies are comparable with the present study.

Systolic Blood Pressure

In this study as shown in table no. 3, Mean basal systolic blood pressure was comparable in both the groups (p=0.463). So changes in mean basal systolic blood pressure was statistically not significant (P>0.05) and at all other points between both groups; changes in mean systolic blood pressure was statistically significant (P<0.05).

A study conducted by Nimmagadda R R Kumar, Nirmala Jonnavithula, Shibani Padhy, Virinchi Sanapala, Vadithe Vasram Naik[9] on evaluation of nebulised dexmedetomidine in blunting haemodynamic response to intubation. They found systolic blood pressure values after nebulization and immediately after intubation were comparable in both groups. The SBP values at 1, 5 and 10 min after intubation were lower in group D in a statistically significant manner with P values of 0.01, 0.02, 0.03, respectively.

Mumtaz Hussain, Nidhi Arun, Sanjeev Kumar, Arvind Kumar, Rajnish Kumar, Saurav Shekhar[10] conducted a study on effect of Dexmedetomidine Nebulization on Attenuation of Haemodynamic Responses to Laryngoscopy. They found comparable mean SBP at baseline in both the groups (p=0.73). Patients in Group- N had statistically higher values of SBP after intubation at all time intervals in comparison to patients of Group - D.

Findings of the above all studies are comparable with the present study.

Diastolic Blood Pressure

In our study as shown in table no. 4, mean basal diastolic blood pressure in both the groups was comparable (p=0.218). So changes in mean basal diastolic blood pressure was statistically not significant (P>0.05) and at all other points between both groups; changes in mean systolic blood pressure was statistically significant (P<0.05).

A study conducted by Nimmagadda R R Kumar, Nirmala Jonnavithula, Shibani Padhy, Virinchi Sanapala, Vadithe Vasram Naik[9] on evaluation of nebulised dexmedetomidine in blunting haemodynamic response to intubation. They found diastolic blood pressure after nebulization and immediately after intubation were comparable in both groups. The DBP values following laryngoscopy and intubation at 1, 5 and 10 min were lower in group D, which was statistically significant with P values of 0.001, 0.001, 0.01, respectively.

Mumtaz Hussain, Nidhi Arun, Sanjeev Kumar, Arvind Kumar, Rajnish Kumar, Saurav Shekhar[10] conducted a study on effect of Dexmedetomidine Nebulization on Attenuation of Haemodynamic Responses to Laryngoscopy. They found mean DBP at baseline was comparable in both the groups (p=0.120). Patients in Group- N had statistically higher values of DBP after intubation at all time intervals in comparison to patients of Group - D.

Findings of the above all studies are comparable with the present study.

Mean Arterial Pressure

In this study as shown in table no. 5, basal Mean arterial pressure in both the groups was comparable (p=0.218). So changes in basal mean arterial pressure was statistically not significant and at all other points between both groups; changes in mean systolic arterial pressure was statistically significant (P<0.05).

A study conducted by Nimmagadda R R Kumar, Nirmala Jonnavithula, Shibani Padhy, Virinchi Sanapala, Vadithe Vasram Naik[9] on evaluation of nebulised dexmedetomidine in blunting haemodynamic response to intubation. They found mean arterial pressure after nebulization and immediately after intubation were comparable in both groups. The MAP values after intubation were lower in group D, which was statistically significant at 1, 5 and 10 mins with p<0.05 at all times.

Mumtaz Hussain, Nidhi Arun, Sanjeev Kumar, Arvind Kumar, Rajnish Kumar, Saurav Shekhar[10] conducted a study on effect of Dexmedetomidine Nebulization on Attenuation of Haemodynamic Responses to Laryngoscopy. They found MAP at baseline was comparable in both the groups (p=0.323). Patients in Group- N had statistically higher values of DBP after intubation at all time intervals in comparison to patients of Group - D.

Findings of the above all studies are comparable with the present study.

CONCLUSION:

Nebulization of dexmedetomidine in a dose of 1 microgram/kg is effective in blunting hemodynamic stress response to laryngoscopy and endotracheal intubation.

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