HAEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION AFTER INTRAVENOUS DEXMEDETOMIDINE: A COMPARISON BETWEEN TWO DOSES

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ABSTRACT

BACKGROUND

Many pharmacological drugs are used to attenuate the haemodynamic response to laryngoscopy and endotracheal intubation. Dexmedetomidine, a highly selective α2 agonist has pharmacological properties like sedation, sympatholysis, analgesic property and less respiratory depression with preservation of the ventilator response to carbon dioxide and makes it an ideal adjuvant drug during general anaesthesia, in comparison to other drugs. In this study we compared the effects of two different doses of Dexmedetomidine on the haemodynamic responses during laryngoscopy and endotracheal intubation.

MATERIALS AND METHODS

Ninety patients of American society of anesthesiologists (ASA) physical grades I and II undergoing general anaesthesia were randomly allocated into three groups of 30 patients each. Values of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure (MAP) were recorded before giving the drug. Group A, Group B and Group C received 20 ml of Inj. Normal Saline, Inj. Dexmedetomidine 0.5 µg/Kg diluted to 20 ml with normal saline and dexmedetomidine 0.75 µg/Kg body weight diluted to 20 ml normal saline respectively as infusion over 10 minutes. Sedation scores were also recorded 1 min and 3 min after giving the test drugs. HR, SBP, DBP, MAP were recorded 1 min, 3 min, 5min, and 10 minutes after laryngoscopy and intubation.

RESULTS

The increase in HR, SBP, DBP and MAP after intubation were significantly less in Group C than Group A and Group and B and lasted longer than Group A and Group B. Sedation score was significantly low in Group C than Group A and Group B

CONCLUSION

Both the doses of Intravenous dexmedetomidine 0.5 µg/Kg body weight and 0.75 µg/Kg body weight attenuate the haemodynamic response of laryngoscopy and endotracheal intubation, but the dose of 0.75 µg/Kg body was found to be more effective than 0.5 µg/Kg body weight.

KEYWORDS

Dexmedetomidine, Laryngoscopy, Intubation, Attenuation, Intubation Response.

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BACKGROUND

Laryngoscopy and endotracheal intubation are one of the most important methods of securing airway for proper ventilation during General anaesthesia and surgery. This laryngoscopy and endotracheal intubation evokes prompt physiological response such as autonomic and activated brain stem reflexes which increase blood pressure, plasma catecholamine levels, heart rate and even leads to dysrhythmias in some cases.[1] Various methods and medications have been used to obtund these hemodynamic changes to laryngoscopy and endotracheal intubation such as-deepening of the depth of anaesthesia, minimizing the duration and attempt of laryngoscopy and intubation (less than 15 sec), administering drugs such as intravenous lidocaine, vasodilators drugs, beta adrenergic blockers, calcium channel blockers etc.[2-10] Some researchers used magnesium sulphate and melatonin and found useful in attenuating the presser response during laryngoscopy intubation.[11-13] Many drugs have been compared to attenuate the presser responses. Dexmedetomidine is an alpha 2 adrenergic receptor agonist which reduces heart rate and blood pressure, has sedative and analgesic effect, decreases cardiovascular responds to laryngoscopy & intubation and surgical stimuli. Premedication with dexmedetomidine 1.0 µg/Kg body wt. obtunds the presser response to laryngoscopy and intubation when used as adjuvant to general anaesthesia.[14-17] Many researchers have compared dexmedetomidine with other drugs such as esmolol, magnesium sulphate, clonidine etc. and found that

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it is superior to these drugs in obtunding the hemodynamic changes during intubation.[18-25] Effects of different doses of dexmedetomidine on intubation response have also been studied. Dexmedetomidine in the doses of 0.5 µg/Kg body wt. and 1.0 µg/Kg body weight given as infusion before the induction of general anaesthesia are found to be effective in attenuating the stress response to laryngoscopy and intubation. Others have used different doses but the higher dose of 1 µg/Kg and above were found to be associated with higher cardiovascular side effects like hypotension and bradycardia and also increased sedation whereas lower doses are less effective in obtunding the hemodynamic changes during laryngoscopy and intubation. Hence, we designed a randomized, prospective study to determine whether dexmedetomidine in the dose of 0.75 µg/Kg can attenuate the haemodynamic response to laryngoscopy and endotracheal intubation with minimization of the unwanted side effects.

Aims and Objectives

This study was undertaken to find out an optimal dose of dexmedetomidine to attenuate the stress responses during laryngoscopy and endotracheal intubation by comparing two doses of dexmedetomidine 0.5 µg/Kg body weight and 0.75 µg/Kg body weight with a placebo.

MATERIALS AND METHODS

It was a randomized double blinded study conducted in three groups of patients aged 18-50 years of either sex, with the American Society of Anaesthesiologist (ASA) physical status I & II scheduled for elective surgeries under General Anaesthesia, and has signed a written informed consent form. Patient with predictable difficult intubation, physically dependent on narcotic, bronchial asthma, drug or alcohol abuser, allergic to either clonidine or dexmedetomidine, cerebrovascular, neurological, respiratory or ischemic heart disease, renal and hepatic dysfunction, hypertension, diabetes mellitus, pheochromocytoma, on beta blockers, antidepressant, anxiolytic, anticonvulsant, antipsychotic were excluded from the study. Bradycardia was defined as HR <50/minutes and Tachycardia was defined as HR>100 beats/minute. Hypotension was defined as systolic blood pressure < 20% of the baseline value

Sample Size

The sample size was estimated with reference to previous study using the mean HR at 5 minutes. At 95% confidence limit and 90% power, a sample size of 26 is obtained in each group by taking the largest mean difference at 7.91 and expected bacKground standard deviation (SD) of 9.1 and presuming 10% non-respondent, the sample size of 26 + 2.6, rounded to 30 patients were included in the study in each group.

Sample Grouping

The patients were randomly (computer- generated) allocated to three groups -Groups A, Group B and Group C. Group A received 20 ml of Normal saline. Group B received dexmedetomidine 0.5 µg/Kg body weight diluted to 20 ml normal saline, Group C received dexmedetomidine 0.75 µg/Kg body weight diluted to 20 ml normal saline.

Anaesthetic Procedure

After obtaining institutional Ethical committee clearance, ninety patients belonging to American society of Anesthesiologists physical status I and II (ASA I and ASA II), in the age group 18 -50 yrs. of either sex, posted for elective surgeries were enrolled for the study. All the patients were evaluated one day before the surgery. The patients were kept nil orally for 8 hours and they received tab Ranitidine 150 mg and tab alprazolam 0.5 mg orally as premedication on the night before surgery. Patients were divided into three groups of thirty each. On the day of surgery, patients were monitored with electrocardiography, pulse oximetry and non-invasive blood pressure. After securing an IV-line, infusion of Inj. Ringer lactate was started and Inj. glycopyrrolate in the dose of 0.004 mg/Kg body wt. IM and Inj. ondansetron 0.1 mg/Kg body wt. IV and Inj. pantoprazole 40 mg iv were given as premedication 30 minutes before induction. The baseline parameters like baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and oxygen saturation (SPO_2) was recorded. Group A received 20 ml Inj. Normal saline as IV infusion over a period of 10 minutes. Group B received iv dexmedetomidine 0.5 µg/Kg diluted to 20 ml with normal saline as infusion over 10 minutes. Group C received IV dexmedetomidine 0.75 µg/Kg body wt. diluted to 20 ml normal saline as infusion over 10 minutes. Sedation score was measured at 1 min and 3 minutes after completion of the infusion of the drug by using Ramsay Sedation scale. Then general anaesthesia was initiated. All patients were preoxygenated with 100% oxygen for 3 minutes. Anaesthesia was induced with 1% Inj. propofol 2 mg/Kg body weight. Inj. succinyl choline 1.5 mg/Kg body was given intravenously to facilitate endotracheal intubation. Following laryngoscopy and intubation the following parameters-HR, SBP, DBP, and MAP and SPO2 were recorded at 1, 3, 5 and 10 minutes after intubation. Anaesthesia was maintained with O_2 and air in the ratio of 1:4 with sevoflurane. Muscle relaxation was maintained with bolus dose of Inj. vecuronium bromide 0.1 mg/Kg body weight and top-up with 0.04 mg/Kg body weight. Inj. diclofenac sodium IM and Inj. paracetamol infusion were given in the intraoperative period. After surgery, the residual effect of neuromuscular blocking drugs was reversed with Inj. neostigmine 0.05 mg/Kg body weight combined with Inj. glycopyrrolate 0.008 mg/Kg body weight and patient was extubated after suctioning of the oropharynx and adequate recovery, judged on clinical ground. After adequate recovery, patients were shifted to post anaesthesia care unit and monitored for 12 hours and later shifted to the ward.

RESULTS

Continuous variables are expressed as Mean ± Standard Deviation and compared across the groups using unpaired t

test. Categorical variables are expressed as Number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes/ Fisher's Exact Test as appropriate. The statistical software SPSS version 20 has been used for the analysis. An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant. The mean and sex distribution of the three groups and their comparisons are shown in table 1 and table 2. The groups are similar in respect to age and gender

Heart Rate

Maximum intubation response in heart rate is seen at 1 minutes after intubation in all three groups with maximum increase in Group A. In Group A, heart rate comes down to near the baseline value at 10 minutes after intubation whereas it comes down near the baseline value after 5 minutes in Group B and Group C. The heart rate goes down below the baseline at 10 minutes after intubation in Group B and Group C. There was significant fall in heart rate in group B and Group C ($p<0.001$) in 1, 3 and 5 minutes after intubation. The fall in heart rate was still significant in Group C at 10 minutes after intubation in comparison to Group A and Group B. So it can be interpreted that Inj. Dexmedetomidine 0.75 µg/Kg body can better obtund the increase in HR than dexmedetomidine 0.5 µg/Kg body wt. Table 3. Shows the comparison of heart rate of the three groups.

Systolic Blood Pressure

There was increase in systolic blood pressure in all the groups till 1 min after laryngoscopy and intubation, but the increase was significantly lower in both the dexmedetomidine groups. Systolic blood pressure comes below the baseline after 3 minutes in both Group B and C while it comes down after 5 minutes of intubation in Group A. Highly Significant fall in systolic blood pressure ($p<0.01$) occurs in Group B and Group C at 1, 3, 5 minutes after intubation. The significant fall in systolic blood pressure persist even 10 minutes after intubation ($p<0.05$) in Group C in comparison to Group A. Table 4 shows the comparison of Systolic Blood pressure (mmHg) among three groups.

Diastolic Blood Pressure (DBP)

There was no significant difference in diastolic blood pressure among the three groups till 3 minutes after intubation. The diastolic blood pressure in Group B and Group C came down below the baseline values after 3 minutes of intubation while it came down below baseline values after 5 minutes of intubation in Group A. There was highly significant fall in diastolic blood pressure in Group B and Group C ($p<0.01$) at 5 minutes after intubation. Significant decrease in Diastolic blood pressure occurred even 10 minutes after intubation in Group C comparison to Group A ($p<0.5$) Table 5 shows the comparison of Diastolic blood pressure among the three group

Mean Arterial Pressure

No significant difference in mean arterial pressure among the three groups was seen till 1 minute after intubation. The Mean arterial pressure came down below the baseline values after 3 minutes of intubation in both Group B and Group C and after 5 minutes in Group A. Mean arterial pressure in Group A was significantly higher than Group B and C at 3, 5 and 10 minutes after intubation ($p<0.05$). No significant difference was seen between Group B and C. Table 6 shows the comparison of Mean arterial pressure among the three groups

Sedation Score

There was significant high sedation score in Group B and Group C ($p<0.05$) than Group A at 1 and 3 minutes after completion of the drug infusion and it was highly significant ($p<0.01$) after 3 minutes in Group C in comparison to Group A. Table 7 shows the Sedation score 1 minute after completing test drug infusion. Table 8 shows the Sedation score 3 minutes after completing test drug infusion.

Age	GROUP					
	Group A	Group B	Group C	p Value		
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	A vs. B	A vs. C	B vs. C
	36.2 ± 9.49	38.1 ± 13.78	34.8 ± 8.52	0.536	0.550	0.269

Table 1. Age Distribution of The Three Groups

		GROUP				p Value		
		Group A	Group B	Group C	Total	A vs. B	A vs. C	B vs. C
Sex	F	28 (93.33)	29 (96.67)	27 (90)	84 (93.33)	0.554	0.640	0.612
	M	2 (6.67)	1 (3.33)	3 (10)	6 (6.67)			
Total		30 (100)	30 (100)	30 (100)	90 (100)			

Table 2. Sex Distribution of The Three Groups

	Group A	Group B	Group C	p Value		
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	A vs. B	A vs. C	B vs. C
HR0	77.4 ± 9.24	80.4 ± 9.64	74.47 ± 12.51	0.223	0.306	0.044
HR1	107.0 ± 11.04	91.17 ± 13.51	85.3 ± 10.27	0.000	0.000	0.063
HR3	97.53 ± 10.21	84.73 ± 11.9	78.17 ± 8.73	0.000	0.000	0.018
HR5	87.2 ± 11.73	80.57 ± 12.52	75.57 ± 8.87	0.038	0.000	0.080
HR10	77.7 ± 13.13	77.9 ± 12.37	70.3 ± 9.86	0.952	0.017	0.011

Table 3. Table Showing Comparison of Heart Rate of The Three Groups

	Group A	Group B	Group C	p Value		
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	A vs. B	A vs. C	B vs. C
SBP-0	122.83 ± 11.96	124.2 ± 12.03	122.5 ± 12.19	0.661	0.915	0.589
SBP-1	146.03 ± 18.24	135.93 ± 17.46	133.3 ± 17.26	0.032	0.007	0.559
SBP-3	127 ± 16.06	114.73 ± 13.61	113.33 ± 11.02	0.002	0.000	0.663
SBP-5	114.7 ± 17.12	103.13 ± 10.45	103.57 ± 9.4	0.003	0.003	0.866
SBP-10	107.43 ± 14.09	101.13 ± 12.14	99.1 ± 10.09	0.069	0.011	0.483

Table 4. Comparison of Systolic Blood Pressure (mmHg) Among Three Groups

SBP 0, 1, 3, 5, 10 = Systolic blood pressure at baseline, 1, 3, 5 and 10 minutes after intubation.

	Group A	Group B	Group C	p Value		
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	A vs. B	A vs. C	B vs. C
DBP-0	78.7 ± 7.19	77.77 ± 9.42	78.7 ± 8.23	0.668	1.000	0.684
DBP-1	95.07 ± 13.52	91.4 ± 14.33	89.37 ± 14.36	0.312	0.119	0.585
DBP-3	80.73 ± 12.95	75.93 ± 10.59	74.7 ± 11.97	0.121	0.066	0.674
DBP-5	74.37 ± 13.1	65.03 ± 10.22	65.7 ± 11.32	0.003	0.008	0.812
DBP-10	70.23 ± 11.92	63.83 ± 13.25	64.13 ± 10.63	0.054	0.041	0.923

Table 5. Comparison of Diastolic Blood Pressure Among the Three Groups

	Group A	Group B	Group C	p Value		
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	A vs. B	A vs. C	B vs. C
MAP-0	93.1 ± 7.05	91.23 ± 8.24	89.67 ± 8.53	0.350	0.095	0.472
MAP-1	110.77 ± 14.97	106.4 ± 16.72	105.1 ± 16.89	0.291	0.174	0.766
MAP-3	96.07 ± 12.92	88.9 ± 10.44	87.73 ± 10.66	0.021	0.008	0.670
MAP-5	87.3 ± 13.39	79.53 ± 9.96	78.37 ± 9.7	0.013	0.004	0.648
MAP10	81.87 ± 11.52	74.93 ± 10.67	75.5 ± 9.44	0.019	0.023	0.828

Table 6. Comparison of Mean Arterial Pressure Among the Three Groups

		Group			Total	p Value		
		Group A	Group B	Group C		A vs. B	A vs. C	B vs. C
SS1	2	30(100)	24(80)	24(80)	78(86.67)	0.024	0.024	1.000
	3	0(0)	6(20)	6(20)	12(13.33)			
Total		30(100)	30(100)	30(100)	90(100)			

Table 7. Sedation Score 1 Minute After Completing Test Drug Infusion

		Group			Total	p Value		
		Group A	Group B	Group C		A vs. B	A vs. C	B vs. C
SS3	2	30(100)	23(76.67)	20(66.67)	73(81.11)	0.011	0.001	0.390
	3	0(0)	7(23.33)	10(33.33)	17(18.89)			
Total		30(100)	30(100)	30(100)	90(100)			

Table 8. Table Showing Sedation Score 3 Minutes After Completing Test Drug Infusion

DISCUSSION

Laryngoscopy and endotracheal intubation causes marked haemodynamic responses like increase in the heart rate and blood pressure,[1] which can be dangerous in patients with co -existing cardiac and neurological diseases like in patients with coronary artery diseases and intracranial aneurysm which necessitate the blunting of these responses. Various techniques and drugs were used to attenuate these intubation-related hemodynamic changes. Many researches have tried many pharmacological agents to obtund these changes.[2-13] Recently many researchers have tried Dexmedetomidine, an alpha 2 adrenergic receptor agonist to blunt these responses. Dexmedetomidine is highly selective alpha 2 receptor adrenergic receptor agonists which acts through three types of receptors-alpha 2A, alpha 2B and alpha 2C situated in the brain and spinal cord. It has unique pharmacological properties like sedation, sympatholysis, analgesic, cardiovascular stabilizing effect and with the advantage to avoid respiratory depression both in paediatric and adult patients. Stimulation of alpha 2A and Alpha 2C in the locus ceruleus in the brain causes sedation. In the spinal cord, activation of both alpha 2A and alpha 2C receptors directly reduces pain transmission by reducing the release of substance P. Premedication with Dexmedetomidine in the dose of 1 µg/Kg significantly reduced heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure and blunted the pressor response during intubation, reduced the opioid requirement.[14-17] Its effectiveness in obtunding the pressor response during intubation has also been compared with other drugs and placebos and found to be more effective than these drugs.[18-25] Dexmedetomidine has been used in different doses in infusion form with or without bolus doses. Some researchers found that Dexmedetomidine given in the dose of 0.25-0.5 µg/Kg body weight only decreased blood pressure while doses of 1-2 µg/Kg was associated with transient increase in blood pressure followed by hypotension and bradycardia with, maximum fall in heart occurred with the dose of 2 µg/Kg body weight.[26] Dexmedetomidine in the doses of 0.7 µg/Kg body weight was found to decrease stress response which was comparable with 1 µg/Kg body weight.[27]

Some studies show that dexmedetomidine 1 µg/Kg body better attenuates the haemodynamic response during intubation,[28-29] while others found that both 0.5 µg/Kg body weight and 1 µg/Kg weight effectively and significantly attenuates cardiovascular and haemodynamic response during endotracheal intubation but the different doses did not cause any significant distinct result in mitigating cardiovascular responses.[30] Another study shows that dexmedetomidine 0.5 µg/Kg has an effective inhibition without respiratory depression on tracheal intubation evoked cardiovascular response.[31] Some researchers found that dexmedetomidine 0.6 µg/Kg body weight completely obtund and provide better attenuation of the haemodynamic responses of laryngoscopy and endotracheal intubation unaccompanied by transient hypertension and bradycardia which is observed in 1 µg/Kg loading dose.[32-33] In most of the study it was found that low doses of the drug are less effective in obtunding the haemodynamic responses during intubation while higher doses produce initial hypertension followed by hypotension and bradycardia. Our study aimed at finding an effective dose of dexmedetomidine which can attenuate the haemodynamic changes during laryngoscopy and intubation but avoids its unwanted effects, by comparing two doses of dexmedetomidine 0.5 µg/Kg body weight and 0.75 µg/Kg body weight.

In our study we found that both 0.5 µg/Kg body wt. and 0.75 µg/Kg body weight significantly attenuate the increase in the heart rate till 5 minutes after intubation which is similar to other's findings. The fall in heart rate still continued till 10 min after intubation in 0.75 µg/Kg body weight group and is significant in comparison to 0.5 µg /Kg. There was no significant bradycardia in both the groups. There is significant fall in the systolic blood pressure in both the groups till 5 minutes after intubation but dexmedetomidine 0.75 µg/Kg body has longer significant action on systolic blood pressure till 10 minutes. In our study we don't find any significant effect on diastolic blood pressure with both the two doses of the drug till 3 minutes after intubation. Significant fall in diastolic blood pressure occurs at 5 minutes after intubation in both the groups but the fall is still significant at 10 minutes after intubation in 0.75 µg/Kg body wt. group.

Both the doses of the drug produced significant attenuation of the Mean arterial blood pressure at 3 and 10 minutes after intubation but there is no significant difference between the two doses even though the mean fall in is more in 0.75 µg/Kg body weight group. The sedation score was similar between the two doses of dexmedetomidine at 1 minutes and 3 minutes after completion of the drug infusion but statically better with 0.75 µg/Kg body weight than 0.5 µg/Kg body weight. The present study was confined to a group of patients who are normotensive and having normal cardiovascular status. Any dose of the study drug within the range of 0.5 µg/Kg body weight and 0.75 µg/Kg body weight can be presumed to be quite effective. Attenuation of the haemodynamic response to laryngoscopy and tracheal intubation is necessary in hypertensive patients and dexmedetomidine infusion within the range of the above two doses can be tried. There were no complications like severe hypertension, hypotension, bradycardia or fall in oxygen saturation during the study.

There were some limitations in our study. First, the present study depends on the haemodynamic parameters for assessment of the attenuation of the cardiovascular responses to airway manipulation without measuring the blood catecholamine and cortisol levels. No Invasive blood pressure monitoring could be done as it is not available at our institute, which could give more accurate value at the appropriate timing. The study timing was confined to 10 minutes after intubation. We don't know how long the drugs can attenuate the haemodynamic responses after 10 minutes.

CONCLUSION

The present study concludes that systolic blood pressure and diastolic blood pressure increases after laryngoscopy and intubation. Both doses of Dexmedetomidine administered at the dose of 0.5 µg/Kg body weight and 0.75 µg/Kg body weight can attenuate the haemodynamic response to laryngoscopy and intubation but dexmedetomidine at the dose of 0.75 µg/Kg body weight can do it better and longer than dexmedetomidine administered at the doses of 0.5 µg/Kg body weight blood without producing any severe side effects like, transient hypertension or reflex hypotension and bradycardia as seen in high doses of the drug, following laryngoscopy and endotracheal intubation.

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