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A STUDY TO COMPARE THREE DIFEERENT DOSES OF INTRAVENOUS DEXMEDETOMIDINE FOR ATTENUATION OF PRESSOR RESPONSE DURING LARYNGOSCOPY AND INTUBATION

Anesthesiology

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ABSTRACT

Background: This study was to compare the effects of three different doses of intravenous dexmedetomidine for attenuation of pressor response during laryngoscopy and endotracheal intubation.

Material and methods: ASA class 1 the patients were divided into three groups randomly by slip draw method. Group 1(n=30) patients received 0.3 mcgkg^{-1} of intravenous dexmedetomidine in 100ml normal saline infusion over 10 minutes before induction. Group 2(n=30) patients received 0.5 mcgkg^{-1} of intravenous dexmedetomidine in 100ml normal saline infusion over 10 minutes before induction. Group 3 (n=30) received 1mcgkg^{-1} of intravenous dexmedetomidine in 100 ml normal saline over 10 minutes before induction. Systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate were recorded at 1 minute (T1), 3 minutes (T3), 5minutes (T5), 7 minutes (T7) and 10 minutes (T10) after laryngoscopy & intubation.

Results: When comparing the three different doses of dexmedetomidine it was observed that 1 µgkg-1 significantly attenuates the press or response in comparison to 0.3 µgkg-1 and 0.5 µgkg-1. Although the incidence of peri operative hypotension and bradycardia was noticed more with the dose 1 µgkg-1, it could be safely managed with adequate monitoring and symptomatic treatment. A significant difference was not seen between the dose of 0.3 µgkg-1, and 0.5 µgkg-1, for attenuation of press or response.

Conclusion: It can be concluded that dexmedetomidine significantly and effectively attenuates the pressor response during laryngoscopy and endotracheal intubation. It reduces the hemodynamic responses in relation to heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure.

KEYWORDS

INTRODUCTION

Endotracheal intubation has never been a risk-free procedure, but is needed to protect airway and for airway access.[1] Laryngoscopy and endotracheal intubation invariably violate patient's protective reflexes as it is a noxious stimulus. Direct laryngoscopy and endotracheal intubation frequently induce a cardiovascular stress response manifesting as hypertension, tachycardia and increase in serum catecholamine.[2]

Although these pressor responses to tracheal stimulation are of little significance in healthy and young individuals, they may cause some deleterious effects in patients with ischaemic heart diseases, hypertension and other vascular co-morbidities.

Some pharmacological measures include intravenous administration of lidocaine or fentanyl administered before laryngoscopy, hypotensive agents like sodium nitroprusside, nitroglycerine, hydralazine, beta blockers and calcium channel blockers.[3]

Dexmedetomidine is a potent α-2 adrenoceptor agonist with sympatholytic, sedative, amnestic, and analgesic properties, which has been described as a useful and safe adjunct in many clinical applications. It is the most recently developed and commercialized agent in this pharmacological class.[4] It provides a unique "conscious sedation" (patients appear to be asleep, but are readily roused), analgesia, without respiratory depression. It decreases central nervous system (CNS) sympathetic outflow in a dose-dependent manner and has analgesic effects best described as opioid-sparing. Evidence proves its organ protective effects against hypoxic injury along with cardioprotection, neuroprotection and renoprotection.[5]

In our study we have evaluated the efficacy of three different doses of dexmedetomidine i.e. 0.3 µgkg^{-1} vs 0.5 µgkg^{-} vs 1 µgkg^{-1} for attenuation pressor response during laryngoscopy and endotracheal intubation. We have undertaken this study in order to find the optimum dose of dexmedetomidine required for blunting the pressor responses.

MATERIAL AND METHODS

This was a hospital based prospective, randomized double blind study in the Department of Anaesthesiology And Critical Care at SGT Medical College, Hospital and Research Institute on ninety patients of either sex aged between 18-50 years belonging to physical status ASA 1 and ASA 2 group according to American Society of Anesthesiologists who were scheduled for elective surgery under general anaesthesia over a period of two years

EXCLUSION CRITERIA:

Unwilling patients, emergency surgeries, anticipated difficult intubation, patients with SBP >140 mm Hg and DBP >90 mm Hg, patients on beta blockers, calcium channel blockers, ACE –inhibitors and anti-hypertensive and patients with known allergy to drugs used in the study were excluded from the study.

METHODOLOGY:

All the patients were examined on the day prior to surgery and were subjected to complete general physical and systemic exam. Routine and special investigations were carried out in all patients. The purpose and protocol of the study was explained and an informed written consent was obtained.

Patients were kept fasting for eight hours and premedication in the form of tablet ranitidine 150 mg at night the day before surgery was given to the patient.

On the day of surgery, anaesthesia machine and circuits were first checked, resuscitation equipment was kept ready. After confirmation of NPO status patients were shifted to the operating room. After connecting to multichannel monitor basal systolic blood pressure (SBP), diastolic blood pressure (DBP), Mean arterial pressure (MAP), heart rate and SpO_2 was recorded just before administration of the drug. Continuous monitoring was done with a visual display of ECG and the vital parameters.

An Intravenous line was secured with IV cannula and henceforth the patients were divided into three groups randomly by slip draw method. Group 1(n=30) patients received 0.3 mcgkg^{-1} of intravenous dexmedetomidine in 100ml normal saline infusion over 10 minutes before induction. Group 2(n=30) patients received 0.5 mcgkg^{-1} of intravenous dexmedetomidine in 100ml normal saline infusion over 10 minutes before induction. Group 3 (n=30) received 1mcgkg^{-1} of intravenous dexmedetomidine in 100 ml normal saline over 10 minutes before induction. Principal investigator did not know about the drug given by double blinding method.

All patients were pre- oxygenated for 3 minutes and anaesthesia was induced with 2mgkg^{-1} propofol with a standardized method (bolus injection at the rate 1mlsec^{-1}) for all three groups. End point of induction was lack of response to verbal command followed by loss of eyelash reflex. After successful trial ventilation with 100% oxygen, Succinyl choline 2 mgkg^{-1} was given to facilitate laryngoscopy & intubation. Oxygenation was continued by positive pressure mask ventilation.

After confirming relaxation, intubation was done using laryngoscope with a Macintosh blade with an appropriate sized, well lubricated, oral endotracheal tube. Patients in whom endotracheal intubation required more than twenty seconds or failure of intubation at first attempt, were excluded from the study. After confirmation of the tube position by bilateral auscultation for air entry, cuff will be inflated, and tube was fixed, connected to anaesthesia machine. Anaesthesia was maintained with 33% Oxygen and Isoflurane (1%) along with long acting muscle relaxant in Nitrous Oxide. Systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate were recorded at 1 minute (T1), 3 minutes (T3), 5minutes (T5), 7 minutes (T7) and 10 minutes (T10) after laryngoscopy & intubation.

Sequence	SBP, DBP, MAP, Heart rate recording
Basal reading just before administration of drug	T0
At 1 min after intubation	T1
At 3min after intubation	T3
At 5min after intubation	T5
At 7min after intubation	T7
At 10min after intubation	T10

Surgical incision stimulus was allowed at the end of 10 min after laryngoscopy & intubation. Anaesthesia was continued with N_2O, O_2, Isoflurane. Injection fentanyl 2mcgkg^{-1} was given for analgesia after all the readings were taken. Vecuronium loading dose (0.1mgkg^{-1}) was given along with top up doses, analgesics & IV fluids (6mlkg^{-1}hr^{-1} for maintenance and deficit) was be administered.

Any peri-operatively hypotension (SBP<90, DBP<60 or MAP less than 20% of the baseline), and bradycardia (HR <50) was noted in all the patients. In case of bradycardia, 0.2mg of injection glycopyrrolate was be give intra-operatively.

At the end of surgery, Isoflurane and N2O was discontinued and residual neuromuscular blockade was reversed with Injection Neostigmine (0.05mgkg^{-1}) & Glycopyrrolate (0.01mkg^{-1}) when the patient had adequate respiratory efforts. Recovery was assessed and extubation was done after oral suction.

Patients were shifted to post anaesthesia care unit after having adequate reflexes and responses. Patients were observed for 2 hours to observe the score of sedation. Post-operative follow-up for 24hrs as done and side effects if any were treated. Sedation score was done based on Ramsay Sedation Score system.

Patient was scored from 1 to 6 according to the following-

Patient is anxious and agitated or restless, or both	1
Patient is co-operative, oriented, and tranquil	2
Patient responds to commands only	3
Patient exhibits brisk response to light glabellar tap or loud auditory stimulus	4
Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus	5
Patient exhibits no response	6

STATISTICALANALYSIS

The data was analyzed on Excel spreadsheet. Descriptive data was presented as Mean ±SD and in percentage. Multiple group comparisons were done. For all the tests a p value of <0.05 was considered for statistical significance. For comparing age, systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate and the sedation score Krystal Wallis test was applied. For comparing hypotension, bradycardia and gender among the three groups Fishers extract test was used.

RESULTS

The study was conducted amongst 90 adult patients undergone laryngoscopy and endotracheal intubation. A total of 96 people were approached, but 6 participants did not participate due to any reason. Thus, 90 study participants were included for the analysis which was equal to the estimated sample size among all three groups. Group were divided 1, 2 and 3 who received dexmedetomidine 0.3mcgkg^{-1} ,0.5 mcgkg^{-1} and 1mcgkg^{-1} respectively.

Table 1: Gender distribution among all the groups

	Male n (%)	Female n (%)	p-value
1	15(50)	15(50)	0.804
2	12(40)	18(60)	
3	13(43.3)	17(56.7)	

Table 2: Comparison of HR among all the groups

group	1.00		2.00		3.00		P_1	P_2	P_3
	Mean	SD	Mean	SD	Mean	SD			
PR0	84.80	9.89	85.40	9.05	79.33	9.09	0.721	0.04	0.02
PR1	123.00	14.60	122.13	12.84	93.87	8.65	0.684	0.001	0.001
PR3	113.00	14.34	113.40	13.35	88.93	7.89	0.917	0.001	0.001
PR5	106.60	12.92	107.67	12.33	84.27	7.53	0.673	0.001	0.001
PR7	100.20	12.09	100.73	11.48	79.73	7.64	0.835	0.001	0.001
PR10	92.40	9.00	93.33	8.73	75.20	7.92	0.743	0.001	0.001

PR was statistically significantly different at every interval from baseline to at the 10 min after intubation between group 1 vs 3 and group 2 vs 3 while there was no statistically difference present when group 1 and group 2 compared. Maximum PR were noticed at 1 min after intubation among all three groups and then gradually reduced in all three groups. PR was noticed less in group 3 at every interval

Table 3: Comparison of SBP among all the groups

group	1.00		2.00		3.00		P_1	P_2	P_3
	Mean	SD	Mean	SD	Mean	SD			
SBP0	130.53	8.68	131.47	9.20	128.60	11.70	0.498	0.598	0.352
SBP1	157.53	10.33	155.60	7.09	141.33	11.48	0.513	0.001	0.001
SBP3	151.40	9.73	149.73	6.70	136.60	10.86	0.716	0.001	0.001
SBP5	146.40	9.10	145.47	6.91	132.40	10.42	0.754	0.001	0.001
SBP7	141.33	8.89	140.53	7.01	127.73	10.37	0.964	0.001	0.001
SBP10	136.93	8.66	136.13	7.75	122.93	10.95	0.870	0.001	0.001

SBP was statistically significantly different at every interval from 1 min after intubation to at the 10 min after intubation between group 1 vs 3 and group 2 vs 3 while there was no statistically difference present when group 1 and group 2 compared and baseline SBP among each other. Maximum SBP were noticed at 1 min after intubation among all three groups and then gradually reduced in all three groups. SBP was noticed less in group 3 at every interval.

Table 4: Comparison of DBP among all the groups

group	1.00		2.00		3.00		P_1	P_2	P_3
	Mean	SD	Mean	SD	Mean	SD			
DBP0	79.20	9.82	81.47	10.71	76.60	10.24	0.301	0.445	0.106
DBP1	104.87	7.35	103.87	6.37	88.07	9.62	0.612	0.001	0.001
DBP3	99.37	6.28	98.70	4.85	83.53	9.51	0.940	0.001	0.001
DBP5	94.00	5.78	93.47	4.90	79.33	8.92	0.729	0.001	0.001
DBP7	89.93	5.93	90.07	4.97	75.40	9.07	0.905	0.001	0.001
DBP10	86.73	6.78	87.20	5.67	71.93	9.04	0.654	0.001	0.001

DBP was statistically significantly different at every interval from 1 min after intubation to at the 10 min after intubation between group 1 vs 3 and group 2 vs 3 while there was no statistically difference present when group 1 and group 2 compared and baseline SBP among each other. Maximum DBP were noticed at 1 min after intubation among all three groups and then gradually reduced in all three groups. DBP was noticed less in group 3 at every interval.

Table 5: Comparison of MAP among all the groups

group	1.00		2.00		3.00		P_1	P_2	P_3
	Mean	SD	Mean	SD	Mean	SD			
MAP0	95.17	8.81	96.73	9.83	93.53	10.38	0.406	0.739	0.377
MAP1	121.53	7.28	119.87	5.00	105.40	9.79	0.583	0.001	0.001
MAP3	116.47	6.74	115.37	4.46	100.93	9.52	0.964	0.001	0.001
MAP5	111.33	6.28	110.63	4.66	96.87	8.81	0.894	0.001	0.001
MAP7	106.77	6.32	106.67	4.79	92.67	9.00	0.905	0.001	0.001
MAP10	103.10	6.71	103.10	5.59	88.53	9.25	0.911	0.001	0.001

MAP was statistically significantly different at every interval from 1 min after intubation to at the 10 min after intubation between group 1 vs 3 and group 2 vs 3 while there was no statistically difference present when group 1 and group 2 compared and baseline SBP among each other. Maximum MAP was noticed at 1 min after intubation among all three groups and then gradually reduced in all three groups. MAP was noticed less in group 3 at every interval.

DISCUSSION

Laryngoscopy and endotracheal intubation are a noxious stimuli for patients and invariably cause marked haemodynamic changes. They are observed as rise in heart rate, systemic blood pressure and autonomic reflex activity. These changes are usually well tolerated among the younger population but they can cause serious risk in older and compromised population. haemodynamic changes and autonomic reflex activity which may be a cause of concern in many high- risk patients. These changes disappear gradually after 5 min as stated by study **Russel WJ et al.**[6]

Various drugs have been found to be effective in blunting the haemodynamic responses to laryngoscopy and endotracheal intubation. Our study has compared the efficacy of different doses of dexmedetomidine for blunting hemodynamic responses to laryngoscopy and endotracheal intubation.

In our study it was seen that PR was statistically significantly different at every interval from baseline to at the 10 min after intubation between group 1 vs 3 and group 2 vs 3 while there was no statistically difference present when group 1 and group 2 compared. Maximum HR were noticed at 1 min after intubation among all three groups and then gradually reduced in all three groups. PR was noticed less in group 3 at every interval. SBP, DBP and MAP was statistically significantly different at every interval from 1 min after intubation to at the 10 min after intubation between group 2 vs 3 and group 2 vs 3 while there was no statistically difference present when group 2 and group 3 compared and baseline SBP among each other. Maximum SBP were noticed at 1 min after intubation among all three groups and then gradually reduced in all three groups. SBP was noticed less in group 3 at every interval.

Similar results were noticed by **Keshri RK et al.**[7]In this study there was no significant change in HR between Group I and Group II. But there was a significant increase in HR in Group II as compared to Group III at T1, T2, and T3, it became comparable in both the groups at T4 and T5. SBP, DBP and MAP was significantly ($P < 0.05$) more among Group I compared to Group II and Group III from T2 to T4. However, SBP was significantly low in Group III as compared to Group II at T4 and T5.

Similar results were also noticed by study conducted by **Smitha KS et al.**[8] In this study dexmedetomidine 1 μgkg^{-1} and 0.5 μgkg^{-1}, SAP, DAP, MAP and HR levels were significantly lower at 60 sec after induction and 5 min after intubation than baseline levels. But at 1 minute after laryngoscopy & intubation, these levels increased in all the three groups. But in 1μgkg^{-1} group, the amount of increase in the vital parameter levels, 60 secs after intubation, was less when compared to 0.5 μgkg^{-1} and very much less than the control group was. Hence, it was found that dexmedetomidine very effective in suppressing the hemodynamic response to laryngoscopy and at dose of 1 μgkg^{-1} better than at dose 0.5 μgkg^{-1}. Studies by **Sagıroglu et al**[9], **Menda et al**[10] and **Pipanmekaporn et al**[11] compared the two different doses of dexmedetomidine to observe the blunting of pressor response to laryngoscopy and intubation and reported that a dose of 1μgkg^{-1} was more effective than a dose of 0.5 μgkg^{-1}. In our study, the hemodynamic response was sufficiently blunted with both the doses of dexmedetomidine.

In contrast to our study, studies by **Ebert TJ et al**[12] and **Scheinin B et al**[13] it is observed that mean arterial pressure was decreased by low doses of dexmedetomidine (0.25-1 μgkg^{-1}) and mean It can be concluded that dexmedetomidine significantly and effectively attenuates the pressor response during laryngoscopy and endotracheal intubation. It reduces the hemodynamic responses in relation to heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure.of (1-4 μgkg^{-1}) dexmedetomidine.

ADVERSE EVENTS:

Dexmedetomidine can lead to a decline in blood pressure and heart rate and thus has a good effect in the control of the surgical stress response. However, dexmedetomidine will cause hypotension and bradycardia, which presents certain risks to patients with original low blood volume or heart block.

Current study revealed that no patient suffered from bradycardia or hypotension in group 1 but theincidence of hypotension and bradycardia was maximum group 3 who received maximum dose of dexmedetomidine followed by group 2 and this difference was noticed statistically significant.

Piao et al[14] in their meta- analysis found the similar adverse event compare to control group. In this observation it was found that the occurrence of adverse effects such as hypotension and bradycardia found them to be significantly higher as compared to controls **Khan et al.**[15] in their comparative study of 1.0 μgkg^{-1} and 0.5 μgkg^{-1} doses of dexmedetomidine reported a higher incidence of hypotension and bradycardia with the use of higher dose of the drug. Similar result was noticed by **Keshri RK et al.**[7] and stated that the use of lower dose was associated with a lesser incidence of both these side effects.

CONCLUSION

It can be concluded that dexmedetomidine significantly and effectively attenuates the pressor response during laryngoscopy and endotracheal intubation. It reduces the hemodynamic responses in relation to heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure. When comparing the three different doses of dexmedetomidine it was observed that 1 µgkg-1 significantly attenuates the press or response in comparison to 0.3 µgkg-1 and 0.5 µgkg-1. Although the incidence of peri operative hypotension and bradycardia was noticed more with the dose 1 µgkg-1, it could be safely managed with adequate monitoring and symptomatic treatment. A significant difference was not seen between the dose of 0.3 µgkg-1, and 0.5 µgkg-1, for attenuation of press or response. The incidence of hypotension and bradycardia among these two groups was found to be low.

REFERENCES

1. DiLorenzo A, Schell R. Morgan & Mikhail's Clinical Anesthesiology, 5th Edition. Anesthesia & Analgesia. 2014;119(2):495-496.
2. Stoelting RK. Circulatory changes during direct laryngoscopy and tracheal intubation: Influence of duration of laryngoscopy with or without prior lidocaine. Anesthesiology 1977;47:381-4
3. Hazarika A,Deori AK, Bora J, Deori J, Tiwari PK. Attenuation of haemodynamic responses to laryngoscopy and intubation: a clinical study of dexmedetomidine. IJCMR 2016;3(12):3536-8.
4. Carollo S, Nossaman D, Ramadhyani U.Dexmedetomidine:a review of clinical applications. Curr Opin Anaesthesiol. 2008;21:457-61.
5. Panzer O, Moitra V, Sladen N. Pharmacology of sedative-analgesic agents: dexmedetomidine, remifentanil, ketamine, volatile anesthetics, and the role of peripheral mu antagonists. Crit Care Clin 2009;25:451-69.
6. Russel W, Morris R, Frewin D and Drew S. Changes in plasma catecholamine concentrations during endotracheal intubation. Br J Anaesth 1981; 53: 837. 6. Onkar Singh, Kumar P, Swarn Kaur. Attenuation of the pressure response to laryngoscopy and tracheal intubation: Comparison of beta blockers and calcium channel blockers. Ind J Anaesth 1993; 41: 320-324.
7. Keshri R, Prasad M, Choudhary A, Jheetay G, Singh Y, Kapoor K. Comparative Evaluation of Different Doses of Intravenous Dexmedetomidine on Hemodynamic Response during Laryngoscopy and Endotracheal Intubation in Geriatric Patients Undergoing Spine Surgeries: A Prospective, Double-Blind Study. *Anesth Essays Res*. 2018;12(4):897-902
8. Smitha K. S,Divya Shukla, Sathesha M, Raghavendra Rao, Nethra S. S, K. Sudheesh. Comparison of two different Doses of Dexmedetomidine in attenuating Hemodynamic Changes during Laryngoscopy. Journal of Evolution of Medical and Dental Sciences 2014; 3(61):13501-13508,
9. Sağıroğlu AE, Celik M, Orhon Z, Yüzer S, Sen B. Dıfferent doses of dexmedetomidine on controlling haemodynamic responses to trachealintubation. Internet J Anesthesiol. 2010;27:2.
10. Koner O, Sayin M, Ture H, Imer P, Aykac B, Menda F. Dexmedetomidine as an adjunct to anesthetic induction to attenuate hemodynamic response to endotracheal intubation in patients undergoing fast-track CABG. Annals of Cardiac Anaesthesia. 2010;13(1):16.
11. Pipanmekaporn T, Punjasawadwong Y, Charuluxananan S, Lapisatepun W, Bunburaphong P. The Effect of Prophylactic Dexmedetomidine on Hemodynamic Disturbances to Double-Lumen Endotracheal Intubation: A Prospective, Randomized, Double-Blind, and Placebo-Controlled Trial. Anesthesiology Research and Practice. 2013;2013:1-8.
12. Ebert TJ et al- The effects of increasing plasma concentrations of dexmedetomidine in humans.2000; Aug; 93 (2): 382-94.
13. Scheinin B, Lindgren L, Randell T, Scheinin H, Scheinin M. Dexmedetomidine attenuates sympathoadrenel responses to tracheal intubation and reduces the need for thiopentone and peroperative fentanyl. Br J Anaesth 1992; 68: 126-131.
14. Piao G, Wu J. Systematic assessment of dexmedetomidine as an anesthetic agent: A meta-analysis of randomized controlled trials. Arch Med Sci. 2014;10:19–24.
15. Khan AA, Kumar N, Singh Y, Singh AK, Mathur SK. To compare the effect of two different doses of dexmedetomidine on the attenuation of airway and pressor response during tracheostomy tube change in traumatic brain injury patients. Anesth Essays Res. 2017; 11:964–8.