Attenuation of Haemodynamic Responses to Laryngoscopy and Intubation with Three Different Doses of Dexmedetomidine - A Randomised Prospective Control Trial

Mousumi Das[1], Saswati Das[2], Debashish Mishra[3], Pradip Kumar Maharana[4]

[1, 2, 4] Department of Anaesthesiology, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India.
[3]Department of Orthopaedics, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India.

ABSTRACT

BACKGROUND
We wanted to study the attenuation of haemodynamic stress responses during laryngoscopy and intubation using safe and effective dose of dexmedetomidine.

METHODS
In this prospective double-blind placebo control interventional study, 120 patients of ASA-I and ASA-II scheduled for elective surgeries under general anaesthesia were divided randomly into four equal groups. Group A, group B, and group C received 0.5 mcg / Kg, 0.75 mcg / Kg and 1 mcg / Kg of dexmedetomidine intra venous (IV) respectively and Group D received 10 mL normal saline (NS) IV as bolus prior to induction of anaesthesia. Haemodynamic parameters were recorded before administration of the study drug, at 5 min with ongoing infusion of study drug, after completion of the study drug (at 10 min.), immediately after induction, during intubation, every minute thereafter up to 5 mins then 10 min after intubation. Data was analysed using SPSS.

RESULTS
Groups were well matched for their demographic data. There was a statistically significant difference ($p < 0.05$) among different doses of dexmedetomidine and normal saline in haemodynamics from infusion of drugs to tracheal intubation and up to 10 minutes after intubation. There were no such adverse effects (hypotension, bradycardia, respiratory depression and fall in oxygen saturation) in any of the patients.

CONCLUSIONS
Dexmedetomidine 0.5 mcg / Kg loading dose is the safe and effective dose to attenuate haemodynamic response to laryngoscopy and endotracheal intubation.

KEYWORDS
Haemodynamic Responses, Laryngoscopy, Intubation, General Anaesthesia, Dexmedetomidine

Corresponding Author:
Dr. Mousumi Das,
Assistant Professor,
Department of Anaesthesiology,
Kalinga Institute of Medical Sciences,
KIIT University Bhubaneswar,
Odisha, India.
E-mail: mousumi.das1503@gmail.com

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BACKGROUND

Endotracheal intubation was introduced by Rowbotham and Magil in 1921 and is still widely practiced even today. In 1940, Reid and Brace, first showed the hemodynamic response to laryngoscopy and intubation.[1] The intubation is a noxious stimulus, which causes tachycardia and hypertension due to intense sympathetic activity.[2] The reflex sympathetic discharge due to epipharyngeal and laryngeal stimulation and are marked by hypertension, tachycardia arrythmias. This hemodynamic response is generally transient and unpredictable. Although such a response would likely be tolerated well by healthy patients, but patient with coronary artery or cerebrovascular diseases may prone for myocardial ischemia and cerebral haemorrhage, which lead to pulmonary edema, myocardial insufficiency and cerebrovascular accident.[3,4] Attenuation of adverse hemodynamic responses to laryngoscopy and intubation has been tried by several techniques, but none of them were found to be ideal.

Earlier studies have used higher doses of the drug (Dexmedetomidine 1 and 2 mcg / Kg) which was associated with bradycardia and hypotension, hence were not studied. So, our present study is designed with three lower doses of Dexmedetomidine (0.5 mcg / Kg, 0.75 mcg / Kg, and 1 mcg / Kg) for attenuating hemodynamic response to laryngoscopy and tracheal intubation with a control group. Objective of the present study is attenuation of haemodynamic stress response during laryngoscopy and intubation using safe and effective dose of dexmedetomidine.

METHODS

This prospective randomised double blind clinical study was undertaken at Kalinga Institute of Medical Sciences, during the period from 15-02-2019 to 14-02-2020. The study was undertaken after obtaining ethical committee clearance (KIMS/KIIT/IEC/ 212/2018) and CTRI registration (CTRI/2019/02/017816) as well as informed consent from all the patients.

Allocation of Groups

Hundred twenty patients of either sex, posted for elective surgeries under general anaesthesia were randomly divided into four groups, 30 patients in each group. Three groups received dexmedetomidine in different doses and control group received normal saline.

- Group A - 0.5 mcg / Kg body weight.
- Group B - 0.75 mcg / Kg body weight.
- Group C - 1 mcg / Kg body weight.
- Group D - received NS.

Inclusion Criteria

Age: 18 to 60 year, ASA-I and II.

Exclusion Criteria

Hypertension, diabetes, chronic obstructive pulmonary disease (COPD), ischemic heart diseases, patients on beta blocker, heart block, cases of base line sinus bradycardia, allergic to study drugs, BMI > 30, pregnancy, difficult airway, & emergency surgeries. Laryngoscopy & intubation taking more than 15 seconds or failing to perform intubation in a single attempt was excluded from the study.

A routine preanaesthetic evaluation of each patient was done a day prior to surgery. Weight of the patient was recorded for calculation of the drug dosage for the study. Patient were kept fasting 6 to 8 hours prior to surgery. All the patients were preoperatively evaluated. After obtaining a good IV access, patients were shifted to the operating room where multiparameter monitor was available. All the vitals (HR, ECG, NIBP, ETCO2, and SpO2) were recorded and patients were premedicated with inj. glycopyrrolate 0.004 mg / Kg, inj. nalbuphine 0.1 mg / Kg & midazolam 20 mcg / Kg. All vitals were recorded after premedication. The study drugs were diluted with NS up to 10 mL and group D received only 10 mL NS given to the patient using infusion pump over 10 minutes. All the patients were then induced with propofol after preoxygenation. Intubation was facilitated using rocuronium 0.6 mg / Kg, and anaesthesia was maintained with oxygen, nitrous oxide & isoflurane. At the end of procedure, all cases were reversed with a mixture of neostigmine and glycopyrrolate in usual doses. No surgical stimulation was allowed for 10 minutes after intubation (till the study period was over). Patients were monitored for incidence of bradycardia (HR < 25 % of baseline value or 50 / min), hypertension (SBP > 25 % of baseline value or SBP > 150 mm Hg) hypotension (SBP < 25 % of baseline value or SBP < 90 mm Hg) and fall in SpO2.

Following Parameters were Noted

HR, SBP and DBP were compared in the four groups

- before administration of the study drug.
- at 5 min with ongoing infusion of study drug.
- after completion of the study drug.
- immediately after induction.
- during intubation.
- every minute up to 5 minutes & 10 min after intubation.

Statistical Analysis

Statistical analysis was performed through SPSS Version 15. Statistical analysis was done with ANOVA and paired t test. Results were expressed as mean ± SD. A p value less than 0.05 was considered as statistically significant.

RESULTS

Demographic profile of patients, i.e. age, weight, BMI (mean ± SD) and sex are mentioned in Table 1. Baseline mean HR were comparable in all four groups. During infusion of the study drug, group A (0.5 mcg / Kg) mean HR was slightly decreased but in group B (0.75 mcg / Kg) and group C (1 mcg / Kg) mean HR was significantly decreased. Group A, group B, group C, showed no significant increase in mean HR after intubation as compared with group D (NS). In group D, there was a significant increase in HR after intubation as shown in Table 2. In Table 3 the baseline mean SBP were comparable in all four groups. During drug infusion, group B (0.75 mcg / Kg) and group C (1 mcg / Kg) showed transient rise in SBP at 5 and 10 minutes which was highly statistically significant but there was a slight fall in SBP in group A (0.5 mcg / Kg), showing that the patients in this group had no marked fluctuations in their SBP. During intubation, maximum rise in mean SBP was seen in group D (NS) as compared to other three groups. The maximum fall in mean SBP was observed in group C (1 mcg / Kg) at 10 minutes following intubation.

Baseline mean DBP was comparable. During drug infusion, there was an increase in mean DBP in group B, and group C, but a slight decrease was noted in group A. During intubation the rise in mean DBP was more significant in group D (NS) as compared to other three groups as shown in Table 4.

Parameter	Group A	Group B	Group C	Group D
Age (Year)	40 ± 11.25	38.83 ± 10.28	38.03 ± 11.36	40.66 ±12.12
Weight (Kg)	57.73 ± 5.86	57.17 ± 5.59	57.56 ± 5.31	58.43 ± 5.62
BMI (Kg / m)	22.80 ± 1.10	22.75 ± 0.84	22.76 ± 0.82	23.22 ± 0.78
Sex (male / female)	12 / 18	16 / 14	13 / 17	14 / 16

Table 1. Demographic Profile of Patient

Heart Rate	Group				P Value	Pairwise Significance		
	Group A Mean ± SD	Group B Mean ± SD	Group C Mean ± SD	Group D Mean ± SD		Group A vs. D	Group B vs. D	Group C vs. D
At baseline	77.13 ± 5.97	75.53 ± 5.72	75.30 ± 6.99	76.40 ± 7.15	0.681	0.668	0.606	0.549
After 5 min of infusion of the study drug	73.13 ± 6.39	69.63 ± 6.36	67.40 ± 4.32	76.20 ± 7.46	0.000	0.093	0.001	0.000
After completion of the study drug	70.03 ± 7.03	63.63 ± 6.33	63.20 ± 3.95	76.13 ± 7.39	0.000	0.002	0.000	0.000
After induction	65.93 ± 6.86	66.20 ± 6.40	68.37 ± 5.11	70.73 ± 7.34	0.016	0.011	0.013	0.153
During intubation	71.83 ± 6.45	72.77 ± 6.12	75.50 ± 4.55	92.60 ± 12.25	0.000	0.000	0.000	0.000
At 1 min. after intubation	70.70 ± 7.09	68.77 ± 6.13	71.60 ± 3.24	90.47 ± 11.37	0.000	0.000	0.000	0.000
At 2 min. after intubation	68.40 ± 6.99	66.43 ± 5.95	69.10 ± 3.50	88.50 ± 10.78	0.000	0.000	0.000	0.000
At 3 min after intubation	66.57 ± 6.63	64.20 ± 5.42	67.10 ± 3.54	86.93 ± 10.35	0.000	0.000	0.000	0.000
At 4 min after intubation	64.73 ± 6.42	62.80 ± 5.51	65.80 ± 3.18	109.03 ± 132.58	0.000	0.000	0.061	0.000
At 5 min after intubation	62.63 ± 6.56	62.90 ± 5.44	63.77 ± 2.82	82.50 ± 9.88	0.000	0.000	0.000	0.000
At 10 min after intubation	60.70 ± 6.29	59.83 ± 5.32	60.57 ± 2.37	79.83 ± 8.72	0.000	0.000	0.000	0.000

Table 2. Comparative Changes of Heart Rate (HR) among Four Groups and Intragroup Change in Mean HR from Baseline HR at Different Time Intervals

SBP	Group				P Value	Pair Wise Significance		
	Group A Mean± SD	Group B Mean± SD	Group C Mean ± SD	Group D Mean ± SD		Group A vs. D	Group B vs. D	Group C vs. D
At baseline	122.23± 7.01	122.17± 5.10	123.47±5.08	122.43 ± 5.56	0.801	0.903	0.847	0.456
After 5 min of infusion of study drug	116.43± 8.14	126.30± 4.89	127.97± 6.62	121.90 ± 5.36	0.000	0.093	0.002	0.000
After completion of the study drug	116.27± 6.55	126.53± 5.17	127.00± 6.98	121.47 ± 6.20	0.000	0.002	0.001	0.002
After induction	113.97± 5.99	121.43± 4.68	111.80± 7.45	117.90 ± 6.12	0.000	0.011	0.015	0.001
During intubation	117.67± 5.35	125.33± 4.22	115.17± 7.27	133.67 ± 9.20	0.000	0.000	0.000	0.000
At 1 min after intubation	117.43± 5.41	124.50± 5.53	113.47± 7.21	131.60 ± 8.67	0.000	0.000	0.000	0.000
At 2 min after intubation	116.13± 5.50	122.00± 3.87	109.7± 6.92	128.70 ± 7.29	0.000	0.000	0.000	0.000
At 3 min after intubation	114.07± 6.09	120.80± 3.02	108.03± 6.05	126.17 ± 6.31	0.000	0.000	0.000	0.000
At 4 min after intubation	112.13± 6.32	118.63± 2.62	106.07± 6.64	123.67 ± 5.36	0.000	0.000	0.000	0.000
At 5 min after intubation	110± 6.84	118.57± 1.72	104.83± 7.05	120.57 ± 3.37	0.000	0.000	0.005	0.000
At 10 min after intubation	108.33± 6.55	116.93± 2.12	104.37 ± 5.60	119.8 ± 2.31	0.000	0.000	0.000	0.000

Table 3. Comparative Changes Mean Systolic Blood Pressure (SBP) among Four Groups and Intragroup Change in Mean SBP from Baseline SBP at Different Time Intervals

DBP	Group				P Value	Pairwise Significance		
	Group A Mean ± SD	Group B Mean ± SD	Group C Mean ± SD	Group D Mean ± SD		Group A vs. D	Group B vs. D	Group C vs. D
At baseline	78.67± 3.31	77.87 ± 3.62	77.77 ± 2.61	79.4 ± 3.84	0.208	0.432	0.117	0.059
After 5 min of infusion of study drug	76.57 ± 3.43	81.03 ± 4.57	83.73 ± 4.14	79.37 ± 4.51	0.000	0.009	0.161	0.000S
After completion of the study drug	76.4 ± 3.52	80.53 ± 4.75	78.47 ± 4.93	79.77 ± 4.76	0.007	0.004	0.156	0.811
After induction	71.87 ± 4.38	73.67 ± 4.92	74.87 ± 3.63	75.5 ± 5.07	0.001	0.004	0.160	0.580
During intubation	76.57 ± 4.01	77.93 ± 4.76	79.43 ± 3.50	89.17 ± 6.35	0.000	0.000	0.000	0.000
At 1 min after intubation	75.87 ± 4.2	75.73 ± 4.91	78.2 ± 3.31	87.9 ± 4.67	0.000	0.000	0.000	0.000
At 2 min after intubation	74.47 ± 4.31	75.53 ± 4.84	76.77 ± 3.33	87.13 ± 4.66	0.000	0.000	0.001	0.000
At 3 min after intubation	72.6 ± 4.42	74.8 ± 4.92	74.93 ± 3.43	86 ± 4.67	0.000	0.000	0.000	0.000
At 4 min after intubation	71.3 ± 4.74	73.13 ± 4.62	71.77 ± 3.66	82.07 ± 3.35	0.000	0.000	0.000	0.000
At 5 min after intubation	70.2 ± 4.63	72.13 ± 4.04	70 ±3.12	80.4 ± 3.2	0.000	0.000	0.000	0.000
At 10 min after intubation	67.53 ± 4.12	69.47 ± 3.44	65.1 ± 3.34	79.13 ± 2.94	0.000	0.000	0.000	0.000

Table 4. Comparative Changes in Mean Diastolic Blood Pressure (DBP) among Four Groups and Intragroup Changes in Mean DBP from Baseline DBP at Different Time Intervals.

DISCUSSION

Laryngoscopy and endotracheal intubation are noxious stimuli which causes haemodynamic changes due to sympathoadrenal response. These changes are usually short lived and well tolerated by normal patients. But in patients with cardiovascular compromise like hypertension, coronary artery disease, cerebrovascular disease and in patients with intracranial aneurysms, even these transient changes in haemodynamics can result in potentially harmful effects[5] which necessitates its control[6] by obtunding the stress response.[7] Distribution half-life of Dexmedetomidine is of approximately 6 min, so can be used successfully for attenuating the stress response to laryngoscopy and intubation.

Dexmedetomidine offers a unique pharmacological profile with sedation, sympatholysis, analgesia, cardiovascular stability and with great advantage to avoid respiratory depression in adult and paediatric patients. It increases the hemodynamic stability by altering the stress induced sympathoadrenal responses to intubation during surgery and during emergence from anesthesia.[8]

In the present study, three different dosages (0.5, 0.75, and 1 μg / Kg) of Dexmedetomidine were studied to evaluate the effective and safe intravenous dose of Dexmedetomidine to attenuate these adverse hemodynamic responses of laryngoscopy and endotracheal intubation.

Similar to our study finding, A Laha et al[9] observed a statistically significant fall in mean HR at 1 and 2 minutes of infusion of Dexmedetomidine at 1 mcg / Kg over 10 minutes. Kenya et al[10] observed transient bradycardia when they used Dexmedetomidine infusion 1 mcg / Kg over 10 minutes prior to induction. Lowrencen et al observed significant transient fall in HR at 1st and 5th minute after administration of single dose of 2 / Kg.[11]

Presynaptic and postsynaptic effects of α2 agonists diminish nor epinephrine release and inhibit the central sympathetic out flow. In the present study, there was a significant decrease in HR in all patients after induction, but it was more marked in patients who received Dexmedetomidine at dosage of 1 μg / Kg as premedication. The primary action of Dexmedetomidine on the heart is a negative chronotropic effect by blocking the cardioaccelerator nerves and by augmenting the vagal nerve. The decrease in HR can be attributed to a reflex response for transient hypertension during the initial part of infusion and subsequently due to a decrease in the central sympathetic outflow.[12]

A study conducted by Menda et al on ischemic heart disease patients, undergoing fast-track coronary artery bypass graft. In their study, they compared Dexmedetomidine 1 mcg / Kg and placebo. They concluded that, in placebo group, the systolic arterial pressure increased significantly after the intubation, compared to pre-intubation period, whereas in Dexmedetomidine group, it did not change significantly.[13] In many studies, transient increase in HR and MAP was noted initially within 3 to 5 min of Dexmedetomidine infusion, which was followed by a decrease [14,15,] most probably due to vasoconstrictive effect of Dexmedetomidine appearing earlier than the central sympathetic action. Our study result are also in accordance with these studies. Yildiz et al.[16] and Keniya et al.[10] studied the effect of Dexmedetomidine on the hemodynamic responses to laryngoscopy and intubation and on the intraoperative anaesthetic requirement. They concluded that the increase in BP and HR was significantly lower in the Dexmedetomidine group than in the placebo group.

Hypotension and bradycardia (HR < 50 / min) were not observed in any patient during our study period. This may be due to premedication with injection glycopyrrolate and adequate preanaesthetic plasma volume expansion. Bijoy Kumar Panda[17] and Shirsendu Mondal et al[18] have also not found any instability of vitals either with Clonidine or dexmedetomidine. Singh et al[19] study also did not show any side effects like bradycardia and sinus pause, which would have warranted the use of atropine.

CONCLUSIONS

Based on the findings of our study, we conclude that, dexmedetomidine 0.5 mcg / Kg loading dose is safe and effective to provide better attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation. 0.5 mcg / Kg loading dose is unaccompanied by transient hypertension and bradycardia which is observed at 0.75 mcg / Kg and 1 mcg / Kg loading doses.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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