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Original Article

COMPARISON BETWEEN EFFECT OF TWO DIFFERENT DOSES OF INTRAVENOUS DEXMEDETOMIDINE IN ATTENUATING HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION IN ELECTIVE GENERAL SURGERIES UNDER GENERAL ANAESTHESIA

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ABSTRACT

Objective: The process of intubation is a noxious stimuli leading to a period of hemodynamic stress and is accompanied with intense sympathetic activity marked by tachycardia, hypertension and arrythmias.

Methods: It was a randomised, prospective, double-blind study. After approval from the ethics committee 60 patients (ASA class 1 and II) were selected randomly, thirty in each group. Group A (n=30) received 0.5 µg/kg of inj. Dexmedetomidine and Group B received 0.75µg/kg of inj. Dexmedetomidine in 20 ml of normal saline as an infusion over 10 min. The patient was induced with inj Fentanyl 1µg/kg, inj. Propofol and inj. Succinylcholine administered and intubated. The primary outcome variables were heart rate and blood pressure at 1, 3, 5, 10, 15 min after intubation. The secondary outcome variables were the effect on the induction dose of propofol and any adverse effect associated with dexmedetomidine. The statistical package used was spss version 22.

Results: The hemodynamic responses were attenuated in both groups after laryngoscopy and endotracheal intubation, with statistical significant difference between both groups and better obtundation of hemodynamic response in terms of heart rate, systolic, diastolic and mean arterial pressure at all points of time with dexmedetomidine 0.75µg/kg. Sedation scores were more with dexmedetomidine 0.75µg/kg. No significant side effects were there in both groups.

Conclusion: Inj. dexmedetomidine 0.75µg/kg is more effective in attenuating the response to laryngoscopy and endotracheal intubation.

Keywords: Laryngoscopy, Endotracheal intubation, Hemodynamic response, Dexmedetomidine

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INTRODUCTION

Laryngoscopy and endotracheal intubation is a conventional measure to secure the airway for proper ventilation of the patient during general anaesthesia and surgery [1]. The process of intubation is a noxious stimuli leading to a period of extreme hemodynamic stress and is accompanied with intense sympathetic activity marked by tachycardia, hypertension and arrythmias [2]. These augmented cardiovascular response of laryngoscopy and intubation in the form of tachycardia and hypertension are transitory, variable and unpredictable and may cause insignificant problems in normal healthy individuals generally but can be detrimental for patients with hypertension, myocardial insufficiency and cerebrovascular disease [3, 4].

Clinically available α_2 adrenergic agonists are Clonidine and Dexmedetomidine. These drugs by virtue of their sympatholytic action i.e. antihypertensive and negative chronotropic, attenuate hemodynamic response following laryngoscopy and endotracheal intubation [5].

Various authors have used dexmedetomidine in a dose of 0.5mcg/kg and 1mcg/kg and found them to be effective in attenuation of stress response to laryngoscopy and endotracheal intubation [6, 7]. Although with promising result yet the higher dose of 1mcg/kg was associated with increased incidence of cardiovascular compromise in the form of hypotension and bradycardia [6, 7].

The present study is aimed to compare two different doses of dexmedetomidine i.e. 0.5mcg/kg and 0.75mcg/kg to arrive at an optimal dose of dexmedetomidine for attenuation of stress response to laryngoscopy and endotracheal intubation in patients posted for elective general surgeries under general anaesthesia without untoward side effects.

MATERIALS AND METHODS

The present study was conducted in department of anaesthesia at our Medical College Hospital, with due permission from the institutional ethics committee and review board. It is a hospital-based, prospective, randomized, double-blind, Interventional study.

The sample size required is sixty cases, thirty cases in each group at 95% Confidence Interval and 80% power to verify the expected minimum difference of 1.27 (±0.97) in variation in heart rate from baseline to one minute after laryngoscopy and intubation in both groups. Patients included in study were those who gave informed written consent, between 18-50 y, of either sex, and ASA Class 1 and Class 2.

Those patients unable to understand the study protocol, on beta-blockers, antidepressants, anxiolytics, anticonvulsant, antipsychotics, known drug allergy to dexmedetomidine, anticipated difficult airway were excluded from study.

After checking fasting status, written informed consent and preanaesthetic checkup, baseline hemodynamic parameters heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, SpO2, ECG were recorded.

Group A received inj. dexmedetomidine 0.5 µg/kg diluted to 20 ml normal saline as an infusion over 10 min. Group B received inj. dexmedetomidine 0.75mcg/kg diluted to 20 ml normal saline as an infusion over 10 min. After study drug infusion, if there was any hypotension as a decrease in mean blood pressure, more than 20% from baseline was supposed to be managed by incremental doses of 3 mg inj. Mephentermine intravenously and bradycardia as heart rate less than 50/min was supposed to be managed by incremental doses of 0.5 mg inj. Atropine intravenously.

After completion of drug infusion, sedation was assessed at 2, 5, 10 min interval using ramsay sedation score. The general anaesthesia technique was standardized for both groups.

All patients were given i. v. inj. Metoclopramide 0.1 mg/kg+inj. Glycopyrrolate 0.004 mg/kg+inj. Midazolam 0.02 mg/kg+inj. Fentanyl 1 µg/kg.

After preoxygenation with 100% oxygen for 3 min, induction was done with 1% inj. Propofol intravenously at the rate of 0.5 ml/sec, which was continued till the patient's verbal response abolished. The dose of propofol was noted. Neuromuscular blockade was achieved with inj. succinylcholine 2 mg/kg intravenously; under direct laryngoscopy endotracheal intubation was done. Then loading dose of inj. Atracurium 0.5 mg/kg i. v. was given and anaesthesia was maintained with 40% O2+60% N2O+Isoflurane 0.4 MAC%+inj. Atracurium 0.1 mg/kg as maintenance dose. vital parameters HR, SBP, DBP, MAP, at 1, 3, 5, 10, 15 min after laryngoscopy and intubation was recorded. At the end of surgery, reversal was achieved with i. v. inj. Neostigmine 0.05 mg/kg and inj. Glycopyrrolate 0.01 mg/kg and after complete reversal, extubation was done. After adequate recovery patients were shifted to post anaesthesia care unit.

Statistical analysis was performed with the SPSS, version 21 for Window statistical software package (SPSS inc., Chicago, IL, USA). The quantitative data was presented as mean and SD and were compared using the student t test. The categorical data was presented as numbers (percent) and were compared among groups using chi square test. The level of significance was kept at 95% for all statistical analysis. Probability was considered to be significant if less than 0.05.

RESULTS

The present study was conducted on 60 patients and were well matched for their demographic profile age, sex and weight (table 1)

Table 1: Demographic profile of study population

Parameters	Group A	Group B	P value
Age (years)	38.10±11.35	40.87±8.52	0.279 (NS)
Sex (M/F)	16/14	17/13	1 (NS)
Weight (kg)	57.93±10.85	59.17±9.33	0.638 (NS)

There was a statistically significant difference between the mean HR in two groups at 10 min after completion of study drug ($p<0.05$) and a significant difference at 1 min, 3 min, 5 min, 10 min, 15 min post intubation ($p<0.05$).

Table 2: Comparison of mean heart (bpm)

	Group A mean±SD	Group B mean±SD	P value
Baseline (T0)	81.80±5.15	81.60±5.13	0.880 (NS)
2 min AD (T1)	79.23±5.19	77.83±5.19	0.300 (NS)
5 min AD (T2)	75.70±5.40	73.27±4.97	0.74 (NS)
10 min AD (T3)	72.07±5.36	68.5±4.89	0.009 (S)
1 min AI (T4)	86.40±4.92	82.67±5.34	0.006 (S)
3 min AI (T5)	84.03±5.09	80.20±5.53	0.007 (S)
5 min AI (T6)	80.60±5.35	76.03±5.24	0.001 (S)
10 min AI (T7)	80.07±5.24	75.50±5.20	0.001 (S)
15 min AI (T8)	79.80±5.27	74.87±5.26	0.0006 (S)

There was a statistically significant difference between the mean SBP in two groups at 1 min, 3 min, 5 min, 10 min, 15 min post intubation ($p<0.05$).

Table 3: Comparison of mean SBP (mmHg)

Time	Group A mean±SD	Group B mean±SD	P value
Baseline (T0)	124.83±6.51	127.13±5.86	0.155 (NS)
2 min AD (T1)	120.87±6.86	122.03±5.99	0.485 (NS)
5 min AD (T2)	116.13±6.47	115.13±6.19	0.365 (NS)
10 min AD (T3)	111.13±6.21	110.07±6.41	0.515 (NS)
1 min AI (T4)	132.33±7.88	127.23±5.96	0.006 (S)
3 min AI (T5)	126.87±7.76	120.57±5.86	0.007 (S)
5 min AI (T6)	122.97±6.95	112.87±5.85	0.001 (S)
10 min AI (T7)	121.60±6.65	112.73±5.74	0.001 (S)
15 min AI (T8)	120.50±6.33	111.90±5.12	0.001 (S)

There was a statistically significant difference between the mean DBP in two groups at 5 min 10 min after completion of study drug ($p<0.05$) and a significant difference at 1 min, 3 min, 5 min, 10 min, 15 min post intubation ($p<0.05$).

Table 4: Comparison of mean DBP (mmHg)

Time	Group A mean±SD	Group B mean±SD	P value
Baseline (T0)	79.60±4.21	80.77±3.92	0.271 (NS)
2 min AD (T1)	76.07±4.46	75.20±3.75	0.418 (NS)
5 min AD (T2)	71.63±4.71	69.20±3.64	0.029 (S)
10 min AD (T3)	66.73±5.16	63.33±3.07	0.002 (S)
1 min AI (T4)	84.43±4.71	80.83±3.74	0.001 (S)
3 min AI (T5)	79.07±4.43	75.83±3.74	0.003 (S)
5 min AI (T6)	77.00±4.01	72.13±4.11	0.001 (S)
10 min AI (T7)	76.10±4.44	71.73±3.91	0.001 (S)
15 min AI (T8)	75.17±4.41	79.90±4.15	0.001 (S)

There was a statistically highly significant difference between the mean MAP in two groups at 1 min ($p<0.001$), and a significant difference at 3 min, 5 min, 10 min, 15 min post intubation ($p<0.05$). There was a statistically significant difference between the mean induction dose of propofol in two groups being low in group B ($p<0.001$).

Table 5: Propofol dose

Dose	Group A	Group B	P value
Mean dose (mg/kg)	1.34±0.12	0.98±10	<0.001 (S)
Range	1.2-1.7	0.8-1.12	

Ramsay Sedation Score between the two study groups at 2 min, and 5 min after completion of study drug (P >0.05), but it was significant (p<0.05) at 10 min after completion of drug being high in group B. There was no fall in SpO2 below 97% in any of the group at any time after drug administration.

DISCUSSION

Dexmedetomidine is a more specific α_2-adrenoreceptor agonist (α_2/α_1= 1620/1) than clonidine (α_2/α_1= 220/1) [8]. Dexmedetomidine causes a reduction in blood pressure, slowing of HR, sedation and analgesia [9, 10]. The fall in blood pressure is mainly due to inhibition of central sympathetic outflow and also due to stimulation of presynaptic α_2 adrenoceptors decreasing norepinephrine release [11]. An important advantage is its minimal respiratory depressant effect with potent sedative and analgesic effects compared with opioids and other sedatives.

In the present study, there was a gradual reduction in heart rate after dexmedetomidine infusion in both group, which was significant 10 min after completion of study drug. After laryngoscopy and intubation, the mean heart rate increased in both groups then started decreasing. when compared at different point of time after intubation, it was found that the mean heart rates in Group B were lower than in Group A with significant differences at all point of time i.e. 1 min, 3 min, 5 min, 10 min, 15 min (p-value<0.05) after intubation.

In group A HR reached to baseline 5 min after intubation while in group B HR reached to baseline or below it at 3 min after intubation. Similar observations were noted by *Bon Sebastian et al.,* (2017) [12], that following laryngoscopy and intubation, there was an increase in heart rate from baseline in both groups of dexmedetomidine. It approaches to baseline at 5 min in dexmedetomidine 0.5µg/kg group while in dexmedetomidine 0.75µg/kg group it approaches to baseline at 3 min and the intubation response was completely obtunded in this group. So, authors concluded dexmedetomidine 0.75µg/kg being most effective with better control of heart rate.

When SBP, DBP and MAP of both groups were studied, it was found that after drug infusion, there was decreased in SBP, DBP MAP in both group and after laryngoscopy and intubation, the mean SBP, DBP, MAP increased at 1 min, in group A while it was almost similar to baseline in group B, then it started decreasing with significant differences at all point of time i.e. 1 min, 3 min, 5 min, 10 min, 15 min (p-value<0.05) after intubation. Dexmedetomidine in a dose of 0.75µg/kg obtunds complete hemodynamic response as compared to dose 0.5µg/kg. *L. Dhanachandra et al.* (2019) [13] also interpreted similar result and concluded that SBP, DBP, MAP, increases after laryngoscopy and intubation; Both doses of dexmedetomidine 0.5µg/kg body weight and 0.75µg/kg body weight can attenuate the hemodynamic response to laryngoscopy and intubation but dexmedetomidine at the dose of 0.75µg/kg body weight can do it better and longer i.e. up to 10 min than dexmedetomidine 0.5µg/kg body weight.

In our study, the patients who received dexmedetomidine 0.75µg/kg had significantly more sedation score as compared to dexmedetomidine 0.5µg/kg (p<0.05). *Bon Sebastian et al., (2017)* found almost similar observation being sedation score were higher in dexmedetomidine 0.75µg/kg group i.e. 6 patient had ss 4 in dexmedetomidine 0.75µg/kg group and 2 patients had ss 4 in dexmedetomidine 0.5µg/kg.

Induction dose of propofol was significantly reduced in dexmedetomidine 0.75µg/kg group being 0.8-1.12 mg/kg as compared to group A (p<0.05). Thus, dexmedetomidine 0.75µg/kg provides more intense sedation along with sparing of propofol dose. *Neha Sharma et al. (2018)* [14], who concluded that the induction dose of propofol required to abolish verbal response was reduced to almost half its dose in the dexmedetomidine group as compared to placebo group.

There was no significant fall in HR, SBP, DBP, MAP in both the groups. None of the patient required treatment of bradycardia, hypotension, hypertension. Also there was no fall in SpO_2 below 97% in any of the patient. Respiratory depression was not observed in any patient among both the groups. *Bon Sebastian et al., (2017)* found similar observation in their study and there was no episode of bradycardia, hypotension, hypertension, respiratory depression in any of the patient.

CONCLUSION

According to our study, inj. dexmedetomidine 0.75µg/kg provides statistically significant attenuation of hemodynamic response to laryngoscopy and endotracheal intubation as compared to inj. dexmedetomidine 0.5µg/kg without having significant adverse effects, with better hemodynamic stability along with dose sparing effect of propofol for induction.

Thus, from the present study, we conclude inj. dexmedetomidine 0.75µg/kg as more effective in attenuating the response to laryngoscopy and endotracheal intubation.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally

CONFLICT OF INTERESTS

Declared none

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