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Original Research Paper

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EFFECT ON HEMODYNAMIC VARIABILITY OF INTRAVENOUS DEXMEDETOMIDINE 0.5μg/kg VS 1μg/kg DURING DIRECT LARYNGOSCOPY & ENDOTRACHEAL INTUBATION IN ELECTIVE SURGERIES UNDER GENERAL ANAESTHESIA: A RANDOMIZED DOUBLE BLIND INTERVENTIONAL STUDY

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KEYWORDS :

INTRODUCTION

Safe airway management is an essential skill for an anaesthesiologist.[1] Laryngoscopy and endotracheal intubation are common measure to secure airway for proper ventilation of patients during surgery under general anaesthesia.[2] Laryngoscopy and intubation evoke a painful stimulus, which causes severe physiological and pathological responses such as autonomic and activated brain stem reflexes.[2] The magnitude of the response is greater with increasing force and duration of laryngoscopy.[3,4] Endotracheal intubation directly affect severe sympathoadrenal responses, which increase arterial blood pressure, plasma catecholamine levels, heart rate and even lead to dysrhythmia in some cases.[5]

The tachycardia and hypertensive response to laryngoscopy and intubation are not of much consequence and short lived in normotensive patients but may prove hazardous in geriatric patients or patients with medical problems like hypertension, ischemic heart disease, thyrotoxicosis and cerebrovascular diseases.[4] In such cases acute left ventricular failure, acute myocardial ischemia and cerebral haemorrhage can occur. These changes may be fatal, and sudden deaths have also been reported in patients with medical problems.

There is need for the availability of a drug that effectively suppresses all the hazardous responses to obnoxious stimuli to blunt the undesirable hemodynamic responses. Drugs acting as α2 agonist like clonidine and dexmedetomidine have been recently used. Dexmedetomidine is 7-10 times more α2 selective and has a shorter duration of action compared to clonidine. Dexmedetomidine activates α2 adrenergic inhibitory neurons in medullary vasomotor centre, thus there is a decrease in sympathetic nervous system outflow from central nervous system to peripheral tissues, which results in peripheral vasodilatation and decrease in systemic blood pressure (BP), heart rate (HR) and cardiac output, and maintain hemodynamic stability.

Premedication with dexmedetomidine provide a stable haemodynamic awake sedation without causing respiratory depression. It is currently used in Intensive Care Unit (ICU) for sedation and analgesia in mechanically ventilated patients and produces rapid recovery after discontinuation. The need for inhalational anaesthetics decreases because of significant drop up to 90% in the minimum alveolar concentration (MAC) of volatile anaesthetics.[6] This not only attenuates hemodynamic response but also decreases thiopentone requirements and improves the recuperation from anaesthesia with no serious hemodynamic or other adverse effect.[7]

The dose of dexmedetomidine used for this purpose varies from 0.5μg/kg to 2μg/kg but the risk of undesirable side effects along with desired advantage is extremely important in evaluating the overall safety of any medications. But very few researchers have studied a comparison between two doses of dexmedetomidine (0.5μg/kg vs 1μg/kg) and it is yet remains undetermined which dose of dexmedetomidine provides better attenuation of haemodynamic surges associated with laryngoscopy and intubation. Thus, we designed a randomized, prospective, double-blinded study to compare hemodynamic responses with two different doses 0.5μg/kg and 1μg/kg of dexmedetomidine and to compare the side effects in first 24 hours of post induction period.

MATERIALS AND METHODS

This hospital based randomized double blinded Interventional study was conducted under the department of Anaesthesia, tertiary care facility Jaipur. Study was conducted for the period of one year from November 2020 to October 2021 after approval from the Institutional Ethical Committee of the institution.

Sample Size

Sample of 38 cases in each group was calculated at 95% confidence interval and 80% power to verify the expected minimum difference of 6±9.2 beats per minute in change in heart rate from baseline to 1 minute post intubation in both study groups.

Patients of 20 to 50 years of age, undergone elective surgery under general anaesthesia, of ASA class I and II, who gave written informed consent were included in our study. Patients with history of hypertension or on any antihypertensive medicine, or history of drug or alcohol abuse, or have allergy to dexmedetomidine were excluded from the study. All eligible patients were randomly allocated into each study group A and B after explaining them about nature and purpose of the study. To ensure unbiased group allocation, the sealed envelope method of randomization was employed in this study. We prepared opaque and securely sealed envelopes, each containing a group assignment and each envelope labelled with a unique identifier or number. The envelopes were identical in appearance to maintain allocation concealment. Randomization occurred by drawing one envelope at a time from the set. The anaesthetist who prepared the study drug and administered the anaesthesia was different from the anaesthetist who observed study variables. Patients were told that anaesthetic agent were given to them to stabilize their vitals, but the dose and details were not discussed. Patients of group A received 0.5 μg/kg of Dexmedetomidine infusion in 20 ml of normal saline over 10 min via infusion pump. Patients of group B received 1.0 μg/kg of Dexmedetomidine infusion in 20 ml of normal saline over 10 min via infusion pump.

Complete medical and surgical history of the patient were noted including any known drug allergy. The baseline vitals were recorded. All patients were given intravenous Metoclopramide 0.1 mg/kg + injectable Glycopyrrolate 0.004

mg/kg + injectable Midazolam 0.02mg/kg + injectable Fentanyl 2 μg/kg. After preoxygenation with 100% oxygen for 3 minutes, induction was done with 2.5% Thiopentone intravenously till the patient's eyelash's response abolished. The dose of Thiopentone required for abolishing this response was noted after which neuromuscular blockade was achieved with succinyl choline 2 mg/kg intravenous under direct laryngoscopy endotracheal intubation was done. Following this vital parameter heart rate, systolic and diastolic blood pressure, and mean arterial pressure at 1, 2,3,5 and 10 minutes were recorded. Then loading dose of Atracurium 0.5 mg/kg intravenous was given and anaesthesia was maintained with 50% O_2 + 50% N_2O + Isoflurane 0.4 MAC% + inj. Atracurium 0.1 mg/kg. At the end of surgery reversal was achieved with intravenous Neostigmine 0.08mg/kg and injectable Glycopyrrolate 0.01mg/kg, and extubation was done. After adequate recovery patient was shifted to recovery room to see immediate postoperative complications and to observe any side effects till next 24 hours post operative periods.

Statistical Analysis

Done using SPSS Trial version 23 and primer. Discrete data were expressed in form of proportion and continuous data expressed as mean and standard deviations. The difference in proportion was analyzed by using chi square test and the difference in means was analyzed using the student t test. The level of significance was kept at 95% for all statistical analysis.

RESULTS

The mean age of participants of group A and B was 35.92±10.36 and 38.97±8.94 years respectively. In group A, 18(47.4%) were male and rest were female, in group B 21(55.3%) were male and rest were female. The mean weight of patients of Group A and Group B were 59.32±10.84 kg and 59.168±9.03 kg respectively. There was no significant difference in age, sex, and weight of participants between both study groups (p value>0.05). In group A, mean induction dose of thiopentone was 262.42±46.47 mg while in group B it was 222.42±35.02 mg. Difference in mean induction dose of thiopentone between both the groups was statistically significant (p value<0.05) which means Group B required less dose of thiopentone for induction. In group A, none of the patient had hypotension, while bradycardia and vomiting each were seen in one patient. While in group B, only one patient had hypotension and no other side effects were seen. [Table I] depicts mean heart rate at different time intervals. Mean heart rate in patients of group A was higher compared to group B, this difference in mean heart rate was significant at 10 minutes after infusion, just before intubation, 1 minutes, 2 minutes, 3 minutes, 5 minutes, and 10 minutes post intubation (p value<0.05). [Table II] depicts mean systolic blood pressure at different time intervals. Mean systolic blood pressure in patients of group A was significantly higher compared to group B at 10 minutes after infusion, just before intubation, 1 minutes, 2 minutes, 3 minutes, 5 minutes, and 10 minutes post intubation (p value<0.05). [Table III] Similarly mean diastolic blood pressure in patients of group A was significantly higher compared to group B at 5 minutes and 10 minutes after infusion, just before intubation, 1 minutes, 2 minutes, 3 minutes, 5 minutes, and 10 minutes post intubation (p value<0.05). [Table IV] Similarly mean arterial pressure in patients of group A was significantly higher compared to group B (p value <0.05).

Table I- Comparison Of Heart Rate (Beats Per Minute) At Various Time Interval

Heart rate	Group A (n=38)	Group B (n=38)	P value
Baseline	81.13±5.61	80.08±5.58	0.415 (NS)
5 min after Infusion	78.63±5.59	76.34±5.49	0.076 (NS)
10 min after infusion	75.13±5.62	70.21±5.56	<0.001 (S)
Just before intubation	71.18±5.68	65.24±4.76	<0.001 (S)
1 min post intubation	86.71±5.64	78.87±5.71	<0.001 (S)
2 min post intubation	83.76±5.61	76.32±5.78	<0.001 (S)
3 min post intubation	80.53±5.62	74.45±5.33	<0.001 (S)
5 min post intubation	79.82±5.73	74.11±5.24	<0.001 (S)
10 min post intubation	79.84±5.41	73.08±5.23	<0.001 (S)

Table II- Comparison Of Systolic Blood Pressure (mm of Hg) At Various Time Interval

Systolic blood pressure	Group A (n=38)	Group B(n=38)	P value
Baseline	125.79±6.12	127.76±5.9	0.157 (NS)
5 min after Infusion	121.21±6.13	120.58±6	0.651 (NS)
10 min after infusion	116.5±6.03	113.61±6.38	0.046 (S)
Just before intubation	110.68±5.86	106.95±6.26	0.009 (S)
1 min post intubation	131±7.43	125.42±6.36	<0.001 (S)
2 min post intubation	126.32±7.29	120.11±6.58	<0.001 (S)
3 min post intubation	122.84±6.65	112.97±6.56	<0.001 (S)
5 min post intubation	121.21±6.5	111.95±6.44	<0.001 (S)
10 min post intubation	120.45±6.35	110.18±5.68	<0.001 (S)

Table III- Comparison Of Diastolic Blood Pressure (mm of Hg) At Various Time Interval

Diastolic blood pressure	Group A (n=38)	Group B (n=38)	P value
Baseline	80.21±4.24	81±4.07	0.411 (NS)
5 min after Infusion	76.39±4.22	73.66±3.58	0.003 (S)
10 min after infusion	72.5±4.67	67.37±3.32	<0.001 (S)
Just before intubation	67.76±5.11	62.29±2.60	<0.001 (S)
1 min post intubation	84.58±4.84	80.71±3.5	<0.001 (S)
2 min post intubation	80±4.76	74.66±3.16	<0.001 (S)
3 min post intubation	76.97±4.54	70.45±3.87	<0.001 (S)
5 min post intubation	76.08±4.87	69.82±3.69	<0.001 (S)
10 min post intubation	75.29±4.63	68.66±3.63	<0.001 (S)

Table IV- Comparison Of Mean Arterial Pressure (mm of Hg) At Various Time Interval

Mean arterial pressure	Group A (n=38)	Group B (n=38)	P value
Baseline	95.11±3.52	96.97±3.48	0.57 (S)
5 min after Infusion	90.5±3.35	90.45±3.44	0.946 (NS)
10 min after infusion	86.24±3.6	84.47±3.52	0.034 (S)
Just before intubation	83.00±3.73	79.97±3.57	0.001 (S)
1 min post intubation	100.42±4.24	97.05±3.22	<0.001 (S)
2 min post intubation	94.76±3.66	92.29±3.31	0.003 (S)
3 min post intubation	91.76±3.64	88.84±3.22	<0.001 (S)
5 min post intubation	90.92±3.78	86.42±2.97	<0.001 (S)
10 min post intubation	90.16±4.03	83.45±4.22	<0.001 (S)

DISCUSSION

Endotracheal intubation is perceived as the most detrimental events giving rise to a transient but marked sympathoadrenal response. 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 anaesthesia.[8]

No statistically significant differences were found with respect to age, gender, ASA grade, and body weight (p value > 0.05). Therefore, clinically insignificant variation in demographic parameters simply helped to alleviate confounding factors for doses of drugs. The mean baseline parameters (HR, SBP, DBP & MAP) were comparable in both the groups (p value > 0.05). Thus, the randomization was done adequately, and the desired study populations were achieved.

Heart Rate

Heart rate values were statistically significantly lower in

the Dexmedetomidine 1μg/kg group at all-time intervals and an increase in heart rate after intubation was observed in all patients in our study, but the increase was more in patients who received lower dose of dexmedetomidine. It indicates that decrease in heart rate was in a dose dependant manner.

Menda F et al[9], Keniya VM et al[10] and Laha A et al[11] reported the efficacy of dexmedetomidine in blunting the hemodynamic responses to laryngoscopy and intubation. Dhanchandra L et al[12] supported the dose dependent effect of dexmedetomidine as they found that dexmedetomidine in dose of 0.75 μg/kg better obtund the increase in HR than dexmedetomidine in dose of 0.5 μg/kg. Saoyroolu et al[13] also found concurrent results with high dose of dexmedetomidine. Parmar et al[14] also showed that there was significant difference in mean HR in high dose group as compared to low dose group.

The primary action of dexmedetomidine on the heart is negative chronotropic effect by blocking the cardio accelerator nerve and by augmenting the 10th nerve. The decrease in heart rate may be attributed to decrease in central sympathetic outflow.

Blood Pressure

It was seen that 1min after intubation, there is rise in SBP, DBP and MAP as compared to pre laryngoscopic values, but the values were lower in high dose group. Annedath R Silpa et al[15] also observed that the incidence of hypertension following intubation was significantly more in low dose group but N Sharma et al[16] and Thapa C et al[17] in contrast to our study found that both the doses were equally effective in blunting the hemodynamic responses. Although they have suggested that the reason is might be use of fentanyl in dose of 2 μg/kg which is also known to attenuate hemodynamic response to laryngoscopy and intubation. Similar observations were observed by Smitha K et al[3] that the Dexmedetomidine 1μg/kg group had a better control of blood pressure than Dexmedetomidine 0.5 μg/kg group and significantly better than the control group.

Mean Induction Dose Of Thiopentone

In our study, patients of group B required less dose of thiopentone for induction compared to group A. The eyelash response was abolished equally with both the doses of dexmedetomidine. The reduction in anesthetic requirement was in concordance with earlier studies conducted by Keniya VM et al[10] and Laha A et al[11].

Thus, dexmedetomidine is a useful anaesthetic adjuvant that can be safely co-administered with thiopentone for its anaesthetic sparing effect. There is evidence that dexmedetomidine alters the pharmacokinetics of IV anaesthetic agents by decreasing cardiac output and regional blood flow.

Adverse Effects

In our study, no significant adverse effects such as respiratory depression, bradycardia and post-operative nausea and vomiting (PONV), were noted in any of the group and none of them required any medical intervention. Considering the adequacy of both the low and high doses in blunting the hemodynamic response, the equal safety of both dose with regard to the adverse effects appears to offer a definite clinical advantage.

Strengths And Limitations

Adequate number of patients were taken in both the groups to establish general ability of the findings. The present study depended on the hemodynamic 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 was done which could give more accurate value at the appropriate timing.

CONCLUSION

Dexmedetomidine when used as an infusion in the loading dose of 1 μg/kg is therapeutically more effective than loading dose of 0.5 μg/kg in attenuating of hemodynamic responses to laryngoscopy and intubation and reducing the induction dose of Thiopentone. But both the doses are devoid of any significant side effects like hypotension and bradycardia. Hence better efficacy and equal safety of dexmedetomidine in dose of 1 μg/kg may offer clinical advantage.

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