Original Research Article

Role of Dexmedetomidine as Premedicant to Attenuate Pressor Response to Laryngoscopy and Intubation

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ABSTRACT

Aims and Objectives: To study the efficacy of intravenous dexmedetomidine in the dose of 1mcg/kg as a premedication for attenuation of pressor response to laryngoscopy for endotracheal intubation, and dose requirements of anesthetics for induction.

Method: Total 60 patients of either sex, ASA grade I, having age between 18-60 years, posted for elective surgery under general anaesthesia requiring endotracheal intubation were randomly allocated in two equal groups. Group A (Dexmedetomidine group)received Inj. dexmedetomidine 1 mcg/kg IV in 100ml of NS given over a period of 10 min in infusion form at constant rate prior to induction. Group B (placebo group) received 100ml of NS over a period of 10 min at constant rate prior to induction. All patients were monitored intra and postoperatively with respect to hemodynamic parameters, rate pressure product and any other side effects.

Results: Group A significantly attenuated the sympathetic response to laryngoscopy and tracheal intubation in terms of heart rate, systolic and diastolic blood pressure, mean arterial pressure and rate pressure product compared to group B. The total dose of propofol for induction of general anesthesia was significantly less in group A as compared to group B. In both the groups, no patient had bradycardia or hypotension.

Conclusion: Intravenous dexmedetomidine used as a premedication in a dose of 1 mcg/kg effectively blunted the pressor response to laryngoscopy and endotracheal intubation without any side effect.

Keywords: Dexmedetomidine, Pressor Response, Laryngoscopy, Endotracheal Intubation

INTRODUCTION

Premedication is an integral part of general anaesthesia which requires laryngoscopy and endotracheal intubation. This premedication is done to attenuate anxiety, pain and certain surgical and anaesthetic stress responses which lead to hyperadrenergic states in patient leading to alteration in hemodynamics like hypertension and tachycardia. [1-3]

Among these responses, laryngoscopy and tracheal intubation (TI) may trigger reflex responses causing profound variation in cardiovascular physiology, and may cause serious complications in patients with underlying coronary artery disease, hypertension, or intracranial neuropathology. [4] Various methods and drugs used for attenuation of pressor response to laryngoscopy and endotracheal intubation but none have been entirely successful. [5,6] The search was continued for an ideal agent, which can reduce the pressor response to intubation as well as to surgical stimuli and to stabilize hemodynamics in intra-operative period.

Dexmedetomidine, the pharmacologically active d-isomer of

medetomidine, is a highly selective a2-adrenoceptor agonist. Its short half-life makes it an ideal drug for intravenous (IV) titration. [7] Various studies have evaluated its hypnotic, analgesic, and anxiolytic properties in the intraoperative period and critical care setting. [8-10] However, there are limited data on its effect on attenuation of pressor response to direct laryngoscopy and TI. Most of the studies have used higher doses of dexmedetomidine, 1-2 mg/kg; [11-16] very few studies have evaluated the role of lower doses of dexmedetomidine (1mcg/kg) in attenuation of pressor responses. The purpose of this study was to evaluate the effects of intravenous dexmedetomidine as a premedication for attenuation of pressor response to laryngoscopy and intubation, and dose requirements of propofol for induction in patients undergoing elective surgery under general anaesthesia.

MATERIALS AND METHODS

After obtaining Institutional Ethics Committee approval and patient's written informed consent, this randomized, prospective, placebo controlled study was conducted on 60 ASA physical status I patients of either sex, aged between 18–60 years, who underwent elective surgeries lasting more than 2 hours under general anaesthesia requiring endotracheal intubation. Patients on any treatment or drugs that affect the heart rate, blood pressure or hormonal stress response, psychiatric patients, patients suffering from hypertension, A-V blocks, cardiac arrhythmias, congestive cardiac failure, coronary artery disease, cerebrovascular disease, COPD, asthm, bronchospasm, acute or chronic hepatic or renal failure, any patients requiring a second attempt of laryngoscopy and intubation or patients in whom duration of laryngoscopy was more than 60 seconds, patients with anticipated difficult intubation, BMI > 30 kg/m2, emergency surgery and patients allergic to study drugs were excluded from the study. A detailed pre-anaesthetic evaluation including history and thorough general and systemic examination and all relevant investigations were done for all the patients. Patients were kept nill by mouth for 8 hours prior to surgery and they received crystalloid Lactated Ringer solution at rate of 2ml/kg for the period of starvation.

In the operation theatre, multipara monitors- electrocardiogram, pulse oximeter and NIBP were applied to the patient and baseline parameters like Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation (SpO2), and respiratory rate (RR)were recorded and mean arterial pressure (MAP) and rate pressure product(RPP) were calculated from the above parameters. After that all patients were divided randomly by computer generated random number charts into two groups of 30 patients each i.e. Group A (Dexmedetomidine group) and Group B (placebo group).Patients in Group A received injection dexmedetomidine hydrochloride 1 mcg/kg IV diluted in 100 ml of sterile NS given over 10 minutes at constant rate with the help of infusion pump whereas patients in group B received plain sterile NS infusion 100 ml given over a period of 10minutes at constant rate with the help of infusion pump. After the end of infusion all patients received remaining premedication i.e. glycopyrrolate 0.004 mg/kg, ondensetron 0.08 mg/kg, midazolam 0.02 mg/kg and ranitidine 1 mg/ kg. Then each patient was induced with propofol in graded doses. The dose of propofol required for induction was noted. After confirming the ability to ventilate, injection vecuronium 0.1 mg/kg was given and each patient was ventilated with 100% O2 for 3 min.

Any surgical interventions like catheterization, nasogastric tube insertion, incision were done10 minutes after intubation to avoid disturbances in data recording. Anaesthesia was maintained with O2 50%, N2O 50% and sevoflurane with vecuronium as relaxant on controlled ventilation with circle absorber system. Injection pentazocin 0.5mg/kg was given 10 min after endotracheal intubation and before incision in both groups. Both the groups

received diclofenac 1.5 mg/kg im for post operative analgesia. After completion of surgery neuromuscular blockade was antagonized with injection neostigmine 0.05 mg/kg and glycopyrrolate 0.008 mg/kg IV, patients were then extubated and shifted to post anaesthesia care unit for observation. All the patients were monitored intraoperatively and postoperatively till the patients completely recovered clinically with respect to HR, SBP, DBP, MAP, RPP, SpO2, sedation score and any other side effects. Patients were observed in post anaesthesia care unit (PACU) for minimum 2 hours and shifted to the ward only when vitals were stable.

Statistical analysis

Data obtained was statistically analyzed by Chi-square test and unpaired or student's t- test and paired t-test where ever applicable. The intergroup comparison was analyzed with unpaired t- test and intra group comparison with Paired t-test. P value of <0.05 was considered as significant. P < 0.001 was considered as highly significant.

OBSERVATIONS AND RESULTS

The demographic profiles of the patients were comparable in both the groups and difference was statistically not significant. The most common surgery performed in group A was Mod. Radical mastoidectomy while in group B was humerus plating. Other type of surgery performed was cholecystectomy but distribution of surgeries in both the groups was statistically insignificant (p>0.05), (Table 1).

Table- 1. Demographic data and Type of surgery

Variable	Group A	Group B	P Value
Age (years)	28.77± 9.4	26.9 ±9.2	0.494
Weight (kgs.)	57.27±4.07	59.57±8.4	0.066
Sex (Male/Female)	19/11	22/8	Total- 41/19
Type of Surgery			Total
Colecystectomy	6(20%)	8(26.66%)	14
Forearm plating	0 (0%)	1 (3.33%)	1
Incisional hernia repair	4 (13.33%)	1 (3.33%)	5
Lap. Appendicectomy	4 (13.33%)	6 (20%)	10
Mandibular cyst exision	0 (0%)	1 (3.33%)	1
Mod. Radicalmastoidectomy	9 (30%)	4 (13.33%)	13
humerus plating	7 (23.33%)	9 (30%)	16

The difference in mean HR and SBP between two groups was not statistically significant at baseline, while it was highly significant at 5min and10 min of infusion, after induction with injection propofol, 3minutes after giving vecuronium, laryngoscopy, intubation, and 1,2,3,4,5,7,10 minutes after intubation between two groups, (p<0.001), (Figure 1).
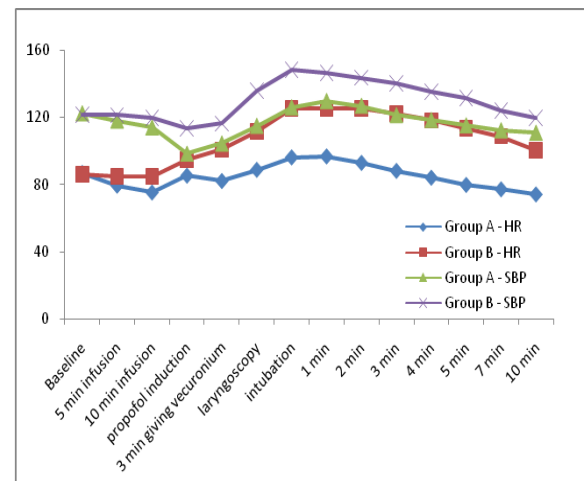

Figure 1. Comparison of Heart Rate and SBP between two groups

Whereas difference in mean DBP and MAP between two groups was not statistically significant at 5min after infusion while highly significant at baseline, 10minutes of infusion, induction with injection propofol, 3minutes after giving vecuronium, laryngoscopy, intubation, and 1,2,3,4,5,7,10 minutes after intubation between two groups, (p<0.001), (Figure 2).
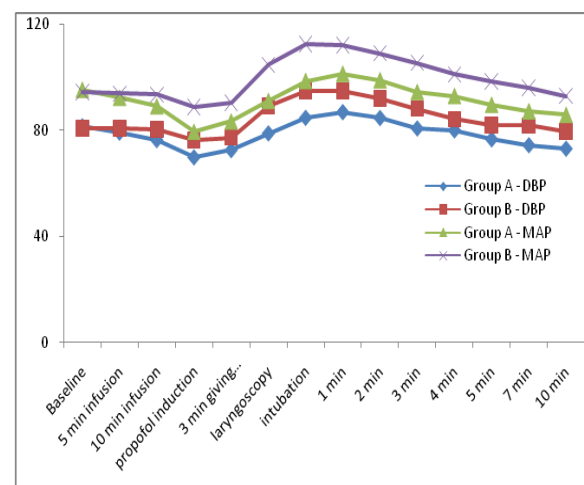

Figure 2. Comparison of DBP and MAP between two groups

The mean rate pressure product (RPP) was statistically significant at baseline.(p=0.042) while highly significant at 5 and 10 minutes of infusion, induction with injection propofol, 3minutes after giving vecuronium, laryngoscopy, intubation, and 1,2,3,4,5,7,10 minutes after intubation.(p<0.001), (Figure 3). There were no significant differences in respiratory rate and SpO2 in both the groups. This suggested that there was no significant respiratory depression in dexmedetomidine premedicated patients neither they suffered from hypoxia. The sedative effect of dexmedetomidine in dose of 1 mcg/kg was not associated with respiratory depression.
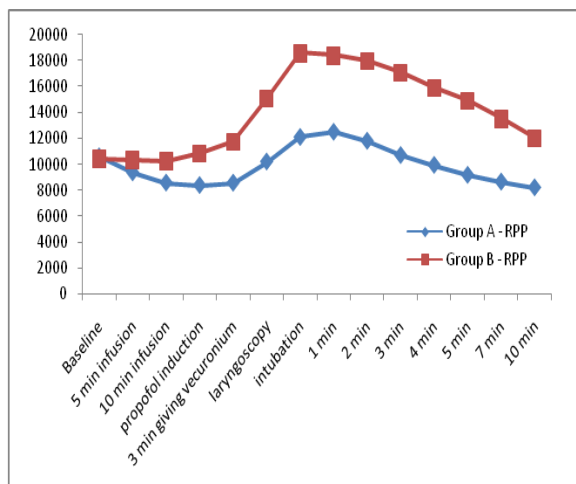

Figure 3. Comparison of RPP between two groups

There was no difference of sedation at initiation of infusion and after propofol induction in both the groups. At 5 min of infusion group A had 2 mean score of sedation while there was 1 score in group B patients. After 10 min of infusion group A had mean sedation score of 2.87 while that of group B was 1. There was statistically significant (p<0.01) score hence the sedation was more in group A at 5min and 10 min of infusion than the group B. The mean dose of propofol required for induction was significantly low in group A(1.55 ± 0.4 mg/kg)as compared to group B (2.11 + 0.28mg/kg), (p<0.001).

DISCUSSION

In the present study, demographic data of the patients in terms of age, weight and sex and duration of surgery being comparable between two groups and seems that it has no influence on outcome of the study. Our study demonstrated that baseline values of hemodynamic parameters were achieved earlier in group A than in group B after the tracheal intubation and also found statistically significant difference in hemodynamic parameters between two groups during the laryngoscopy and tracheal intubation.

In group A the heart rate was decreasedfrom5 minute after starting infusion till 10 minutes after intubation as compared to group B, also decreased in HR as compared to the baseline was seen at 5 minutes and 10 minutes after starting infusion. After propofol induction and 3 minutes after IPPV, there was increased in HR in group B than group A and in group A HR was near baseline values after propofol. The dose of propofol required for induction was less in group A compared to group B, this was statistically highly significant and probably resulted in lesser decrease in cardiac output, this fact along with effect of dexmedetomidine prevented the rise in HR in group A. At the time of laryngoscopy and tracheal intubation and 10 minutes thereafter, the HR was decreased in group A compared to group B and was near baseline at the time of laryngoscopy. There was statistically significant increase in HR in group A at the time of tracheal intubation compared to its baseline. This trend continued till3 minutes after intubation then HR returned to its baseline value.

Five min after premedication, 5 and 10 min of infusion, after induction with propofol and 3 minutes of IPPV with injection vecuronium there was fall in SBP in group A as compared to group B, also fall in SBP observed in group A10minutes after starting infusion and after propofol induction as compared to its baseline and it continued till 3 minutes of IPPV with injection vecuronium. This may be attributable to the combined effect of propofol and dexmedetomidine on cardiac output. However, the cause of hypotension

after dexmedetomidine is usually hypovolemia unmasked by the reduction of sympathetic tone. This can be easily treated by administration of IV fluids. The fall in SBP in dexmedetomidine during induction was without reflex tachycardia. Thus dexmedetomidine provided the controlled hypotension prior to intubation. Dexmedetomidine provided stable hemodynamics at the time of laryngoscopy and intubation. The SBP came to its near baseline value at 3minutes after tracheal intubation in group A compared to group B which took 10 minutes after tracheal intubation. This showed that the rise in SBP was short lived in group A as compared to group B. Changes observed in SBP in our study were compared with study of Ghodki et al. [17]

After 10 minutes of infusion, there was decreased in DBP in group A as compared to group B and at the end of infusion again decreased in DBP in group A compared to its baseline. This fall in DBP was due to sympatholytic effect of dexmedetomidine, sedation and anxiolytic effect of it and distribution t1/2 of the drug which is 6 minutes. After induction and 3 minutes of IPPV with vecuronium, there was highly significant decrease in DBP in group A compared to group B. At the time of laryngoscopy and tracheal intubation and till 10 minutes thereafter there was decrease in DBP in group A compared to group B. At the time of laryngoscopy DBP in group A was significantly low compared to baseline but 1minute after tracheal intubation, the DBP was significantly higher compared to baseline. The DBP again reached near baseline value 3 minutes after intubation. Thereafter, DBP remained significantly low than the baseline. The rise in DBP was short lived in group A compared to group B.

Similarly, 5 minutes after starting the infusion there was significantly decrease in MAP in group A as compared to group B. In group A the MAP was significantly decreased as compared to baseline after 10minutes of starting infusion. This may be attributed to sedation and anxiolytic property of the drug and its action on sympathetic nervous system. After induction with propofol and IPPV for 3 minutes after vecuronium, there was decreased in MAP in group A as compared to group B and its baseline. At the time of laryngoscopy and tracheal intubation and 10 minutes thereafter, there was significantly low MAP found in the group A as compared to group B. At the time of laryngoscopy in group A, the MAP was significantly lower than baseline but 1 minute after tracheal intubation, the MAP was high as compared to the baseline. This trend continued till 2minutes after intubation. The MAP was significantly low after 4 minutes of intubation and remained so till 10 minutes thereafter in group A.

We found decreased in RPP in group A as compared to group B after starting the infusion. In group A there was significant decrease in RPP after 10 minutes of premedication as compared to baseline. This fall is attributed to the decrease in the mean HR and SBP by dexmedetomidine and its anxiolytic and sedative property. After induction and at 3 minutes of IPPV with vecuronium there was significantly fall in RPP in group A as compared to group B, also we observed fall in RPP in group A compared to its baseline value after propofol induction. This was due to combined effect of propofol and dexmedetomidine as dexmedetomidine prevented the reflex tachycardia in response to hypotension induced by propofol induction. At the time of laryngoscopy and intubation, we found lower mean RPP in group A as compared to group B. This trend continued till the end of observation period. In group A, there was no significant rise in RPP at the time of laryngoscopy but significant rise observed at the time of tracheal intubation from baseline. However this rise was transient and short lived. Also it was significantly lower than rise in group B. The RPP reached to near baseline value at 3 minutes of intubation. Thereafter RPP was significantly low compared to baseline till the end of observation period. This can be

attributed to the effect of dexmedetomidine on HR and SBP. The blockade of sympathetic nervous system by dexmedetomidine resulted in the decrease HR and controlled hypotension eventually leading to lower RPP. The RPP is an indirect measure of myocardial oxygen demand. It increases progressively with the exercise and stress and the peak RPP can be used to characterise the cardiovascular performance. The most normal individuals develop peak RPP of 20,000 to 35,000 without any changes on EGG. [18]

Intra operative hemodynamics was stable in both the groups and all patients were extubated without any complications. All the patients were observed in post anaesthesia care unit for 2hours and shifted in the wards after they fulfilled the criteria of shifting. No patient had bradycardia (HR< 50/min) or hypotension (BP< 90/60 mmHg i.e. MAP<70mmHg) during post-operative period. None of the patient had any ECG changes intra operatively and post operatively.

CONCLUSION

In conclusion, intravenous dexmedetomidine used as a premedication in a dose of 1 mcg/kg given as an infusion over 10 minutes prior to induction of anaesthesia effectively blunted the pressor response to laryngoscopy and endotracheal intubation in ASA physical status 1 patients. It also reduced the dose of propofol required for induction of anaesthesia. It produces sedation, without any undesirable side effect like respiratory depression.

Thus intravenous dexmedetomidine in the dose of 1 mcg/kg is an effective, readily available drug with low side effects; which can be used as pre anaesthetic medication in ASA I patients posted for elective surgery before administration of general anaesthesia with endotracheal tube.

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