Research Article

Dexmedetomidine attenuates pressor response to tracheal intubation and reduces the need for propofol and perioperatrive fentanyl

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Abstract

Background: Dexmedetomidine is a new highly selective alpha- 2 adrenoceptor agonist. It is known for its sedative, sympatholytic and cardiovascular effects. **Material and methods:** we assessed the safety and efficacy of dexmedetomidine as a preanaesthetic agent and in attenuating pressor response during laryngoscopy and intubation and requirement of induction agent and opioids during perioperative period. 60 Adult patients (ASA- 1) were enrolled in the study and randomized into two groups. **Group – I** (Dexmedetomidine group) received isoflurane - opioid – dexmedetomidine as part of balanced anaesthesia. **Group - II** (Saline group) received isoflurane – opioid - saline as a part of balanced anaesthesia. ECG, heart rate, blood pressure were recorded as a basal value, pre-induction, induction, 0 min after intubation, 5 min after intubation. Total required doses of propofol and opioids were recorded during perioperative period. Statistical evaluation was performed using analysis of variance (ANOVA) for repeated measurements with one between factor (drug)and one within factor (time). Data were analysed with student t test, Mann-Whitney U test. P less than 0.05 was considered statistically significant. **Results**: The two groups were comparable in terms of patient's characteristics (age, weight, sex, duration of surgery and type of surgery). Total propofol requirement during induction was significantly decreased in dexmedetomidine group. Isoflurane, opioids requirement during perioperative period was also significantly decreased in dexmedetomidine group. Maximum average rise in systolic, diastolic and heart rate from basal value to 0 mins after intubation is 7.6% ,10%, 15% in dexmedetomidine group and 22%, 18%, 24% in control group respectively. **Conclusion:** Dexmedetomidine as a preanaesthetic agent and perioperative infusion is effective in attenuating pressor response to endotracheal intubation and has significant anaesthetic and opioid sparing effect.

Key Word: alpha-2 adrenoceptor, Control, Dexmedetomidine, Pressor response.

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INTRODUCTION

Since the time of introduction of general anaesthesia in the last quarter of 19th century endotracheal intubation has become one of the commonly performed procedures in the practice of anaesthesia. Endotracheal intubation is translaryngeal placement of a tube into the trachea via nose or mouth. This procedure includes process of laryngoscopy and intubation which constitute a period of extreme haemodynamic stress and is associated with intense sympathetic activity marked by tachycardia and hypertension. This pressor response to endotracheal intubation is very common problem in routine anaesthesia practice. It is particularly more significant in case of cardiac and neurosurgical patients. According to review of literature a lot of maneuvers like local blocks, drugs are being employed to attenuate this response. In drugs, clonidine has been investigated extensively as an adjunct to anaesthesia. It provides improved haemodynamic,

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metabolic and hormonal stability by attenuating the sympathoadrenal activation elicited by anaesthesia, tracheal intubation and surgery but causes sedation and delayed emergence.[1-4] Besides this, drugs like fentanyl, alfentanyl, xylocard are also helpful in current clinicial anaesthesia practice to attenuate pressor response. Dexmedetomidine is a new, highly selective and potent alpha –2 adrenoceptor agonist.[5,6] Animal experiments have indicated that it has prominent anaesthetic effects[6]. Studies in human volunteers also demonstrated that dexmedetomidine has sedative, sympatholytic and cardiovascular effects.[7,8] In recent studies in patients, dexmedetomidine has been shown to have clinically significant effects on anaesthetic requirements and on the sympathoadrenal and haemodynamic responses induced by anaesthesia and surgery.[8 –11]

AIMS AND OBJECTIVES

To investigate the safety and efficacy of dexmedetomidine as a preanaesthetic agent and its effects on the pressor response to laryngoscopy and intubation and on requirements of opioids and induction agents during perioperatrive period.

MATERIAL AND METHODS

We investigated 60 (ASA I) patients undergoing elective surgery. The study was approved by the Ethics Committe of the Hospital and written informed consent was obtained from all patients. Patients taking any medication, with child bearing potential or with a known drug allergy were excluded from the study. The patients were randomly divided into two groups.

Group – I (Dexmedetomidine group): Isoflurane–opioid-dexmedetomidine.

Group – II (Saline group): Isoflurane–opioid- saline.

The patients were premedicated with oral diazepam 0.2 mg/kg 60-90 min before induction of anaesthesia. Patient was shifted to operation theatre. After shifting to operation theatre intravenous cannulation was done with 20G I.V cannula. Another venous cannula was inserted on the dorsum of the hand. ECG, SPO_2 Probe, NIBP [(non invasive blood pressure) cuff were attached. After the monitoring equipment had been attached, the patient was allowed to rest for 5 minutes. Cardiovascular recordings (baseline) were made. The patients were allocated randomly to receive either dexmedetomidine (n= 30) Group 1 or saline (n =30) Group 2. In group 1, inj. dexmedetomidine 1µg/kg over a period of 10 min prior to induction of anaesthesia through an infusion pump was administered. In group 2, same volume of normal saline was given through infusion pump over a period of 10 minutes preceded by glycopyrrolate 0.01 mg/kg and inj. ondansetron 4 mg intravenously. After the trial drug was given, grades of sedation and alertness were recorded for 10 min according to Ramsay sedation score. Then a dose of propofol (1.5- 2.5 mg/kg) sufficient to the loss of verebal commands was injected into the intravenous cannula attached to a fast running infusion of Ringer's lactate, followed by vecuronium 0.1 mg/kg to provide necuromuscular block. The lungs were ventilated with 50% nitrous oxide in oxygen for 3 min. Laryngoscopy lasting 10 sec. was performed with a Macintosh laryngoscope and the trachea was intubated. During surgery, anaesthesia was maintained with isoflurane and 70% nitrous oxide in oxygen. The inspiratory concentration of isoflurane was adjusted in steps of 0.2% when needed as judged by lacrimation or an increase in heart rate, blood pressure exceeding 30% of preanaesthetic values or a reduction in arterial pressure of 20% of the earlier value. Injection fentanyl 1-2 µ/kg in the increments was given immediately when 1% inspiratory isoflurane was needed. The isoflurane concentration was decreased 1 min after administration of fentanyl. The mean inspiratory concentration was calculated as the sum of the products of inspiratory concentration divided by total anaesthesia time. Neuro-muscular block was maintained with intermittent doses of vecuronium and the dosage controlled using a nerve stimulator. The dexmedetomidine infusion was continued after intubation in a dosage of 0.2 µg/kg/hr in group 1, till the start of skin closure. Residual neuromuscular block was antagonized with neostigmine 0.05 mg/kg preceded by glycopyrrolate 0.01 mg/kg intravenously. The interval from discontinuation of inhalation of nitrous oxide at the end of surgery to the when the patient opened the eyes on command was recorded as the recovery time. All patients were observed in the recovery room for 2 hrs. After surgery. Injection diclofenac 1.5 mg/kg was given intravenously when the patient complained of pain in the recovery room. ECG, heart rate and blood pressure were recorded at the following times: basal value, pre - induction, induction, 0 mins after intubation and 5mins after intubation.

STATISTICAL ANALYSIS

Statistical evaluation was performed using analysis of variance (ANOVA) for repeated measurements with one between factor (drug)and one within factor (time). When a statistically significant drug X time interaction was found, the analysis was continued by calculating contrasts for each time point Vs baseline. Data were analysed with student t test, Mann-Whitney U test. P less than 0.05 was considered statistically significant.

OBSERVATION AND RESULTS

The two groups were comparable in patients characteristics and type of surgery (Table I). Besides these characterstics, dexmedetomidine was well tolerated and no drug related adverse events were observed in dexmedetomidine group. About 5 mins. after receiving the trial drug, patients were drowsy but arousable.(Ramsay sedation score 2)

Table 1: Patient characteristics and type of surgery (mean)

Variables	Dexmedetomidine group	Control group	p- value
Sex (M/F)	14/16	12/18	>0.05
Age (yrs)	30	31	0.34
Weight (kg)	51	50	0.35
Height (cm)	165	170	>0.05
Type of Surgery			
Breast	4	5	
Orofacial	4	7	
Laminectomy	9	5	
ENT	10	9	>0.05
Thyroid	3	4	

ANAESTHETIC REQUIREMENTS

The mean sleep dose of propofol was significantly greater in the control group than in the dexmedetomidine group. The mean inspiratory concentration of isofluane was more in the control group. Mean dose of fentanyl requirement as an perioperative analgesic was also significantly increased in control than dexmedetomidine group. (Table II).

Table 2: Anaesthesia characteristics (mean)

Variables	Dexmedetomidine group	Control group	p-value
Propofol (mg/kg)	1.7	2.2	<0.01
Fentanyl(µg/kg)	1.1	1.7	<0.01
Isoflurane (mean, insp. conc. (%)	0.57	0.95	<0.01
Duration of surgery (min.)	109	114	0.24
Recovery times (min.)	9	8	>0.05
No. of patients requiring Inj. diclofenac (1.5 mg/kg)	5/30	22/30	<0.05

CARDIOVASCULAR RESPONSES

Dexmedetomidine results slight decreases in blood pressure and heart rate. It also attenuated the pressor response induced by laryngoscopy and intubation, revealed by significant drug x time interactions in ANOVA (fig. 1(A), 1(B), 1(C)). Maximal average increases during intubation from baseline were 7% and 22% in systolic, 10% and 18% in diastolic blood pressure and 15% and 24% in heart rate in the dexmedetomidine and saline groups, respectively. The difference of rise on inter group comparison was also statistically significant (student t test). (Table - III)

Table 3: Difference and percentage rise in mean values of systolic and diastolic blood pressure, heart rate (basal value to 0min after intubation) in Dexmedetomidine and Control group

Variables	Dexmedetomidine Group	Control group	Percentagerise (Dexmedetomidine)	Percentagerise (Control)	P –value
Systolic blood pressure	9.3	27	7.6	22	<0.01
Diastolic Blood Pressure	8.06	15	10	18	<0.01
Heart Rate	11.36	19	15	24	<0.01

Variation in mean values of systolic, diastolic blood pressure, heart rate during perioperative period (Basal value [B], PREINDUCTION [PI], Induction [I], 0 min. after intubation [0 min. AI], 5 mins. after intubation (5 min. AI])

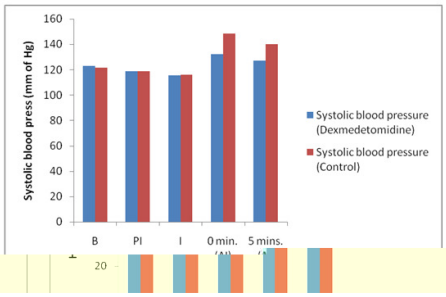

Figure 1(A)

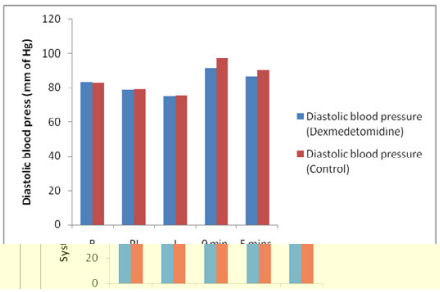

Figure 1(B)

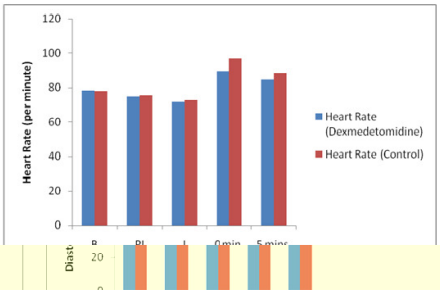

Figure 1(C)

RECOVERY AND ANALGESIC REQUIREMENTS

The duration of recovery was similar in both groups (table II). In the recovery room_there was no difference between the groups in the patients opinions of their drowsiness. The need for diclofenac during the first 2hours after operation was greater in the control group than in the dexmedetomidine group (table II).

DISCUSSION

Endotracheal intubation results in rise in blood pressure, heart rate and plasma catecholamine levels[13]. In the present study, pretreatment with dexmedetomidine 0.1 µg/kg attenuated, but did not totally obtund the cardiovascular response to tracheal intubation after induction of anaesthesia. Intubation induced increases in blood pressure and heart rate observed in the group in the present study were similar to those reported in earlier studies in patients where opioids were not used as part of the anaesthesia medication[14,15]. The dose of propofol needed for induction was reduced significantly in the patients receiving dexmedetomidine as found also by Aantaa and coworkers[9,10]**.** demonstrating the anaesthesia potentiating effects of the drug. In our study, isoflurane ,propofol was used as the main anaesthetic agent. Significant difference was observed between two groups in isoflurane and propofol requirements. The total amount of fentanyl required was greater in the control than in the dexmedetomidine group. The significant smaller doses of diclofenac needed by the dexmedetomidine patients in the recovery room suggests analgesic efficacy. Analgesic properties have been also demonstrated earlier in a study with dexmedetomidine as the sole analgesic after surgery[12].Previous clinical studies with dexmedetomidine have reported mainly on patients undergoing minor surgery under propofol-nitrous oxide anaesthesia[9,10]. In addition to the beneficial property of α-2 agonists, they have also been reported to increase the risk of hypotension and bradycardia[16]. These effects have been most oftenly observed in young healthy volunteers on rapid bolus administration[16]. In our study, bradycardia was observed in two patients receiving dexmedetomidine, with no fall in blood pressure which responded promptly to IV atropine. Nakagava and co-workers[17] have suggested that spinal noradrenergic systems are involved together with serotonin in the modulation of ascending nocioceptive stimulation, possibly through an alpha 2-adrenergic mechanism. The alpha 2- agonists would thus offer a new, interesting possibility for suppression of pain. It is not clear if the reduced opioid requirements after administration of the alpha 2 – adrenergic agonists in our study reflect potentiation of opioid- induced analgesia or other mechanisms.

CONCLUSION

Dexmedetomidine as a preanaesthetic medication and intraoperative infusion decreases requirement of induction agents and volatile anaesthetics.Besides this, dexmedetomidine also has opioid sparing effect.It significantly attenuates pressor response to endotracheal intubation and continuous intraoperative infusion during surgery maintains haemodynamic stability.

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