Evaluation of Heamodynamic Responses upon Using Dexmedetomidine Infusion in Hypertensive Patients under General Anaesthesia

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Abstract

Background: *The objective of this study was to compare the effects of intravenous dexmedetomidine and saline placebo on intra operative haemodynamics in hypertensive patients.*

Methods: *In a double blinded trial, forty hypertensive patients were randomly allocated to receive either dexmedetomidine 0.5 μg /kg/h (Group D) (n = 20) or saline placebo (Group N) (n = 20) intra-venously, started immediately after intubation. Heart rate (HR) and mean arterial pressures (MAPs) were recorded throughout.*

Results: *Dexmedetomidine caused significant fall in MAP, 15 min after starting infusion (P<0.001). Also, patients in group D had fall in heart rate and MAP (P= 0.244) while in Group N showed mild increase in heart rate and a highly significant fluctuation in MAP (P<0.001).*

Conclusion: *These findings suggest that an infusion of dexmedetomidine in hypertensive patients attenuates circulatory reflexes during surgery and at extubation, thus provided stable haemodynamics both intra operatively and at extubation.*

Keywords: *Dexmedetomidine; hypertension; responses; tracheal; extubation.*

Introduction

The perioperative management of hypertensive patients is quite challenging. The progressive ventricular hypertrophy with its consequent diastolic dysfunction is known to occur in hypertensive patients [1].Tachycardia could occur in association with stress responses induced by surgery and anaesthetic manoeuvres like direct laryngoscopy, tracheal intubation and extubation due to severe sympathetic stimulation. The haemodynamic changes predispose the myocardium to ischemia that may be life threatening in a vulnerable hypertensive [1] patient. Modern anaesthesia practices, therefore, plan to prevent sympathetic discharge and provide haemodynamic stability perioperatively. In last few years, a great enthusiasm has been shown towards the use of α2 agonists in anaesthesia practice because of their anxiolytic, sedative, sympatholytic and analgesic sparing properties[3,18,21]. Dexmedetomidine, introduced in 1999 for human use, is a selective α2 agonist

possessing all the properties of α2 agonist without respiratory depression[2]. Intravenous use of dexmedetomidine in the perioperative period is found to decrease serum catecholamine levels by 90%, to blunt the haemodynamic response to laryngoscopy, tracheal intubation and extubation, to provide sedation, without respiratory depression. In poorly controlled hypertensive, a more severe haemodynamic response to laryngoscopy and intubation is seen [1].

The primary aim of this study was therefore, to evaluate the effects of dexmedetomidine infusion on haemodynamic response to laryngoscopy, endotracheal intubation and extubation in hypertensive patients undergoing major surgery. The secondary aims were to observe the occurrence of adverse effects[4,5,,6].

Methods

This prospective, randomised, double blind, placebo controlled clinical study was done on forty hypertensive patients between 18 and 65 years, of either sex and posted for major surgery under general anaesthesia. Patients with decreased autonomic control such as the elderly, diabetic patients, full stomach patients like pregnant or lactating women, patients with uncontrolled hypertension (systolic blood pressure [BP] >160mmHg or diastolic BP>100 mmHg), history of ischemic heart disease, cerebrovascular disease, impaired liver or renal functions were not considered for the study.

The patients were randomly allocated into two groups of 20 patients each, Group N (patients receiving normal saline 0.9% infusion), Group D (patients receiving dexmedetomidine infusion 0.5 mcg/kg/h). Infusion was prepared according to the group allotted. To prepare the infusion, dexmedetomidine 1 ml containing 100 μg of the drug was withdrawn in a 50 ml syringe and was diluted up to 50 ml with normal saline resulting in the final concentration of 2 mcg/ml. Dexmedetomidine or normal saline infusion was given through syringe infusion pump. Depending on the weight of the patient, the pump was set so as to deliver the targeted infusion rate. Thus, the syringe was same, volume of prepared solution was same, only the rate of injection was different according to the weight and group of patient.

Premedication was administered with tablet ranitidine 150 mg and tablet diazepam 5 mg on the night before and on the morning of surgery. All anti-hypertensives except angiotensin – converting enzyme inhibitors were continued. Before induction of anaesthesia, premedication in the form of injection glycopyrrolate 8 mcg/kg IV and injection midazolam 1 mg and morphine 0.1mg/kg IV was given as per the institutional protocol. A multipara monitor was attached and the baseline pulse rate (PR), mean arterial pressure (MAP) and oxygen saturation were noted down. A wide bore intravenous cannula was inserted for giving the intravenous fluids.

Pre-oxygenation was performed for 3 min. Patients were induced with injection propofol 2 mg/kg intravenously followed by injection succinyl choline 1.5 mg/kg intravenously. Trachea was intubated with appropriate size cuffed endotracheal tube. Anaesthesia was maintained with O_2: N_2O (3:1), and injection vecuronium bromide [0.1 mg/kg] as a muscle relaxant. Drug infusion at the rate of 0.5 μg /kg/h was started as soon as the induction and intubation was over .Drug infusion and anaesthetic agents were stopped at the end of surgery. Reversal was carried out as also extubation by conventional methods. All the patients were observed for vital parameters like PR, MAP and SpO_2 at regular intervals including before starting the infusion (baseline), 15 min after starting the infusion, at the time of extubation, 1 minute and 5 minutes after extubation.

Throughout the study, patients were observed for any adverse effects like bradycardia, tachycardia (PR less than or more than 20% of pre-operative level respectively on two consecutive readings), hypo and hypertension (MAP less than or more than 20% of pre-operative level respectively on two consecutive readings). None of the patients in both the groups showed such changes.

We took 20 patients in each group. The results were tabulated and statistically analysed using SPSS (Statistical Package for Social Sciences) Software version 17.0, Chi-square test was used for qualitative data (sex, PR, blood pressure) and the results were expressed as mean ± standard deviation. $P >0.05$ was considered insignificant, <0.05 as significant and highly significant if P<0.001.

Results

All the three groups under study were comparable to each other with respect to age, sex, weight, duration of surgery and anaesthesia [Table 3]. There was no significant difference among the three groupsin reference to the baseline PR and the MAP.

Table 3 Demographic Data.

| Parameters	Group D (n=20)	Group N (n=20)	P
Age in years (mean±SD)	49±9	58.9±5.2	
Sex			
Male	12(20)	11(20)	0.749
Female	8(20)	9(20)	
Weight in kg (mean±SD)	59.7±7.7	55.9±4.7	0.071
Duration of anaesthesia (in hours)	1.6±0.7	1.6±0.5	0.632
Duration of surgery (in hours)	1.6±0.7	1.6 ± 0.5	0.632
Time to extubation	10.00±1.214	5.70±1.342	<0.001
Time to recovery	7.5±1.3	4.5±1.8	<0.001

Heart Rate

In the dexmedetomidine group, after starting the infusion, the PR remained almost the same as the pre-infusion level [Table 4]. After intubation and extubation, the PR and MAP increased above the pre-infusion level in normal saline group (P = 0.133) [Figure 1]. Increasing age and low baseline arterial blood pressure were associated with the development of hemodynamic instability. This was found to be true in this study.

Table 4 changes in PR (beats per minute) (mean±SD)

| HR	Group D	Group N	P
Before starting infusion	72.2±9.7	70.1±5.5	0.416
15 minutes after starting infusion	65.3±11.7	68.9±7.3	0.244
At extubation	75.5±9.1	71.8±5.9	0.137
1 minute after extubation	73.8±8.3	71.4±5.9	0.311
5 minutes after extubation	71.0±10.6	75.4±6.9	0.133

HR-heart rate, SD- standard deviation.

Figure 1 Heart rate variation over time
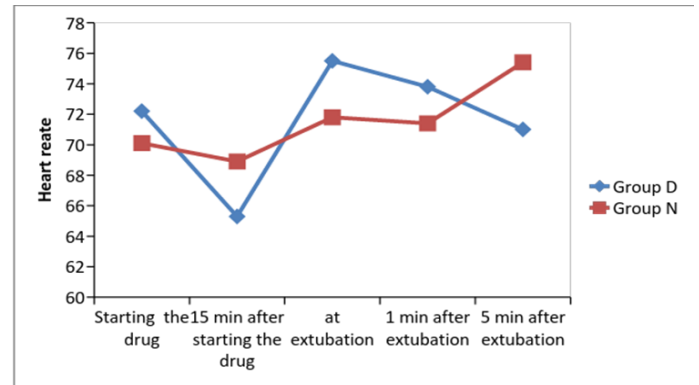
Mean arterial pressure

Base line MAP in both the groups were comparable. (P=0.386). Fluctuating levels of MAP was seen in Group N (97.5 ±3.8 to 90.5±8.6 mmHg) P<0.001. In Dexmedetomidine group, MAP reduced significantly 15 min after starting the drug P<0.001, but then, remained almost the same even 5 minutes after extubation;[Figure 2];97.0±3.7 baseline to 83.1±5.9 mmHg at 15 min after starting infusion and 86.9 ±7.0 mmHg, 5 min after extubation.

Figure 2 Mean arterial pressure variation over time
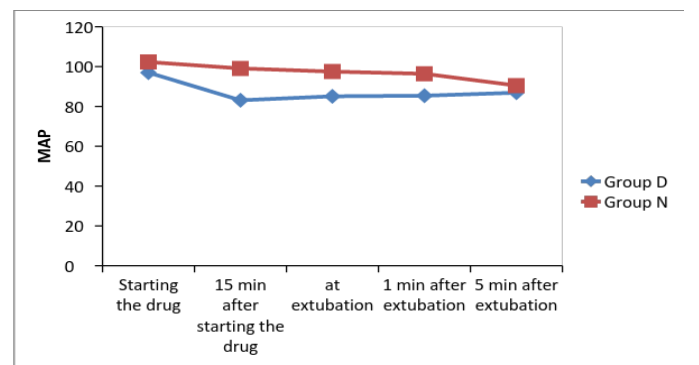
Discussion

Dexmedetomidine offers the benefit of producing light sedation with minimal respiratory depression, in attenuating airway reflex responses to tracheal extubation and maintaining hemodynamic stability without prolonging recovery when used in the absence of other sedative or analgesic agents[1,7] .The anaesthetic- and analgesic-sparing effects of dexmedetomidine have been well documented in animal and human studies[12,13]. Dutta et al[16] reported that a dexmedetomidine plasma concentration of 0.66 ng/mL reduced the propofol dose required for sedation and induction of anaesthesia by 40% to 70%.

Haemodynamic stability is of paramount importance in hypertensive patients [1, 2, 17] especially when there is anassociated diastolic dysfunction. In the present study, we compared the dexmedetomidine group with saline for perioperative haemodynamic stability. Infusion rates with or without bolus dose varying from 0.1 to 10 µg /kg/h [1,2,3,9] have been studied. The reported incidence of hypotension and bradycardia in patients receiving dexmedeto-midine for sedation commonly exceeds 50 %[7]. Low dose infusion of 0.25-0.5 µg/kg/h results in a monophasic response of 10-15% fall in mean arterial blood pressure and HR [1,4,5,6,9,12]. A recent echocardiographic assessment of the cardiac function [9,11] of patients receiving dexmedeto-midine infusion did not demonstrate an impairment in systolic or diastolic function but did find areduction in cardiac output because of a negative chronotropic effect of dexmedeto-midine. Of note, these data were obtained in younger, otherwise-healthy patients undergoing procedural anaesthesia for orthopaedic surgery.

However, further investigation into the mechanism of dexmedetomidine-associated hemo-dynamic instability is warranted [7].

In our study, we first studied using saline placebo infusions for maintenance of anaesthesia. Though it showed not much rise in HR and MAP at intubation, the control was not very effective at the time of surgery and extubation, and the HR and MAP both increased above pre-infusion levels and MAP showed fluctuations throughout surgery and at extubation[6,17]. Then we studied with dexmedetomidine infusion at 0.5 µg /kg/h .The results were quite satisfactory with this dose regime, HR and MAP were always below pre-infusion levels in group D ($P<0.001$).

Pry's Roberts and his colleagues established that poorly controlled hypertensive patients have a more vigorous cardiovascular response to laryngoscopy and intubation than do normoten-sives or well controlled hypertensives[7]. Our study confirms the fact that critical incidences like laryngoscopy and intubation, and extubation do cause significantly high fluctuations in the MAP and HR in hypertensive patients undergoing major surgery as seen in group N. Dexmedetomidine attenuates this sympathoadrenal response and provides haemodynamic stability [2,7,16,20]. The effective attenuation dose with minimum side effects like postoperative nausea and vomiting, noted in our study, was 0.5µg/kg/h infusion [11, 16]. Apart from providing stress response attenuation, the added effects of dexmedetomidine are sedation and analgesia.. It is better to observe patients for 120 min as elimination half-life of dexmedetomidine is 2 h

Conclusion

Low dose infusion of dexmedetomidine at the rate of 0.5 mcg/kg/h without any bolus dose serves as a very useful technique to control haemodynamic stress response to surgery and extubation in hypertensive patients undergoing major surgery. It also provides lighter sedation and reduces the post-operative analgesic requirements without any significant adverse effects.

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