Dexmedetomidine: An Advantage for Reducing Intraoperative Anaesthetic Demand

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Original Research Article

ABSTRACT

The aim of this study was to determine whether dexmedetomidine attenuates hemodynamic response to intubation & reduces perioperative anaesthetic requirement. Sixty ASA I & II patients scheduled for elective surgery of duration 3 hrs or more were randomly selected. Patients were divided into two groups: Group A (n=30) received halothane-fentanyl-saline and group B (n=30) received halothane-fentanyl-dexmedetomidine. Dexmedetomidine infusion in a dose of 1 µg / kg was given over 10 min. before induction of anaesthesia and was continued in dose of 0.2-0.7 µg / kg / hr. until skin closure. All patients were induced with thiopentone, fentanyl and rocuronium. Hemodynamic variables were continuously recorded. The need for thiopentone and halothane was decreased by 25% and 30%, respectively, in dexmedetomidine group as compared to the control group. After tracheal intubation, maximal average increase in systolic, diastolic blood pressure and heart rate was 10%, 10% and 5%, in dexmedetomidine group, as compared to 35%, 30% and 25% in control group, respectively. Fentanyl requirement were 33% less in dexmedetomidine group. It is inferred that dexmedetomidine attenuates hemodynamic response to intubation and has anaesthetic sparing effect.

KEY WORDS: dexmedetomidine, fentanyl, hemodynamic response, halothane, tracheal intubation

INTRODUCTION:

Various drug regimen and techniques have been used from time to time for attenuating the stress response to laryngoscopy and intubation including opioids[2], barbiturates, benzodiazepines, beta blockers[4], calcium channel blockers[1], vasodilator[3] etc .

α2 agonist like clonidine has been introduced to clinical anaesthesia for its sympatholytic, sedative, anaesthetic sparing effects and hemodynamic stabilising properties[5-7]. Dexmedetomidine is a new α2 agonist having eight times more affinity for α2 adrenoceptors as compared with clonidine[8]. The α2 : α1 binding selectivity ratio of dexmedetomidine is 1620 : 1 compared to 220 : 1 for clonidine. In recent studies, dexmedetomidine has been shown to have clinically significant effects on anaesthetic requirements & hemodynamic responses induced by anaesthesia and surgery.

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MATERIALS AND METHODS:

After obtaining approval from the institutional ethical committee at Rama Medical College and Hospital, Kanpur, a randomised controlled study was conducted. The study population comprised of 60 patients with ASA physical status I & II aged 20-60 years, scheduled for elective surgery of duration 3 hours. or more. Written informed consent was taken from each patients. Patients with cardio vascular diseases, epilepsy, hypertension, chronic obstructive pulmonary disease, pregnant and nursing women, morbid obesity, diabetes, renal disease, patients taking any antipsychotic medication, history of allergy to any drug and patients in whom intubation attempts lasted longer than 30 sec were excluded from the study. The patients were randomly assigned to one of the two groups each containing 30 patients using computer -generated coded envelops.

(Group A: Control Group:Halothane - Fentanyl-Saline anaesthesia; Group B: Dexmedetomidine Group:

Halothane - Fentanyl Dexmedetomidine anaesthesia).

On arrival in the operating room, a good intra venous access was secured and baseline HR, blood pressure, oxygen saturation (SpO_2), respiratory rate & ECG were recorded. All the patients in group B received Inj. Dexmedetomidine 1 µg / kg over a period of 10 min prior to induction of anaesthesia via an infusion pump. During the infusion heart rate, systolic blood pressure, diastolic blood pressure, respiratory rate, oxygen saturation and sedation score were recorded at 5 min interval and at 10 min (end of infusion). All the patients in group A received saline through an infusion pump.

All the patients received Inj. Glycopyrolate 0.2 mg i.m. 30 min. before induction of anesthesia and Inj rantac 50 mg and Inj. Metoclopramide 10 mg, Inj. fentanyl 1µg / kg and Inj. midazolam 1 mg I.V. before induction of anaesthesia. Then, a dose of inj. thiopentone sufficient to abolish eyelash reflex was injected followed by inj. rocuronium 0.8mg / kg to facilitate laryngoscopy and tracheal intubation. The lungs were ventilated by 50 % N_2O in O_2 with bains circuit for next 3 minutes. Laryngoscopy was perfomed with a macintosh laryngoscope and intubation done with appropriate size endotracheal tube. Anaeshesia was maintained with N_2O in O_2 (60 : 40), halothane, inj. fentanyl & inj. rocuronium.

The halothane was used in lowest possible concentration necessary to keep the blood presure and heart rate with in 20% limits of patient's pre operative basline values. The inspiratory concentration of halothane was adjusted in steps of 0.2% when needed to keep the hemodynamic parameters to acceptable values. Inj. fentanyl in increment of 0.4 µg/kg was given when inspiratory halothane concentration exceeded by 1%. The dexmedetomidine infusion was continued after intubation in a dosage of 0.2-0.7 µg/kg/hour in group B, till the start of skin closure. All the patients in group B received halothane in minimum concentration of 0.2%, which was further increased when requirement of Inj. Dexmedetomidine exceeded 0.7 µg/kg/hr to keep the hemodynamic parameters within acceptable range. Similarly, halothane was terminated at the start of skin closure and N_2O was discontinued after skin closure.

At the end of anaesthesia, the neuromuscular blockade was antagonised with inj. neostigmine 0.04 mg/kg and inj. glycopyrrolate 0.02 mg/kg intravenously. Patients were extubated when respiration was deemed sufficient and patients were able to obey simple commands.

All the parameters and the results from the two groups (group A and group B) were entered in the predesigned study proforma sheet. The studies parameters included:

1) Sedation score at 5 min and 10 min after administration of loading dose of dexmedetomidine in group B according to Ramsay sedation score; 2) Heart rate, systolic and diastolic blood pressure, SpO_2 at 5 min and 10 min after dexmedetomidine administration, preinduction, induction, 0 min, 1 min, 5 min after intubation; 3) The dose of the Inj. thiopentone for induction of anaesthesia; 4) Total fentanyl requirement throughout the operative procedure; 5) The average inspiratory halothane concentrations was calculated as the sum of the products of inspiratory concentrations and times divided by total anaesthesia time; 6) The intraoperative need for adjuvants such as Inj. diclofenac sodium and propofol.

Statistical analysis was conducted with SPSS (version 10, 2010) for Windows statistical package using paired student's *t* test. The results were expressed as Mean±SD. $p<0.05$ was regarded as statistically significant, $p<0.001$ was taken as highly significant, and $p>0.05$ was regarded as nonsignificant. A sample size of 20 patients per group was needed to detect an intergroup difference of at least 20% with two-sample *t*-test.

RESULTS:

The two groups were comparable in patient characteristics. Dexmedetomidine was well tolerated and no drug-related adverse events were observed. About 5 & 10 min after receiving dexmedetomidine, patients were drowsy but arousable (sedation score 2).

Table 1: Type of surgeries.

Type of surgeries	Group - A	Group - B
Laminectomy	11	09
Ca Breast	04	04
Craniotomy	03	03
ENT Surgery	05	05
Oro - maxillofacial	04	05
Thyroid	03	04

The mean sleep dose of inj. thiopentone required in group A was 5.5 mg/kg, while it was 4.1 mg/kg in group B (Table 2). The decrease in the dose requirement was by 25% in dexmedetomidine group as compared to control group ($p=0.00$).

Table 2: Anaesthesia characteristics [mean (SD)].

Anaesthesia characteristics	Group -A	Group -B	p
Inj. Thiopentone	5.5(0.72)	4.1(0.8)	0.001
Inj. Fentanyl(µg/kg)	1.5(0.23)	1.0(0.34)	0.001
Average Halothane	0.6(0.081)	0.42(0.135)	0.001
Total Duration(min)	230(30)	240(45)	NS

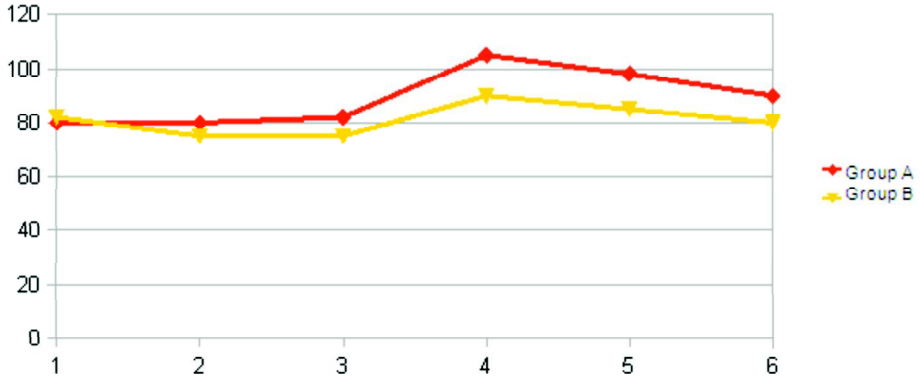

Figure1: Heart rate changes during tracheal intubation in group A and group B. HR(Beat per minute).

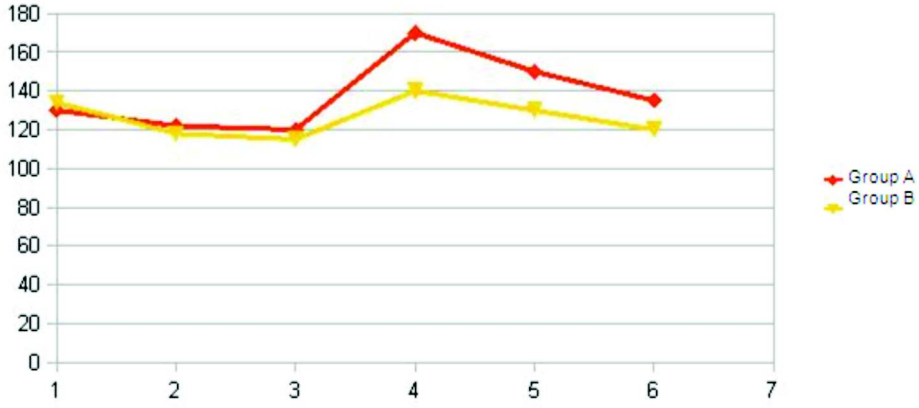

Figure 2:systolic blood pressure changes during tracheal intubation in groupA and group B (SBP mm Hg)

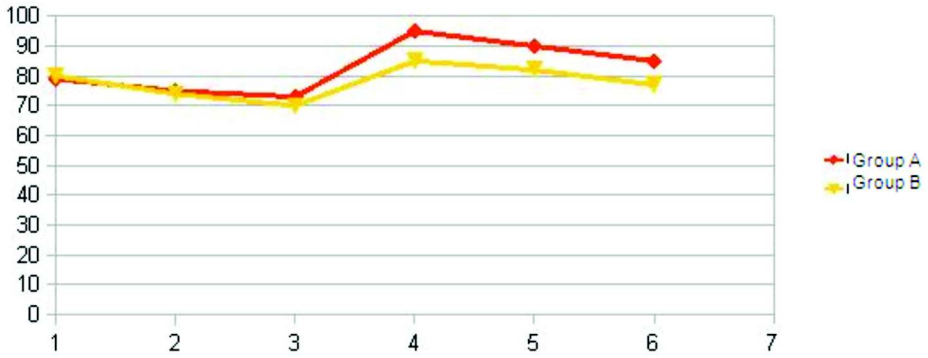

Figure 3: Diastolic blood pressure changes during tracheal intubation in group A and group B**.** Time points: 1 = baseline; 2 = preinduction; 3 = induction; 4 = 0 min after intubation; 5 = 1 min after intubation; 6 = 5 min after intubation DBP (mm Hg).

The average inspiratory concentration of halothane required during anaesthetic maintenance was 0.6% in group A and 0.42% in group B. A decrease of 30% was observed in group B compared to group A (p=0.00).

Also, the requirement of inj. fentanyl was 1.5 μg/kg in group A as opposed to 1.0 μg/kg in group B. (Table 2).

Table 3: Ramsay Sedation Score.

Score	Response
1	Anxious or restless or both
2	Cooperative, Orientated and Tranquil
3	Responding to Command
4	Brisk response to stimulus
5	Sluggish response to stimulus
6	No response to stimulus

In group B patients receiving dexmedetomidine loading infusion, a fall in the heart rate and blood pressure was observed, which was not more than 6% of the baseline. Patients were sedated but arousable with sedation score of 2.

In both the groups, the maximal increase in heart rate and blood pressure occurred immediately after tracheal intubation (0 min) when compared to the baseline arterial blood pressure. The increase in heart rate after intubation was 25% in group A as compared to 5% in group B (p=0.00). Similarly, significant increase in systolic pressure was observed in group A which was 35% as compared to 10% in group B (p=0.00), while increase in diastolic pressure was 30% and 10% in group A and group B, respectively (p=0.001).

25 out of 30 patients in group A required inj. diclofenac sodium 75 mg intravenously, while 5 out of 30 patients in group B required inj. diclofenac sodium 75 mg. 15 patients out of 30 in group A were supplemented with inj. propofol in an average of 150 mg. None of the patients required inj. propofol in group B.

Bradycardia was observed in two patients in group B intraoperatively, which promptly responded to inj. atropine 0.6 mg intravenously. No fall in blood pressure was observed in either of the patients.

The duration of recovery was similar in both the groups. All the patients were immediately able to obey commands upon arrival into recovery room.

In the recovery room, three patients in group B and two patients in group A experienced nausea. None of the patients had explicit recall of awareness or complained of any discomfort when interviewed after operation.

DISCUSSION:

Dexmedetomidine is a highly selective α2 agonist that has been shown to have sedative, analgesic and anaesthetic sparing effects [10-11] . It causes a dose dependent decrease in blood pressure and heart rate. It is successfully used in intravenous doses, varying from 0.25 to 1 μg / kg for attenuating intubation response[12-14]. Optimal dose for attenuating pressure response seems to be 1 μg / kg with lesser doses not being effective.

Dose of thiopentone needed for induction was reduced (25%) by dexmedetomidine, demonstrating the anaesthesia potentiating effects[15]. Similarly dexmedetomidine has an opioid sparing effect with fentanyl requirement reduced by 33% as also found by scheinin et al[16] . Scheinin B et al studied the effect of dexmedetomidine on tracheal intubation and perioperative anaesthetic requirement of Thiopentone and fentanyl . He found that dexmedetomidine reduces the cardiovascular response to intubation and it decreases the perioperative anaesthetic requirement of thiopentone and fentanyl. By virtue of its effect on α2 receptors dexmedetomidine mediates its analgesic effects.

Halothane requirement was reduced by 30% in our study, similar result were noted by segal et al, while studing effect of dexmedetomidine on halothane MAC in rats[17]. Thiopentone Sevoflurane and Isoflurane requirement are also reduced by dexmedetomidine [21-23], and tracheal extubation was faster without respiratory depression [24]. Keniya et al conducted a similar study He studied the effect of Dexmedetomidine on tracheal intubation and perioperative anaesthetic requirement He found that perioperative infusion of Dexmedetomidine is effective in attenuating sympatoadrenal response to intubation. It has significant anaesthetic and opioid sparing effect[18-19]. Clonidine and Dexmedetomidine also causes dose dependent decrease in SBP, DBP, HR & Blood norepinephrine level while plasma cortisol, rennin, ANP & Vasopressin level were unaffected [25-26]. In our study, pretreatment with dexmedetomidine 1 μg / kg attenuated the hemodynamic response to tracheal intubation. Other studies have shown similar results. Aho M Lehtinen et al studied the effect of dexmidetomidine on perioperative hemodynamics

and isoflurane requirement in patients undergoing hysterectomy. They found that in patients receiving higher dose (0.6μg/kg) of dexmeditomidine the increase in heart rate and B.P. and mean endtidal isoflurane concentration was significantly less than in those receiving saline or fentanyl[9].

Bradycardia responsive to atropine was observed in 2 patients with no incidence of hypotension, it may be due to the fact that we used dexmedetomidine as infusion while bradycardia and hypotension are more common on rapid bolus administration [20]. This bradycardia and hypotension is due to decreased central sympathetic outflow.

In our study, three patients were of craniotomies The perioperative haemodynamic stability is of utmost importance in such surgeries. Increase or decrease in blood pressure may cause bleeding or edema or predispose the patient to cerebral ischaemia. The haemodynamic responses to emergence from anaesthesia and extubation are blunted with dexmedetomidine and the centrally mediated sympatholytic effect is continued well in postoperative period, which was advantageous in these patients.

The present study findings corroborate with those of previous studies. No major adverse effects from the drug were seen in the present study.

CONCLUSION :

Dexmedetomidine, as a pre-anaesthetic medication and intraoperative infusion, decreases intraoperative anaesthetic requirement. It has significant opioid and anaesthetic sparing property. It significantly attenuates hemodynamic response to tracheal intubation. In addition, continuous intraoperative administration of dexmedetomidine does not affect intraoperative cardiovascular stability.

LIMITATIONS OF THE STUDY:

A possible limitation of our study is that we used clinical signs to judge anaesthesia depth and requirement of anaesthetic agents, while intraoperative bispectral index (BIS) monitoring would have been definitely a better option for it. Also end tidal halothane con. would have been ideal than inspired dial concentration to indicate depth. of anaesthesia, however there was no case of awareness suggesting adequate depth of anaeshesia.

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