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ORIGINAL ARTICLE

DEXMEDETOMIDINE ATTENUATES THE STRESS RESPONSE TO LARYNGOSCOPY, ENDOTRACHEAL INTUBATION AND REDUCES THE DOSE OF THIOPENTONE

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ABSTRACT: BACKGROUND: Dexmedetomidine, an α-2 adrenoreceptor agonist, is gaining popularity for its sympatholytic, anaesthetic sparing and haemodynamic stabilizing properties without significant respiratory depression. **METHODS:** We assessed the efficacy of dexmedetomidine in attenuating stress response to laryngoscopy, endotracheal intubation and analyzed reduction in the dose of thiopentone. Sixty patients scheduled for elective general abdominal surgeries were randomly selected. Control group (C) received isoflurane–opioid-saline and study group (D) received isoflurane–opioid-dexmedetomidine anaesthesia. Dexmedetomidine infusion in a dose of 1 μg/kg and Saline (at same rate-ml/hr.) was given over 10 min before the induction of anaesthesia. All patients were induced with thiopentone, fentanyl and vecuronium. Haemodynamic variables were recorded at different time intervals. **RESULTS:** The need for thiopentone was decreased by 22.96% in the dexmedetomidine group as compared to the control group. After laryngoscopy and endotracheal intubation, maximal average increase was 8.18% in systolic and 10.07% in diastolic blood pressure in dexmedetomidine group, as compared to 33.81% and 24.02%, respectively, in the control group. Similarly, average increase in heart rate was 7.48% and 19.28% in the dexmedetomidine and control groups, respectively. **CONCLUSION:** Preoperative infusion of dexmedetomidine is effective in attenuating the stress response to laryngoscopy and endotracheal intubation. It has significant anaesthetic sparing effect.

KEYWORDS: α-2 adrenoreceptor, dexmedetomidine, stress response, laryngoscopy, endotracheal intubation

INTRODUCTION: Clonidine, α-2 agonist, has been introduced to clinical anaesthesia for its sympatholytic, sedative, anaesthetic sparing effects and haemodynamic stabilizing properties.[1-4] Dexmedetomidine, the pharmacologically active d-isomer of medetomidine(4,[5]-[1-(2,3-dimethylphenyl)) -ethyl] imidazole is a highly specific and selective α-2 adrenoreceptor agonist.[5, 6] The α-2: α-1 binding selectivity ratio of dexmedetomidine is 1620:1 compared to 220:1 for clonidine.[6] Animal experiments have indicated that it has prominent anaesthetic effect.[7] Studies in human volunteers have demonstrated clonidine like analgesic, sedative, sympatholytic and cardiovascular effects.[8-10] In recent studies, dexmedetomidine has been shown to have clinically significant effects on anaesthetic requirements, haemodynamic responses induced by anaesthesia and surgery in patients.[11] It has also been observed that an infusion of dexmedetomidine combined with inhalation anaesthetics provided satisfactory intraoperative conditions without adverse haemodynamic effects.[12]

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The study was undertaken to assess the efficacy and safety of dexmedetomidine in attenuating the stress response to laryngoscopy, endotracheal intubation and to analyse reduction in the dose of thiopentone.

METHODS: After obtaining approval from hospital ethics committee, a written informed consent was taken from the patients for participation in the study. 60 patients of either sex in the age group of 18-65 years, belonging to ASA class I scheduled for elective general abdominal surgeries were selected for this study. Pregnant and lactating women, difficult intubation (Mallampati Class III to IV or Laryngoscopic grade III to IV) , prolonged laryngoscopic time >30 seconds, patients with more than one attempt at intubation, patients on antihypertensive agents like β-blockers, antidepressants and patients allergic to such medication were excluded from the study. None of the patients were on any significant drug therapy preoperatively.

Patients were randomly divided into two equal groups (30 each) according to simple random sampling and were allocated to one of the two groups as follows:

1. Group C – Isoflurane – Opioid – Saline infusion.
2. Group D – Isoflurane – Opioid – Dexmedetomidine.

All the patients were premedicated with injection glycopyrrolate 0.2mg intramuscularly 30 minutes prior to induction of anaesthesia. On arrival in the operating room, the patient's baseline heart rate, blood pressure and SPO_2 were recorded by connecting the patient to multi-channel monitor after 5 minutes of settling in the operating room. A 16G or 18G intravenous cannula was inserted for drug and continuous fluid infusion. All the patients in group D received injection dexmedetomidine in a dose of 1μg/kg over a period of 10 minutes,[13-15] prior to induction of anaesthesia through an infusion pump. During infusion, heart rate, systolic blood pressure, diastolic blood pressure and SPO_2 at 5 minutes and at 10 minutes interval (end of infusion) were recorded. All the patients in the group C received saline (Same volume as that of dexmedetomidine) through infusion pump over a period of 10 minutes.

All the patients received Injection ondansetron 4mg, Injection midazolam 1mg, Injection Fentanyl 1μg/kg intravenously just before the induction of anaesthesia. Then a dose of injection thiopentone sufficient to abolish eyelash reflex was injected followed by injection vecuronium 0.1mg/kg to facilitate laryngoscopy and tracheal intubation. The patients were ventilated by facemask for at least 3 minutes using 100% O_2. Laryngoscopy was performed with Macintosh laryngoscope and trachea was intubated with appropriate size endotracheal tube. No stimulus was applied for first 5 minutes. Any complication during this period viz. vomiting, involuntary movements, laryngospasm and coughing were noted. Anaesthesia was maintained by nitrous oxide, oxygen, isoflurane, injection fentanyl, injection vecuronium. At the end of surgical procedure the neuromuscular blockade was antagonized with injection Neostigmine 0.05mg/kg and injection glycopyrrolate 0.01mg/kg intravenously. Patients were extubated when respiratory effort was deemed sufficient and patients were able to obey simple commands.

The following parameters were observed and recorded:

The Heart Rate (HR), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) were recorded at following intervals as described below:

1. Baseline,
2. 5 minutes after dexmedetomidine/Saline infusion,
3. 10 minutes after dexmedetomidine/Saline infusion,

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4. Pre-induction,
5. Just before laryngoscopy and endotracheal intubation,
6. Immediately after endotracheal intubation,
7. 1 minute after endotracheal intubation,
8. 5 minutes after endotracheal intubation.

Also the dose of thiopentone (mg/Kg) needed for induction of general anaesthesia was noted in both group D and group C.

STATISTICAL ANALYSIS: Statistical analysis was conducted with SPSS (version 19) for Windows statistical package using paired, unpaired student's t and chi-square test (sex). The results were expressed as Mean ± SD. P<0.05 was regarded as statistically significant and P >0.05 was regarded as insignificant.

RESULTS: The two groups were comparable in patient characteristics [Table 1]. Dexmedetomidine was well tolerated and no drug-related adverse events were observed.

Observation	Group D n= 30	Group C n= 30
Age in years (Males: Females)	35.92±1.98: 34.59±3.95	35.33±4.17: 32.13±3.87
Weight in Kgs (Males: Females)	60.23±2.52: 57.29±2.31	60.67±1.91: 57.60±3.07
Sex ratio (Males: Females)	13:17	15:15

Table 1: Patient Characteristics Mean±SD

The mean sleeping dose of injection thiopentone required in group C was 6.01 mg/kg while it was 4.63 mg/kg in group D [Table 2]. The decrease in the dose requirement was by 22.96% in dexmedetomidine group as compared to control group (P=0.00).

Mean Dose of Thiopentone (mg/kg)	
Groups	Mean ±SD
Group D	4.63±2.65
Group C	6.01±3.24

Table 2: Anaesthesia Characteristics Mean±SD

Before administration of the study drugs in the operating room, heart rate and blood pressure values between the two groups did not differ.

In both the groups, the maximal increase in heart rate and blood pressure occurred immediately after laryngoscopy and endotracheal intubation when compared to the baseline arterial blood pressure. The increase in heart rate after laryngoscopy and endotracheal intubation was 19.28% in group C as compared to 7.48% in group D (P=0.00) [Figure 1]. Similarly, significant increase in systolic pressure was observed in group C which was 33.81% as compared to 8.18% in

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group D (P=0.00) [Figure 2]., while increase in diastolic pressure was 24.02% and 10.07% in group C and group D, respectively (P=0.000) [Figure 3].

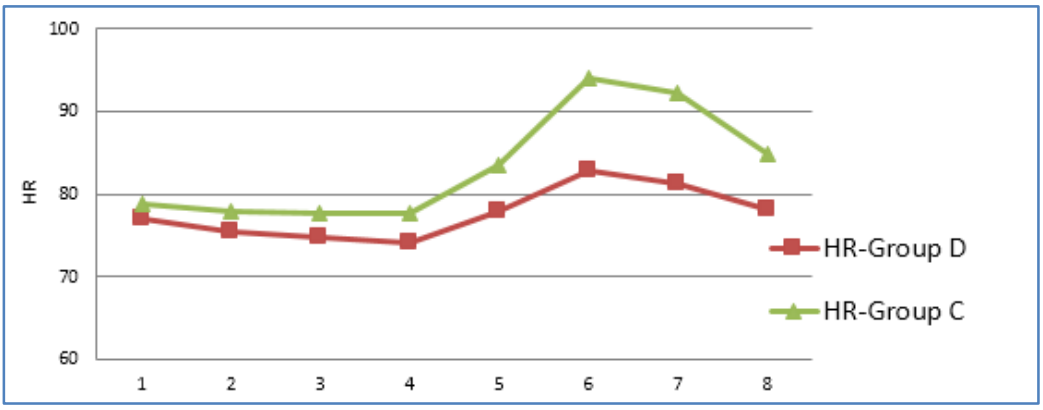

Fig. 1: Shows heart rate of studied patients at different time points

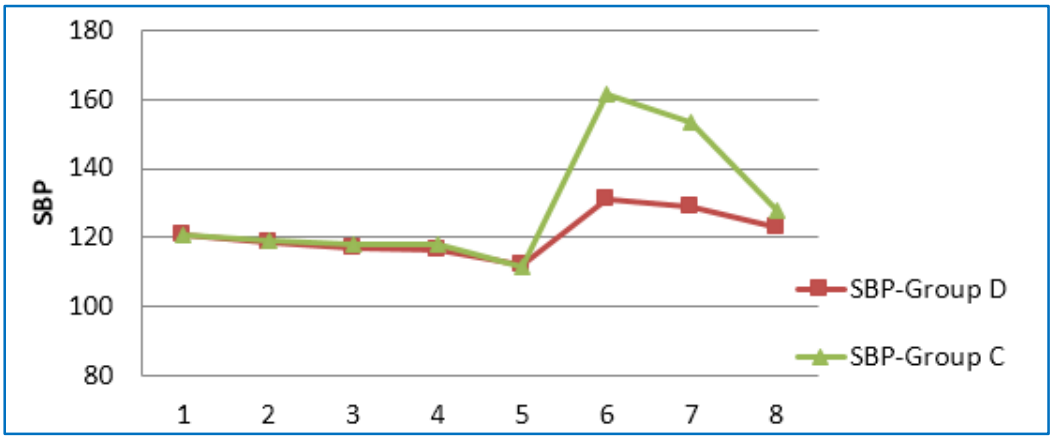

Fig. 2: Shows systolic blood pressure (SBP) at different time points

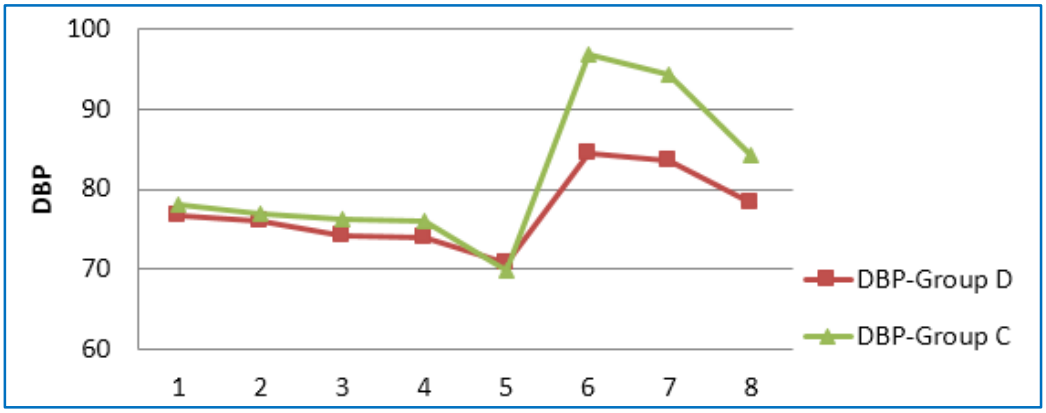

Fig. 3: Shows diastolic blood pressure (DBP) at different time

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Cardiovascular stress response after laryngoscopy and endotracheal intubation in group C and group D. HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure. Time points; -1= Baseline, -2=5 minutes after dexmedetomidine/Saline infusion, -3=10 minutes after dexmedetomidine/Saline infusion, -4 =Pre-induction, -5=Just before laryngoscopy and endotracheal intubation, -6= immediately after endotracheal intubation, -7=1 minute after endotracheal intubation, -8=5 minutes after endotracheal intubation.

In our study, intraoperatively bradycardia was observed in three patients receiving dexmedetomidine, without fall in blood pressure, which responded promptly to IV atropine. All the patients were immediately able to obey commands upon arrival into recovery room.

None of the patients had explicit recall of awareness or complained of any discomfort when interviewed after operation.

DISCUSSION: We conducted this prospective randomized study in an attempt to examine whether administration of dexmedetomidine to a commonly administered balanced anaesthetic regimen attenuates the stress response to laryngoscopy and endotracheal intubation. It would also reduce the induction dose of thiopentone.

Dexmedetomidine is a highly selective α-2 agonist that has been shown to have anaesthetic sparing effects.[16, 17] It causes a dose-dependent decrease in arterial blood pressure and heart rate, associated with decrease in serum norepinephrine concentration.

Dexmedetomidine was well tolerated, and no serious side effects or adverse reactions occurred in the present study.

The dose of thiopentone needed for induction was reduced significantly (22.96%) in the patients receiving dexmedetomidine, as also found by Aantaa and coworkers, demonstrating the anaesthesia potentiating effects of the drug.[18]

Tracheal intubation is associated with increases in arterial pressure, heart rate and plasma catecholamine concentrations.[19] Increases in arterial pressure and heart rate observed in the control group in the present study were almost similar to those reported in earlier studies.[19]

In the present study, pretreatment with dexmedetomidine 1 μg/kg attenuated, but not totally obtunded, the cardiovascular response to tracheal intubation after induction of anaesthesia. In patients undergoing general or gynaecological surgery, numerous studies have shown that dexmedetomidine blunts cardiovascular response to intubation,[20,21,22] and our findings are in accordance with them. In addition to this beneficial property of α-2 agonists, they have also been reported to increase the risk of hypotension and bradycardia.[21] These effects have most often been seen in young healthy volunteers on rapid bolus administration.[21,23] In our study, bradycardia was observed in three patients receiving dexmedetomidine, with no fall in blood pressure, which responded promptly to IV atropine.

A possible limitation of our study may have been the use of subjective criteria to determine the induction dose of thiopentone for each patient. Estimating anaesthesia depth by changes mediated by autonomic nervous system is difficult during dexmedetomidine infusion as it increases the haemodynamic stability. Intraoperative Bi-spectral index (BIS) monitoring would have been definitely more objective in deciding the depth of anaesthesia and the requirement of anaesthetic agent. Also, measurement of QT interval and plasma catecholamine levels, more objective means of haemodynamic response,[24] was not done because of practical difficulty.

The present study findings corroborate with those of previous studies. No adverse cardiovascular effects from the drug were seen in the present study. Bradycardia, a possible consequence of administration of α-2 agonist, was counteracted by the use of atropine. There was no case of awareness suggesting adequate depth of anaesthesia.

CONCLUSION: Dexmedetomidine, as a pre-anaesthetic medication, decreases the induction dose of thiopentone. It has significant anaesthetic sparing property. It also significantly attenuates the stress response to laryngoscopy and endotracheal intubation.

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