Original Research Article

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Effect of Dexmedetomidine on Induction and Hemodynamic Response to Laryngoscopy and Intubation with Propofol and Sevoflurane: A Randomized Clinical Trial

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Abstract

Background: Induction of anaesthesia, laryngoscopy and intubation are critical events and hemodynamic stability is an important factor during this period. This study aims to evaluate the effect of dexmedetomidine on induction with respect to hemodynamic response, induction time and smoothness of induction also to evaluate the combined effect of dexmedetomidine with propofol and sevoflurane on cardiovascular response to laryngoscopy and intubation. *Methods*: A total of 120 American Society of Anaesthesiologists physical status I and II patients undergoing elective surgical procedures under general anaesthesia were randomized into two groups. Both the groups received dexmedetomidine 1.0µg/kg diluted to 10ml, infused over 10min, 10min before induction. Group DP (Dexmedetomidine Propofol) received Inj propofol 1.5-2mg/kg titrated till the loss of verbal response (n= 60) andGroup DS (Dexmedetomidine Sevoflurane) were induced with sevoflurane 8% till loss of verbal response (n =60). Heart rate (HR) Mean arterial pressure (MAP) and rate pressure product (RPP) were recorded at baseline (T0), 2 min after administration of drug (T1), 1min after induction (T2) and at 1, 3, 5 and 10 min after intubation (T3, T4, T5 and T6 respectively). *Results*: There was a significant decrease in mean arterial pressure and heart rate from pre-induction values within both groups after induction. The reduction in MAP and RPP was significantly more in group DP at 1min to 5min after intubation than group DS ($p < 0.05$). *Conclusion*: Induction of anesthesia with Propofol and dexmedetomidine demonstrated a shorter induction time and greater decrease in mean arterial pressure at laryngoscopy and intubation.

Keywords: Induction; Propofol; Sevoflurane; Dexmedetomidine; Hemodynamics; Laryngoscopy.

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Introduction

Anesthetic induction is a critical event and hemodynamic stability is an important component of smooth anesthetic induction [1,2]. Stress response under anesthesia has long been universally recognized phenomenon which may be in the form of endocrine or autonomic disturbance. There is increase in heart rate, blood pressure and arrhythmias [3]. Increase in intraocular and intracranial pressure is also noted [4]. These changes are maximum at 1 min after intubation and last for 5-10 min.Various pharmacological [5,6] methods have been aimed to suppress this pressor response but the search for the ideal drug for attenuation of cardiovascular response during laryngoscopy and tracheal intubation continues as the stress may not be tolerated by patients with compromised cardiac status.

Propofol is one of the most widely used intravenous induction agent because of its rapid onset time, short action duration and lesser side

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effects. Sevoflurane has low blood gas solubility coefficient (0.69) and is a nonpungent inhaled anesthetic [7,8].

There are many studies on dexmedetomidine [9-11] for attenuation of stress response during laryngoscopy and intubation, majority of them using intravenous induction agents. None of the studies evaluate the effect of dexmedetomidine with different induction agents. This study aims to evaluate the effect of dexmedetomidine on induction with IVpropofol and inhalational agent sevoflurane with respect to hemodynamic response, time required and smoothness of induction and also to evaluate the combined effect of dexmedetomidine with propofol and sevoflurane on cardiovascular response to laryngoscopy and intubation.

Materials and Methods

After obtaining approval from the institutional ethics committee the study was registered in the Clinical Trial Registry of India as CTRI/2018/02/012009. A written informed consent was taken from each patient who met the inclusion criteria, before enrolment into the study. This was a prospective, randomized, single-blind study. A total of 120 ASA I and II patients of either gender between 18 to 65 years of age undergoing elective surgery under general anesthesia requiring endotracheal intubation were included. Patients with a history of allergy to volatile anesthetics or Propofol, anticipated difficult mask ventilation, communication problems, baseline mean arterial pressure (MAP) less than 70 mmHg and heart rate (HR) less than 60 beats per minute (bpm), Concomitant use of medications which may exaggerate the heart rate response of dexmedetomidine including digoxin or β–adrenergic antagonists, predicted difficulty in intubation, pregnancy, nursing women, morbid obesity and patients with coronary artery disease, ischemic heart disease, heart blocks were excluded from the study.

A computer-generated randomisation table was generated prior to commencement of the study and concealed in sealed opaque envelopes. Patients were randomly, in a single blinded fashion allocated into Group DP= Dexmedetomidine Propofol group, received Dexmedetomidine (1.0µg/kg) diluted to 10 ml with normal saline, .infused over 10min, 10 min prior induction and Inj propofol 1.5-2mg/kg titrated till the loss of verbal response (n= 60) and Group DS= Dexmedetomidine Sevoflurane group recieved Dexmedetomidine (1.0µg/kg) diluted to 10 ml with normal saline, infused over 10min, 10min before induction and induced with sevoflurane 8% till loss of verbal response (n =60).

On arrival in the operating room, routine standard monitors such as continuous ECG, NIBP and pulse oximeter were established and the patients' baseline heart rate, blood pressure and oxygen saturation (SpO_2) were recorded after 5 min of settling in the operative room. A 20G intravenous cannula was inserted for drug and continuous fluid administration.

All patients were premedicated with intravenous (IV) Glycopyrrolate (0.05mg/kg), IV midazolam 0.03mg/kg, IV Fentanyl (2µg/kg) for analgesia. 10mins prior induction both the groups received dexmedetomidine 1.0µg / kg diluted to 10 ml with normal saline infused over 10 mins. Based on randomisation, Group DP patients were induced with titrating dose of 1% Propofol injected manually at the rate of 1.5 ml every 5 seconds till loss of verbal response. Group DS patients were induced with (8%) Sevoflurane at tidal breathing, using circle system till loss of verbal response. The circuit was primed with 8% Sevoflurane in oxygen at six litres per minute for 30 seconds. Face mask was then applied to obtain adequate seal. The patients were asked to breathe normally. The time of start of injection of propofol or mask placement with sevoflurane 8% was considered as 'starting point of induction'. Loss of verbal response was defined as 'induction end point'. The time taken for anesthetic induction was recorded for both groups. For group DS patients, Sevoflurane was reduced to 4% and subsequently adjusted between 0.5 and 2% to maintain adequate depth of anesthesia clinically. For Group DP patients, 10 to 20 mg increments were administered if the anesthetic depth was clinically judged to be inadequate (indicated by patient movement, swallowing, tachycardia, or MAP >20% pre- induction)

After ensuring the ability to ventilate, patients were relaxed with IV vecuronium (0.1 mg/kg). Laryngoscopy was done with appropriate sized Mac-Intosh blade and intubation with appropriate sized cuffed endotracheal tube within 15 seconds at single attempt by the same anaesthesiologist. Ventilator settings were adjusted to maintain SpO_2>95% and $ETCO_2$ 30-35mmHg. Anaesthesia was maintained with oxygen, N_2O,isoflurane intermittent positive pressure ventilation and vecuronium. At the end of surgery residual neuromuscular blockade was reversed with

neostigmine 0.05 mg/kg and glycopyrrolate 0.02 mg/kg.

Induction time, intubating conditions, attempts for intubation, Hemodynamic response and complications i.e. coughing/gagging, laryngospasm/bronchospasm, patient's movement during endotracheal intubation were noted. The heart rate through ECG, systolic blood pressure, diastolic blood pressure, mean arterial pressure NIBP in mm/Hg, SpO_2 using pulse oximeter, and ECG were monitored continuously and HR, MAP and rate pressure product (RPP) calculated by formula (SBPX HR)/1000 were recorded at baseline (T0) and 2 min after administration of drug (T1),1min after induction (T2) and at 1 min (T3), 3 min (T4), 5 min (T5) and 10 min (T6) after intubation. Complications during the study period were recorded and managed accordingly. Hypotension was considered significant when MAP was less than 20% below pre-induction values and was managed by decreasing the delivery of anesthetic agents, administration of IV fluids and ephedrine 6 mg dose increments when needed. Bradycardia (HR <60 bpm), if associated with low MAP or HR <20% pre-induction values, was treated with atropine 0.6 mg. Tachycardia (HR >20% pre-induction values) was managed by increasing the anesthetic depth and treatment of any other possible cause such as inadequate oxygenation, ventilation or analgesia. Cases were excluded from study if Cormack Lehanne > 2, more than one attempt at laryngoscopy and intubation. Intubating conditions were graded using Cooper's score (annexure 1) in to excellent (Score 8-9), good (Score 6-7), poor (Score 3-5) or inadequate (Score 0-2), considering the criteria of jaw relaxation, condition of vocal cords and response to intubation. Excellent & good (Score>5) were considered as clinically acceptable intubating condition. Demographic data were analysed by student t test and chi square test. Paired sample T-test was used for comparison of MAP and HR within each group. Intergroup comparison was done by independent sample t test. Power analysis was carried out by statistical software package (SPSS version 16). A sample size of 60 patients per group was required to detect a 15% difference MAP, with a power of 90% and 5% significance level. All data were expressed as mean standard deviation (95%

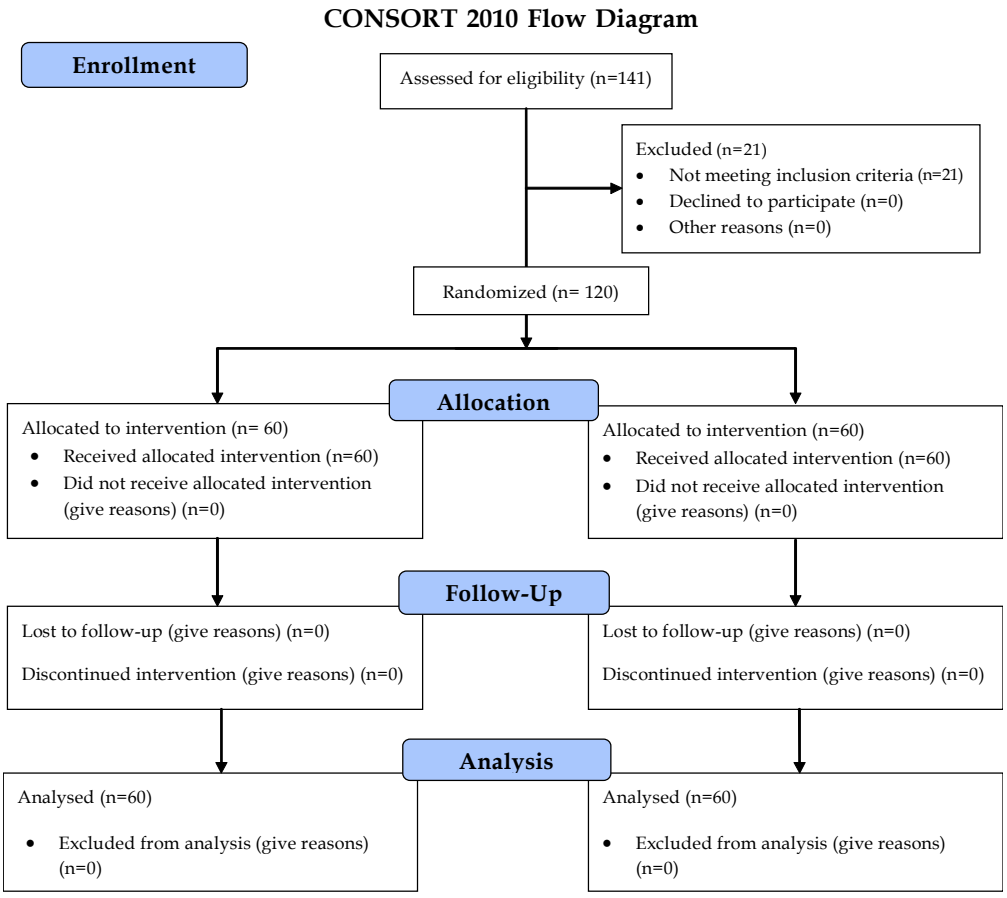

Fig. 1: CONSORT flow diagram of patients included in the study

confidence interval) and p<0.005 was considered significant.

Results

Figure 1 shows flow diagram for this study where 141 patients were assessed for eligibility and 120 patients were included and their results were analysed.The two groups were comparable in patient characteristics with respect to age, mean weight and gender (p>0.05) [Table 1].

The HR at Baseline and 2 min after dexmedetomidine infusion were comparable between the two groups. After induction there was a reduction in heart rates in both the groups but significantly more reduction in group DP, Following laryngoscopy and intubation the HR was comparable in both the groups (Figure 1)

The MAP and RPP were comparable between both the groups at baseline and T1.The fall in MAP and RPP was significantly more after induction in group DP(MAP 78.2±9.291vs 83.2±10.544) than group DS (p<0.05). The MAP and RPP was higher in group DS than group DP (MAP 85.9±10.054 vs91.4± 11.013 in

Table 1: Demographic characteristics amongst two groups

Parameters	Group DP	Group DS
Age [years] (mean ± SD)	35.06 ± 11.794	35.78 ± 10.719
Weight [kg] (mean ± SD)	55.20 ± 8.983	58.06 ± 9.527
Gender [Male / Female]	24/36	22/38

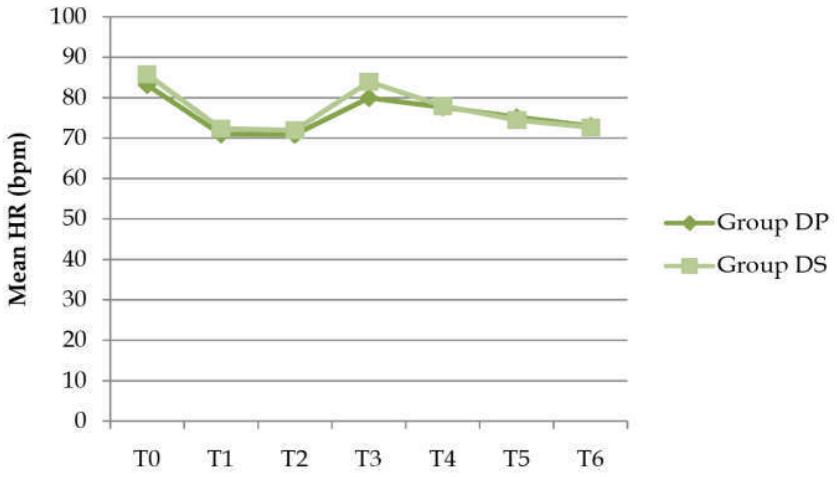

Fig. 1: Inter group comparison of mean heart rate

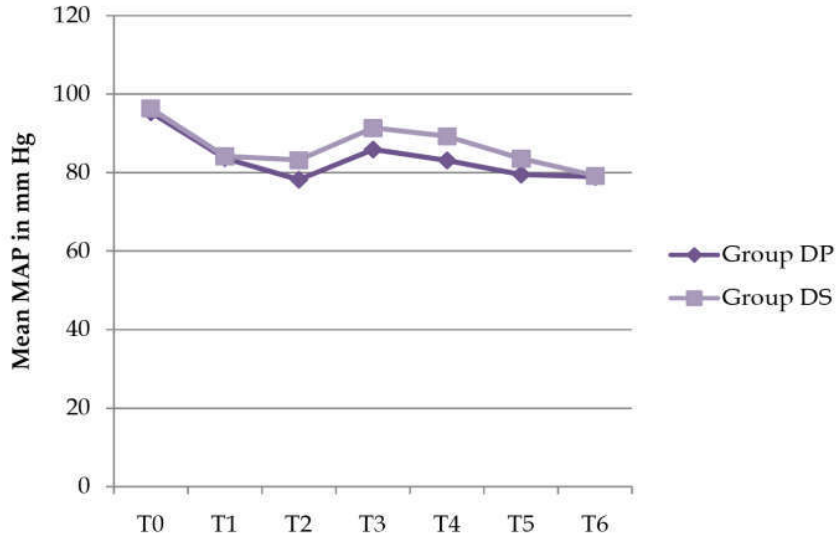

Fig. 2: Inter group comparison of mean MAP(mm Hg)

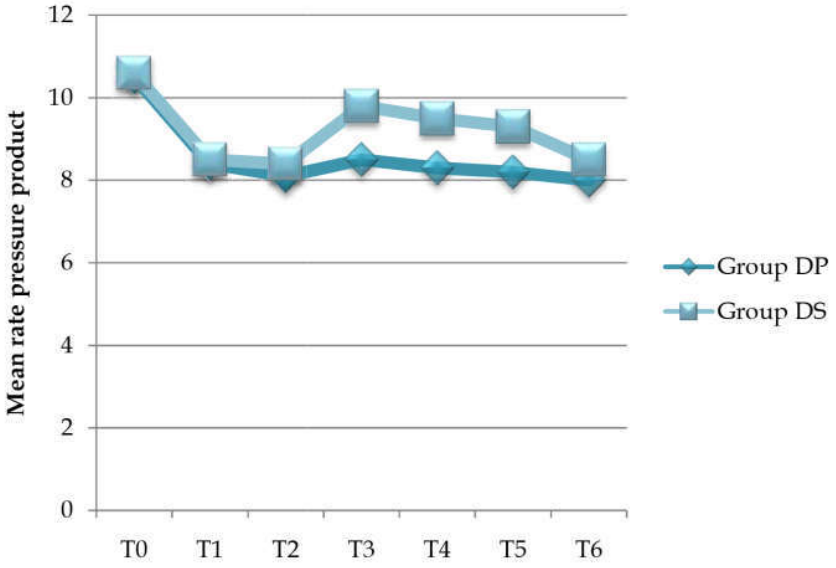

Fig. 3: Inter group comparison of mean rate presssure product

group DP and group DS respectively at T3) after intubation and were comparable at 10 mins (Figure 2 and 3).

The mean induction time was 52.36±13.24 sec in Group DS and 24.5±7.70 sec in Group DP. The mean popofol requirement was 62.64±12.8 mg. Both the groups had excellent intubating conditions cooper score (>8). Complications such as coughing, gagging, laryngospasm or bronchospasm were not observed in any patients. All patients had SpO_2>98% throughout the study period. Only one patient in group DP had bradycardia requiring IV atropine 0.6mg.

Discussion

Hemodynamic stability is an integral component of an ideal anesthetic induction. Patients with cardiovascular diseases and elderly patients are more liable to hemodynamic changes during anesthetic induction [1,2].

Inhalation induction is commonly performed in children. Inhalation induction is also preferred over intravenous induction in patients with anticipated difficult airway where spontaneous ventilation is preferred during induction. Sevoflurane is an inhalational anesthetic with comparable properties to IV Propofol for anesthetic induction, maintenance and recovery.

Non-invasive methods of blood pressure measurement by oscillatory method measures MAP better than systolic or diastolic blood pressure [14]. Rate pressure product is a term used in cardiology, as well as exercise physiology, to measure workload or oxygen demand of the heart and thus a good measure of energy consumption of heart. Hence, we compared MAP and RPP between the two groups in our study.

Dexmedetomidine has sedative, anxiolytic, analgesic and sympatholytic effects and may blunt the cardiovascular responses in the peri operative period without causing significant respiratory depression. Jaakola used 0.6 μg/kg dexmedetomidine and thiopentone induction and noted that after intubation the maximum heart rate was 18% less (p=0.036) in group D compared to placebo group and by 10 min after intubation maximum systolic and diastolic pressures were also significantly (p=0.013 and p=0.020) less in dexmedetomidine group [9].

Scheinin et al. used 0.6 μg/kg dexmedetomidine and showed that dexmedetomidine decreased, but did not completely suppress, the hemodynamic response to tracheal intubation in healthy individuals [10].

Our study showed similar results to Guptaa K et al. [11] where 1 μg/kg dexmedetomidine attenuated the adverse hemodynamic responses of laryngoscopy and intubation adequately, the fall in MAP was higher than study conducted by Gupta, which is probably due to use of fentanyl in our study. Thwaities S [12]

observed that induction of anesthesia with propofol was associated with decreased in MAP more than sevoflurane group. Volatile agents potentiate the effects of non-depolarizing muscle relaxants but in our study the intubating conditions were comparable in both groups (p=0.11) [13].

In this study dexmedetomidine 1 mcg/kg infusion before induction of anesthesia suppressed the hemodynamic response to tracheal intubation in normotensive patients. This suppression in cardiovascular responses was found to be greater with propofol than sevoflurane.

Conclusion

This study concludes that in patients premedicated with dexmedetomidine both the induction agents, sevoflurane and propofol provides good quality of intubating condition. Induction time and hemodynamic response was less in group DP than group DS. Both sevoflurane and propofol with dexmedetomidine showed lesser raise in cardiovascular response to laryngoscopy and intubation but Dexmedetomidine with propofol induction attenuated cardiovascular response better than dexmedetomidine with sevoflurane.

Annexure 1:

Cooper scoring system			
Score	**Jaw relaxation**	**Vocal cards**	**Response tointubation**
0	Impossible to open	Closed (adducted)	Severe coughing orbucking
1	Opens with difficulty	Closing	Mild coughing
2	Moderate opening	Moving	Slight diaphragmaticm ovement
3	Easy opening	Open (relaxed)	No movement

Conflict of Interest : None declared

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