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A comparative study of two different doses of dexmedetomidine for attenuating the hemodynamic response to tracheal intubation

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Abstract

Background: According to the majority of current research, a loading dosage of 1 µg/kg dexmedetomidine is superior to lesser levels in this regard. However, taking a lesser dose may be advantageous because it reduces the risk of undesirable effects such as hypotension and bradycardia, which are more likely when a greater dose is used, as well as being more cost-effective.

Objectives: The aim of the study was to evaluate and compare the effect of loading doses of 1 µg/kg and 0.5 µg/kg dexmedetomidine on attenuation of hemodynamic response to laryngoscopy and intubation

Materials and Methods: One hundred twenty patients scheduled for elective surgery under general anaesthesia were to participate in a randomised, double-blind, placebo-controlled research. Three groups of patients were formed. Before induction, two groups received different loading dosages of dexmedetomidine infusion, while the third group served as a control group. The intubating circumstances and hemodynamic responsiveness of all patients were examined. Using SPSS 26.0 software, nonparametric data were compared using the Chi-square test, and parametric data were compared using the Student's t-test.

Results: Both the loading doses of 1 µg/kg and 0.5 µg/kg dexmedetomidine were equally effective in reducing the induction dose of propofol, improving the intubating conditions and blunting the hemodynamic response to laryngoscopy and intubation. The incidence of adverse effects such as hypotension and bradycardia was lesser with the loading dose of 0.5 µg/kg.

Conclusions: Infusions of dexmedetomidine in the loading dose of 0.5 µg/kg are therapeutically equivalent to infusions of 1.0 µg/kg in terms of providing good intubating circumstances and blunting the hemodynamic response to intubation. A lower dose is linked to a lower risk of negative effects like hypotension and bradycardia.

Keywords: Dexmedetomidine, hemodynamic response, intubating conditions.

Introduction

Anesthesiologists frequently worry about the hemodynamic response after laryngoscopy and tracheal intubation, especially in high-risk patients. Dexmedetomidine has been proven to be effective in obtunding this response, as well as improving intubating circumstances and lowering the dose of additional anaesthetic medications. Dexmedetomidine, the S-enantiomer of medetomidine, is a relatively novel alpha 2 adrenoreceptor agonist that was first used as a sedative during premedication in ICUs in 1999.[1-3]

However, with the passage of time, dexmedetomidine has proved to be a novel drug which is currently used for the purpose of analgesia, day-care surgeries, short procedures such as colonoscopies, and as an adjunct to general anesthesia for the purpose of co-induction.[4-8]

The term co-induction of anesthesia has been applied to the use of two or more drugs to induce anesthesia. Co-induction of anesthesia is practiced by anesthesiologists exploiting drug interactions, particularly synergism. It can produce an improvement in all phases of anesthesia including induction, maintenance, and recovery. Till date, no perfect drug or drug combination that would blunt the hemodynamic response completely without causing unwanted side effects has been found, but dexmedetomidine promises to be a good option.[9,10]

Patients sedated with dexmedetomidine were shown to be easily aroused for procedure compliance, and it may protect against myocardial ischemia and lessen the need for opioid analgesia. Furthermore, in the presence of dexmedetomidine, the dose of induction drugs such as propofol and thiopentone for sedation and anaesthesia induction may need to be lowered. The hemodynamic response to laryngoscopy and intubation is also reduced when dexmedetomidine is given. Comparative studies of different dexmedetomidine dosages in blunting the hemodynamic response have revealed that a greater loading dose of 1 µg/kg is more effective than lesser doses, and have urged for the use of higher doses.[11-16]

However, this advantage may be offset by adverse effects such as hypotension and bradycardia which are likelier to occur with higher dose. A lower dose of 0.5 µg/kg, besides blunting the hemodynamic response, would be safer in terms of having a reduced incidence of adverse effects and being more cost-effective.

Our study was conceptualized to evaluate and compare the effects of two different doses of dexmedetomidine, i.e. 1 µg/kg and 0.5 µg/kg not only for attenuation of hemodynamic response to laryngoscopy & intubation but also for achieving better intubating conditions.

Materials and Methods

This study was conducted in a tertiary care teaching hospital over a period of 6 months. Informed written consent was obtained from 120 patients between the ages of 18 and 65 years categorized as physical status Class I and II according to American Society of Anesthesiologists(ASA), scheduled to undergo endotracheal intubation and general anesthesia for elective surgery.

Exclusion criteria: Patients with age 65 years or with the previous history of difficult or failed intubation, physical characteristics suggesting difficult intubation – Mallampatti Grade III and IV, body mass index >30, history of uncontrolled hypertension, cardiovascular disorders, and pregnant patients were excluded from the study.

A preanesthetic checkup of all included patients was conducted 1 day before the surgery which included a detailed history, a thorough physical examination, and both general and systemic with basic/relevant investigations. Patients were randomly assigned using a computer-generated block randomization schedule, to compose three groups of thirty patients each.

a) Group I received loading dose of 1 µg/kg body weight of dexmedetomidine in 10 ml saline over 10 min intravenously before induction
b) Group II received a loading dose of 0.5 µg/kg body weight of dexmedetomidine in 10 ml saline over 10 min intravenously before induction
c) Group III: Control group received normal saline 10 ml bolus before induction over 10 min intravenously before induction.

The patient as well as the anesthesiologist performing intubation was not aware of the group to which the patient belonged and the study drug was prepared by an anesthesiologist who was not participating in the study. Hence, our study was double-blinded. However, in case of any adverse event related to the study drug, the anesthesiologist who prepared the drug was authorized to reveal the drug. All patients received premedication with pantoprazole 40 mg perorally, a proton-pump inhibitor for acid prophylaxis and Alprazolam 0.25 mg, a benzodiazepine for anxiolysis perorally on the eve of surgery. All the patients were kept fasting overnight for 8 h.

On the day of surgery, all the patients (n = 120) included in the study were started with Ringer's lactate infusion at the rate of 60 ml/h. Subsequently, injection fentanyl (a potent synthetic opioid analgesic with a short duration of action) in the dose of 1 µg/kg body weight, followed by injection ondansetron (a serotonin 5HT3 receptor antagonist for the prevention of postoperative nausea and vomiting) in the dose of 0.1 mg/kg body weight was administered intravenously. Following this, study drug was infused intravenously over a period of 10 min, and all the patients were preoxygenated during this time using a face mask. As soon as the study drug infusion was over, the induction of anesthesia began with 1% propofol intravenously at the rate of 0.5 ml/s which continued till the patient's verbal response was abolished. The dose of propofol required for abolishing this response was noted after which neuromuscular blockade was achieved with injection rocuronium administered intravenously in the dose of 0.9 mg/kg body weight. Subsequently, endotracheal intubation was attempted after 90 s. While intubation was performed, all patients were assessed for five variables – face mask ventilation, jaw relaxation, positioning of vocal cords, movement of vocal cords on intubation, and reflex movement on tracheal intubation. Baseline electrocardiography, heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), and oxygen saturation (SPO2) were recorded at the time of starting study drug and then after every 2 min till intubation.

Subsequently, vitals were recorded at 2, 5, and 10 min after intubation. Any variation in BP and HR was recorded. Hypotension (reduction in arterial pressure of 20% or more from baseline) was noted and planned to be treated primarily by increasing the intravenous (IV) infusion rate and was followed by 10 mg bolus dose of ephedrine (a sympathomimetic amine) as per requirement. Hypertension (increase in arterial pressure 20% or more from baseline) was treated by deepening the level of anesthesia with inhalational anesthetic agent isoflurane. Bradycardia (HR 100 beats/min or 20% increase from baseline) was planned to be treated by injection esmolol 0.2 mg/kg an ultra-short acting cardioselective β1 receptor blocker.

Other side effects such as erythema, allergic reactions, or arrhythmias were also evaluated and dealt with accordingly. Anesthesia was maintained with oxygen, nitrous oxide, and halothane. Top-up doses of rocuronium were also given for maintenance. At the end of surgery, the neuromuscular blocking agent was antagonized with a combination of neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. Patients were transferred to postanesthesia care unit after the completion of surgery. All the observations made in the study were recorded and compared for each parameter at different intervals as per protocol. All the data were analyzed and subjected to statistical analysis for significance. Nonparametric data were compared using the Chi-square test and parametric data were compared using Student's t-test using SPSS 16.0 software. $P < 0.05$ was considered statistically significant.

Results

The three groups were comparable with respect to age, sex, and ASA status. The various parameters such as HR, SBP, DBP, MAP, and SPO2 were noted during the infusion of study drug after laryngoscopy and intubation. The conditions during intubation such as ease of mask ventilation, jaw relaxation, position of vocal cords and reflex movement on intubation, and dose of propofol required to abolish the verbal response during intubation were recorded.

During the infusion of loading dose of 1µg/kg dexmedetomidine given in an infusion over 10 min, the HR showed a 20.05 % decline as compared to the control. The comparison was statistically highly significant ($P < 0.01$) with the control group. When a loading dose of 0.5 µg/kg of dexmedetomidine was given in an infusion, an 8.45% fall of HR was seen. This comparison was also found to be significant ($P < 0.01$) as compared to the control. The DBP showed a fall of 20.15 % fall when 1 µg/kg dexmedetomidine was given ($P < 0.01$) and 8.55% when 0.5 µg/kg was given ($P < 0.01$) whereas Dexmedetomidine did not have any significant effect on SBP and MBP. [Figure-1].

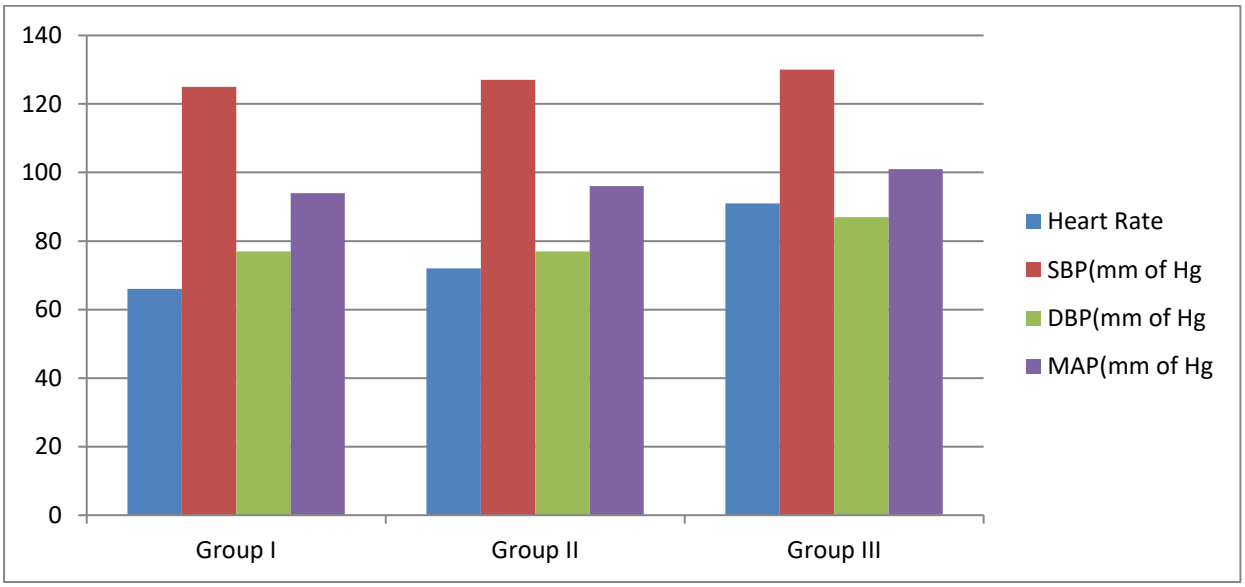

Figure-1: Distribution of various hemodynamic variables in different groups

Following laryngoscopy and intubation, there was a fall of 11.25% ($P < 0.01$) and 7.25% ($P < 0.01$) in the HR with 1 µg/kg and 0.5 µg/kg dexmedetomidine, respectively. The SBP, DBP, and MBP also showed a significant decline with both the doses of dexmedetomidine ($P < 0.01$) when compared to the control group. It was seen that the SPO2 was unaffected during the infusion of the study drug as well as following laryngoscopy and intubation.

Variables		Group I		Group II		Group III		P Value
		n	%	n	%	n	%	
Mask Ventilation	Easy	37	92.5	36	90	35	87.5	0.75
	Difficult	3	7.5	4	10	5	12.5	
Jaw Relaxation	Relaxed	40	100	38	95	36	90	0.12
	Not Relaxed	0	0	2	5	4	10	
Vocal cord Position	Para-Med	39	97.5	36	90	34	85	0.14
	Moving	1	2.5	4	10	6	15	
Movement of Vocal Cord	Nil	39	97.5	40	100	35	87.5	0.02
	Yes	1	2.5	0	0	5	12.5	
Relax movement on intubation	Yes	5	12.5	6	15	10	25	0.29
	Nil	35	87.5	34	85	30	75	
Side effects	Hypotension	1	2.5	0	0	0	0	0.22
	Bradycardia	3	7.5	1	2.5	0	0	
	Nil	36	90	39	97.5	40	100	
Total		40	100	40	100	40	100	

Table-1: Distribution of various responses in different groups

The comparison of variables of mask ventilation showed that mask ventilation was easy in 37 (92.5%) patients of Group I as compared to 36 (90%) patients of Group II and 35 (87.5%) patients III. The comparison was statistically not significant (P =0.75). During the study, jaw was found to be relaxed in all patients receiving 1 µg/kg dose and 38 (95%) patients receiving 0.5 µg/kg dose as compared to 36 (90.00%) patients in the control group (P =0.12) . Position of vocal cords was significantly affected by dexmedetomidine infusion, being paramedian in 39 (97.5%), 36 (90.00%), and 34 (85.0%) patients in each group, respectively (P =0.14). Furthermore, reflex movement of vocal cords was seen in only 1 (2.5%) patient of Group I as compared to none of the patients of Group II and 5 (12.5%) patients of Group III (P =0.02). Five (12.5%), 6 (15.0%), and 10 (25.0%) patients, respectively, of Group I, II, and III showed reflex limb movement during laryngoscopy and intubation or immediately following it (P =0.29). Side effects such as hypotension were seen in 1 (2.5%) patient in Group I compared to none of the patients in the other two groups. Another side effect encountered was bradycardia seen in 3 (7.5%) patients in Group I and 1 (2.5%) patient in Group II and none in Group III, respectively(P =0.22). [Table-1]

Discussion

Intubation of the trachea causes catecholamine release and a pressor reaction, which causes an increase in heart rate and blood pressure. Dexmedetomidine has been used to decrease this reaction and reduce the dose of anaesthetic agent in a number of previous studies.[15-20] With the use of dexmedetomidine, the hemodynamic response was greatly reduced but not totally eliminated in our study. Dexmedetomidine's impact on postsynaptic α2 receptors in the locus coeruleus and activation of the endogenous sleep-promoting pathway could explain this effect. This impact is especially beneficial in patients with cerebrovascular disease, cardiovascular disease, and hypertension.

Sağıroğlu et al[16] in their comparative studies of two different doses of dexmedetomidine reported that a dose of 1.0 µg/kg was more effective than a dose of 0.5 µg/kg in blunting the hemodynamic response to laryngoscopy and intubation. In our study, the hemodynamic response was sufficiently blunted with both the doses of dexmedetomidine. HR and blood

pressure remained stable and showed an increase not >20%. In a meta-analysis of assessment of dexmedetomidine as an anesthetic agent by Piao and Wu et al[21] the occurrence of adverse effects such as hypotension and bradycardia with dexmedetomidine was found to be higher as compared to controls. Khan et al[22] in their comparative study of 1.0 µg/kg and 0.5 µg/kg doses of dexmedetomidine, reported a higher incidence of hypotension and bradycardia with the use of higher dose of the drug. The administration of a lower dose was linked to a decreased occurrence of both of these side effects in our study. Given that both low and high dosages are effective at blunting the hemodynamic response, the relative safety of the lower dose in terms of these side effects appears to give a clear clinical advantage, particularly in patients with low blood volume and heart block. The anesthesiologist had better intubating conditions in our trial, with improved mask ventilation and jaw relaxation. When dexmedetomidine was given as an adjuvant with propofol, the position of the vocal cords was likewise suitable for intubation, with minimal movement of the vocal cords and limbs. These effects were achieved equally well with dosages of 1 µg/kg and 0.5 µg/kg.

Conclusions

Dexmedetomidine used as an infusion in the loading dose of 0.5 µg/kg is therapeutically as effective as when used in the dose of 1.0 µg/kg in providing good intubating conditions and blunting the hemodynamic response to intubation for better anaesthetic results. A smaller dose is not only more cost-effective, but it also avoids adverse effects including hypotension and bradycardia, which are common with the greater dose of 1 µg/kg dexmedetomidine infusion.

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