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Anaesthesiology

Dexmedetomidine, the ideal drug for attenuating hemodynamic response to laryngoscopy and endotracheal intubation.

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ABSTRACT

AIM OF THE STUDY: To evaluate the efficacy of Dexmedetomidine in the dose of 0.6µg/kg body weight in attenuation of the hemodynamic response to laryngoscopy and endotracheal intubation.

MATERIALS AND METHODS: 100 normotensive patients aged 18-50 years old were assigned randomly into two groups control group C and Dexmedetomidine group D. 10 min before induction these two groups received, group C (n=50): received 10 ml normal saline (NS) IV over 10 min, group D (n=50): received dexmedetomidine 0.6µg/kg body weight diluted to 10 ml NS IV over 10 min. After induction of anesthesia, HR, SBP, DBP and MAP were recorded at various time intervals 2^{nd},5^{th},8^{th} min before induction and 1^{st}, 3^{rd}, 5^{th} and 10^{th} min after intubation.

RESULTS: It was found that in control group there was a significant rise in hemodynamic parameters heart rate(HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure in response to laryngoscopy and endotracheal intubation. There was significant attenuation of hemodynamic response to laryngoscopy and endotracheal intubation in study group who received Dexmedetomidine 0.6 µg/kg body weight 10 minutes before induction ($p<0.05$). In addition, dexmedetomidine reduced the requirement of thiopentone and produced arousable sedation after extubation without any side effects like bradycardia and hypotension ($p<0.05$).

CONCLUSION: Dexmedetomidine (0.6µg/kg) IV given 10 min before induction was seen to effectively attenuate the hemodynamic response to laryngoscopy and tracheal intubation without any side effect.

KEYWORDS : Dexmedetomidine, Laryngoscopy, Tracheal intubation, Hemodynamic response,

INTRODUCTION

Laryngoscopy and tracheal intubation in adults are commonly accompanied by increase in arterial blood pressure and heart rate.[1] The magnitude of hemodynamic changes observed may be dependent on various factors such as depth of anesthesia, whether any measures are taken prior to airway manipulation, the anesthetic agent used, the duration of laryngoscopy and intubation. To date, the exact mechanism of hemodynamic responses to laryngoscopy and intubation has not been clarified. The principle mechanism in hypertension and tachycardia is the sympathetic response[2, 3] which may be the result of increase in catecholamine activity.[4] The increase in the pulse rate and blood pressure are usually transitory, variable and unpredictable. Transitory hypertension and tachycardia are probably of no consequence in healthy individuals but either or both may be hazardous to those with hypertension, myocardial insufficiency or cerebrovascular diseases.[4] This laryngoscopic reaction in such individuals may predispose to development of pulmonary edema, myocardial insufficiency and cerebrovascular accident.[5,6]

Pressor response is exaggerated in hypertensive patients even though rendered normotensive pre-operatively by antihypertensive medication.[7] Pressor response may result in intra-operative myocardial infarction,[8] acute left ventricular failure,[8] dysrrhythmias[9] and intracranial bleed[8] in individuals with end organ decompensation. Intravenous anesthetic induction agents do not adequately or predictably suppress the circulatory responses evolved by endotracheal intubation.[10] So prior to initiating laryngoscopy, additional pharmacological measures like use of volatile anesthetics, topical and intravenous lidocaine, opioids, vasodilators – Sodium nitroprusside, Nitroglycerine, Calcium channel blockers and β-blockers have been tried by various authors. Besides minimizing the cardiovascular response, anesthesia induction for patients at risk must also satisfy the following requirements i.e. it must be applicable regardless of patients group, prevent impairment of cerebral blood flow and avoid awareness of the patient. It should neither be time consuming nor affect the duration or modality of the ensuing anesthesia and should not have any effect on the recovery. None of these drugs mentioned above have been found to be effective in attenuating the pressor response to intubation. Hence there is a need of find out the drug which can attenuate pressor response. α2 agonists is being used for attenuating the pressor response[11] and among α2 agonists both clonidine and dexmedetomidine appear to fulfill all the above criteria. Both clonidine and dexmedetomidine have actions on both α1 and α2 receptors but dexmedetomidine is highly specific and selective α2 adrenoceptor agonist with α2: α1 binding selectivity ratio of 1620:1 compared to 220:1 for clonidine.[12] The advantage of intravenous dexmedetomidine as premedicant in anesthesia includes sedation, analgesia, anxiolysis and improved hemodynamic stability. Because of these beneficial properties, it has been found that the minimum alveolar concentration (MAC) of volatile anesthetics also decreases significantly up to 90% and hence decreases the requirement of anesthetic agents.[13,1]

AIMS AND OBJECTIVES

1. To study changes in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure associated with laryngoscopy and intubation.
2. To evaluate the efficacy of intravenous Dexmedetomidine in the dose of 0.6µg/kg body weight in attenuating the hemodynamic responses to laryngoscopy and endotracheal intubation.
3. To study the effects of Dexmedetomidine on the dose requirement of thiopentone sodium for induction of anesthesia.
4. To study any adverse effects associated with Dexmedetomidine

MATERIALS AND METHODS

After obtaining ethical committee clearance as well as informed consent from all patients, 100 patients, scheduled for various elective surgical procedures belonging to ASA grade I and II of both the sex were included in the study. The patients were normotensive with age varying from18 to 50. Patients with cardiac, coronary, renal, hepatic, cerebral, peripheral vascular diseases, hypertension, heart blocks, difficult airway and obese patients (BMI>30) and endocrinal diseases like hyperthyroidism, hypothyroidism, diabetes mellitus were excluded from the study. The patients were randomly allocated into two groups with 50 patients in each group. 10 min prior to induction, group C - Control group (n=50): received 10 ml of NS IV over 10 min using syringe pump, group D - Dexmedetomidine (n=50): received injection dexmedetomidine 0.6µg/kg body wt. diluted to 10 ml NS IV over 10 min using syringe pump. Pre-anaesthetic evaluation was done for all the patients and routine investigations like complete blood count, blood grouping and typing, complete Urine examination, electrocardiogram, chest x ray blood sugar urea serum creatinine of all the patients were done. All patients included in the study were pre-medicated with tablet Alprazolam 0.5 mg and tablet Ranitidine 150 mg orally at bed time the previous night before surgery. They were kept nil orally 10 pm onwards on the previous night.

On arrival of the patient in the pre-operating room, an 18-gauge

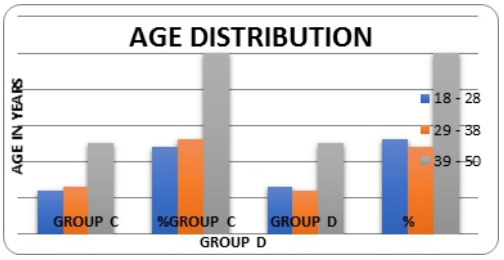
intravenous cannula was inserted and an infusion of ringer lactate was started. The patients were connected to multiparameter monitor with HR, non-invasive measurements of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), end tidal carbon dioxide (EtCO2) and continuous ECG monitoring and oxygen saturation. After recording the baseline reading, 10 min before induction, patients in group D received dexmedetomidine 0.6µg/kg body wt. diluted in 10 ml NS IV over 10 min using syringe pump and patients in group C received 10 ml NS IV using syringe pump. The study drug was prepared by the anaesthesiologist who was blinded with the study. A solution of 5 µg/ml of dexmedetomidine was prepared. Depending on the body wt., volume of the diluted drug in saline or NS was infused through a syringe pump. All the patients were premedicated with Inj glycopyrrolate 0.008mg/kg body weight, injection. midazolam 0.02mg/kg body weight and injection fentanyl 1µ/kg body weight IV after test drug administration. Patients were preoxygenated with 100 % for 3 min. ninety seconds before intubation all patients received IV lignocaine 1.5mg/kg body weight. Patients were induced with thiopentone 5 mg/ kg, as a 2.5% solution till loss of eye lash reflex occurred and dose of thiopentone required for loss of eye lash reflex recorded. Endotracheal intubation was facilitated with injection vecuronium 0.1mg /kg IV. Laryngoscopy was performed using Macintosh blade lasting for not more than 15 seconds and intubation with portex endotracheal tube (ETT), after confirmation of bilateral equal air entry, ETT was fixed. If time for laryngoscopy and intubation exceeded for 15 seconds, such patients are excluded from the study. Anaesthesia was maintained with intermittent positive pressure ventilation with 66% nitrous oxide and 33% of oxygen and sevoflurane 1 %, vecuronium using circle absorber system connected to Boyle's machine. After the patients recovered from loading dose of vecuronium further neuromuscular blockade was maintained with vecuronium 0.02 mg/ kg body weight. No surgical or any other stimulus was applied during 10 minutes of study period and vecuronium was the only additional drug given during this 10 minutes' period. At the end of the procedure patients were reversed with injection Neostigmine 0.05 mg/kg body weight and injection glycopyrrolate 0.01 mg/ kg body weight. Sedation at the end of the surgery was assessed using Ramsay sedation score. Vital parameters like HR, SBP, DBP and MBP were recorded before induction, after induction and 1, 3, 5 and 10 min after laryngoscopy and intubation. Hypotension was defined as SBP ≤ 20% of baseline value. Tachycardia was defined as HR > 25% of baseline value. Bradycardia was defined as HR < 20% of base and dysrhythmia was defined as any rhythm other than sinus. Incidences of all these parameters were recorded in both the groups. The side effects of the study drug like hypotension, bradycardia and sedation were noted.

STATISTICALANALYSIS

The sample size was determined by power analysis performed by a pilot study. A sample size of 50 patients per group was required to detect a 20% change in heart rate, blood pressure and pulmonary artery pressure between baseline and intubation time, with a power of 80% at the 5% significance level. Data are expressed as the mean± standard deviation. Independent t-test was used to compare the study group and the control group. Paired t-test was used to compare the variable before and after the intervention. Chi-square test was used to analyze the categorical data and for testing the association between the variables. Nonparametric tests (Wilcoxon signed rank tests [two tailed]) were used whenever the mean value was less than two times the standard deviation. ANOVA was used to measure the related variable that represent different measurements of the same attribute. A P value of less than 0.05 was considered statistically significant. The package SPSS 17.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

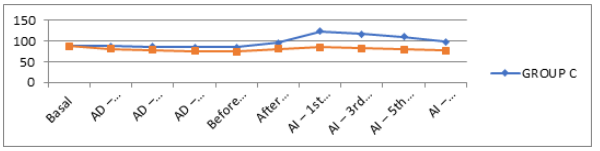
OBSERVATION

The groups were well-matched for their demographic data (Graph 1).



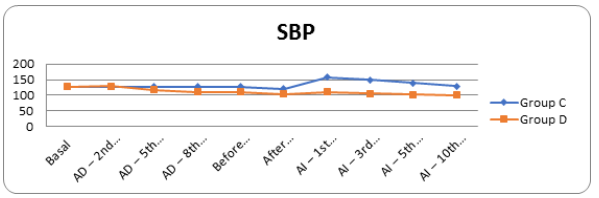
Graph1: shows age distribution of the patients in both the groups.

The basal heart rate was comparable in both groups (p=1.000). Statistical evaluation between the groups showed a significant fall in HR in group D at 2, 5 and 8 minutes of drug administration and before and after induction. The mean HR increase observed at 1, 3, 5 and 10 minutes after intubation in group C was statistically highly significant compared to mean HR in group D (p=0.000). (Graph 2)



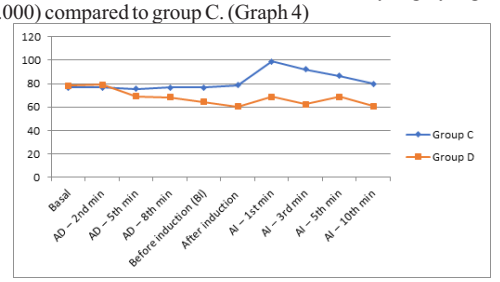
Graph 2: Showing the intergroup comparison of mean heart rate (bpm) changes in response to laryngoscopy and intubation between Control group and Dexmedetomidine group

The mean SBP were comparable in both groups (p=0.734). After 2 min of drug administration the change in SBP was not significant (0.456). The mean SBP values at 5 and 8 minutes of drug administration, before and after induction were significantly low (p=0.000) compared to group C. The increase in SBP in group C at 1, 3, 5 and 10 minutes after intubation was statistically highly significant (p=0.000) compared to group D. (Graph 3)



Graph 3 Showing comparison of systolic blood pressure (SBP in mmHg) changes between Control group and Dexmedetomidine group

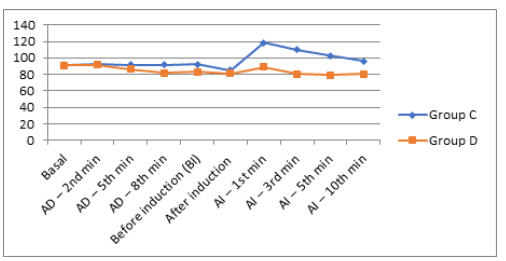
The mean basal DBP are comparable in both groups (p=0.223). The mean DBP, 2 min after drug administration was statistically not significant (p=0.674). The mean DBP values at 5 and 8 minutes of drug administration, before and after induction were significantly low (p=0.000) compared to group C. The increase in DBP in group C at 1, 3, 5 and 10 minutes after intubation was statistically highly significant (p=0.000) compared to group C. (Graph 4)



Graph 4: Showing comparison of diastolic blood pressure (DBP in mmHg) changes between Control and Dexmedetomidine group. AI-After intubation

The mean basal MBP are comparable in both groups (p=1.000). After 2 min of drug administration the change in MBP was statistically not significant (p=0.812).

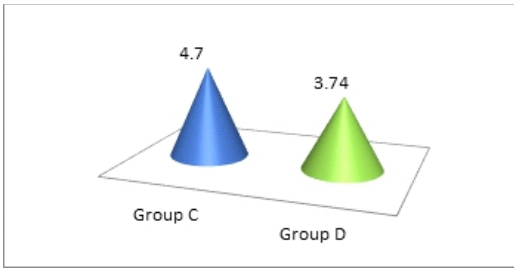
There was a significant difference in MBP values at 5th min, 8th min after drug administration and before and after induction which was statistically highly significant (p=0.000). The increase in MBP in group C was statistically highly significant at 1 min and 3, 5 and 10 minutes after intubation (p=0.000) compared to group C. (graph 5)



Graph 5: Showing comparison of mean blood pressure (MAP in mmHg) changes between Control and Dexmedetomidine group. AI- - After intubation

Table 1. Showing the dose of thiopentone required for induction in Control and Dexmedetomidine group. (p<0.01)- Highly significant (HS); (p<0.05)- Significant (S); (p>0.05) -Not significant (NS

	Mean Dose of thiopentone required for induction(mg)
Group C	278±34.49
Group D	170.5±30.17
p-value	0.000 (HS)



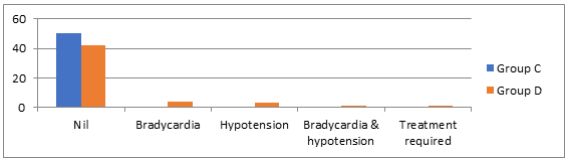
Graph 6: Showing the total dose of vecuronium bromide required for muscle relaxationin Control and Dexmedetomidine group. (p<0.01)- Highly significant (HS); (p<0.05)- Significant (S); (p>0.05) -Not significant (NS*)*

In group C sedation score was 2.62±0.49 and in group D the score was 2.52±0.43. Statistical evaluation showed no difference in the sedation score between the two groups.

Table 2. Showing the sedation score between Control and Dexmedetomidine group. (p<0.01)- Highly significant (HS); (p<0.05)- Significant (S); (p>0.05) -Not significant (NS)

	Sedation score
Group C	2.62±0.49
Group D	2.52±0.43
p-value	0.087 (NS)

4 patients had bradycardia, 3 had hypotension and one patient had both bradycardia and hypotension in dexmedetomidine group which did not need any treatment, while none with control (Graph 7)



Graph 7 Showing the side effects between Control and Dexmedetomidine group. (p<0.01)- Highly significant (HS); (p<0.05)- Significant (S);(p>0.05) -Not significant (NS)

HR values were statistically significantly lower in the dexmedetomidine group at all time intervals when compared with the control group. There was a statistical significance in the systolic arterial pressure, mean arterial pressure and diastolic arterial pressure between groups after drug at the 1st, 3rd, 5th and 8th min post intubation. The dexmedetomidine group had a better control of heart rate and blood pressure than the control group.

Statistical evaluation between the groups showed a statistically highly significant reduction in dose of thiopentone sodium required for induction (p=0.000) (Table 1), reduction in dose of vecuronium bromide for muscle relaxation (p=0.000) (Graph 6). Sedation score between the two groups was not significant (Table 2).

DISCUSSION

Laryngoscopy and endotracheal intubation are considered as the most critical events during general anaesthesia. They provoke a transient, but marked, sympathetic and sympathoadrenal response. But in patients with cardiovascular compromise like hypertension, ischemic heart disease, and cerebrovascular disease and in patients with intracranial aneurysms, even these transient changes in haemodynamic can result in potentially harmful effects like left ventricular failure,[8] pulmonary edema, myocardial ischemia,[8] ventricular dysrhythmias[9] and cerebral haemorrhage. α2 adrenergic drugs, such as clonidine or dexmedetomidine, attenuate these potentially harmful cardiovascular reactions during induction of anaesthesia. In our study, we compared dexmedetomidine, a newer α2 agonist, with additional properties such as sedation, anxiolysis and sympatholysis for attenuating the hemodynamic response to laryngoscopy and tracheal intubation. Dexmedetomidine offers a unique pharmacological profile with sedation, sympatholysis, analgesia, cardiovascular stability and with great advantage to avoid respiratory depression. Interaction with the patient. All these above-said aspects of its pharmacological profile render it suitable as an anaesthetic adjuvant and as intensive care unit sedation. Dexmedetomidine increases the hemodynamic stability by altering the stress induced sympathoadrenal responses to intubation during surgery and during emergence from anesthesia.[14] Jaakola et al.,[15] in their study concluded that dexmedetomidine attenuates the increase in heart rate and blood pressure during intubation. The dose used for this study was like the dose used by us. Scheinin et al., [16] studied the effect of dexmedetomidine on tracheal intubation, required dose of induction agent and preoperative analgesic requirements. They concluded that the required dose of thiopentone was significantly lower in the dexmedetomidine group and the drug attenuated the hemodynamic responses to intubation. The concentration of noradrenaline in mixed venous plasma was lesser in the dexmedetomidine group. Lawrence et al., [17] found that a single dose of 2 µg/kg of dexmedetomidine before induction of anaesthesia attenuated the hemodynamic response to intubation as well as that to extubation. Bradycardia was observed at the 1st and 5th min after administration. This might have been due to bolus administration. Sulaiman, et al.[21] studied the effects of dexmedetomidine on attenuation of stress response to endotracheal intubation in patients undergoing elective off pump coronary artery bypass grafting (CABG), they concluded that pre-treatment with dexmedetomidine at a dose of 0.5 µg/kg as 10 min infusion prior to induction of anaesthesia attenuate the hemodynamic response to laryngoscopy and intubation. Dexmedetomidine can be considered before induction of general anaesthesia in patients undergoing myocardial revascularization, even if the patients are receiving beta blockers. It is a well-known fact that depression of sympathetic response against laryngoscopy and intubation is an dexmedetomidine can provide a dose dependent cooperative sedation that allows ready important advantage, especially in high risk patients. The hypotension and bradycardia caused by dexmedetomidine, theoretically, could limit its usage in previously beta blocked ischemia heart patients. Few studies used dexmedetomidine as an anaesthetic adjuvant in CABG patients receiving beta blockers, and reported that the intraoperative incidence of bradycardia requiring treatment was not more common in the dexmedetomidine group than in the control group.[17,18] A biphasic cardiovascular response has been described after the administration of dexmedetomidine.[19] A bolus of 1 µg/kg results in a transient increase in arterial blood pressure and reflex decrease in heart rate in young healthy patients. Initial response is due to α2 receptor stimulation of vascular smooth muscle. This response can be markedly decreased by slow infusion over 10 min. In our study, this effect was not noticed due to the slow infusion of the drug over 10 min. Studies suggest that perioperative use of dexmedetomidine may result in a decreased risk of adverse cardiac events, including myocardial ischemia.20 α adrenoreceptors stimulation can beneficially modulate coronary blood flow during myocardial ischemia by preventing transmural redistribution of blood flow away from the ischemic endocardium, by specific epicardial vasoconstrictive effects, leading to improvement in endocardial perfusion (the reverse steal effect) and by decreasing heart rate. This property along with hemodynamic stability and attenuation of intubation response makes dexmedetomidine an ideal anaesthetic adjuvant, particularly for patients undergoing coronary bypass grafting. In Dexmedetomidine group, 4 patients developed bradycardia which was after 30 minutes of the drug administration and significant hypotension in 3 patients which was 20 minutes after intubation. The limitations regarding this study are that we did not measure the plasma norepinephrine levels and extubation response was not studied.

CONCLUSION

Dexmedetomidine at a dose of 0.6µg/kg in 10 ml NS, given 10 min before induction significantly obtunds the hemodynamic response to laryngoscopy and tracheal intubation in adult. It also decreases the requirement of induction dose of thiopentone and the requirement of

the total dose of vecuronium bromide for muscle relaxation without significant side effects.

REFERENCES

1. Reid, Brace: Irritation of respiratory tract and its reflex effect on heart-Surgery Gynaecology Obstetrics. 1940; 70:157.
2. Kayhan Z, Aldemir D, Metler H, Ogus E. Which is responsible for the haemodynamic response due to the laryngoscopy and endotracheal intubation? Catecholamines, vasopressin or angiotensin? European Journal of Anaesthesiology 2005; 22:7805.
3. Morin AM, Gelbner G, Schwarz U, Kahl M, Adams HA, Hulf H, et al. Factors influencing pre-operative stress responses in coronary artery bypass graft patients. BMC Anaesthesiology 2004; 4(7).
4. Kovac AL. Controlling the haemodynamic response to laryngoscopy and endotracheal intubation. Journal of Clinical Anaesthesia 1996; 8:63-79.
5. Prys-Roberts C, Green LT, Meloche R, Foex P. Studies of anaesthesia in relation to hypertension II. Haemodynamic consequences of induction and endotracheal intubation. Br J Anaesth 1971; 43:531-47.
6. Dalton B, Guiney T. Myocardial ischemia from tachycardia and hypertension in coronary heart disease – Patients undergoing anaesthesia. Boston: Ann Mtg American Society of Anaesthesiologists; 1972. pp. 201-2.
7. Cedric Preys Roberts. Anaesthesia and hypertension. Br J Anaesth 1984; 56:711-24.
8. Fox EJ, Sklar GS, Hill CH, Villanue Var, King BD. Complications related to the pressor response to endotracheal intubation. Anaesthesiology. 1977; 47:524-5.
9. Ronald D Miller. Miller's Anesthesia volume 2 Seventh edition 2010.
10. Stoelting RK, Stephan F Dierdorf. Anaesthesia and co-existing disease. 4th ed. 2002.
11. Kulka PJ, Tryba M, Zenz M. Dose response effects of intravenous clonidine on stress response during induction of anaesthesia in coronary artery bypass graft patients. Anaesth Analg 1995; 80:263-8.
12. Ralph Getler, Clieghton H Brown, Mitchel H, Silvius N. Dexmedetomidine: a novel sedative analgesic agent. Baylor University Medical Centre Proceedings. 2001; 14(1).
13. Aho M, Lehtnen AM, Erkola O, Scheinin H, Lehtinen A, Kallio A, et al. The effect of intravenously administered dexmedetomidine on perioperative haemodynamics and isoflurane requirements in patients undergoing abdominal hysterectomy. Anaesthesiology 1991; 74:997-1002.
14. Scheinin B, Lindgren L, Randell T, Scheinin H, Scheinin M. Dexmedetomidine attenuates sympatoadrenal responses to tracheal intubation and reduces the need for thiopentone and peroperative fentanyl. Br J Anaesth 1992; 68:126-31.
15. Jaakola ML, Ali-Melkkila T, Kanto J, Kallio A, Scheinin H, Scheinin M. Dexmedetomidine reduces intraocular pressure, intubation responses, and anaesthetic requirements in patients undergoing ophthalmic surgery. Br J Anaesth 1992; 68:570-5.
16. Lawrence CJ, De Lange S. Effects of a single pre-operative dexmedetomidine dose on isoflurane requirements and peri-operative haemodynamics stability. Anaesthesia 1997; 52:736-44.
17. Menda F, Köner O, Sayin M, Türe H, Imer P, Aykaç B. Dexmedetomidine as an adjuvant to anesthetic induction to attenuate hemodynamic response to endotracheal intubation in patients undergoing fast tract CABG. Ann Card Anaesth 2010; 13:16-21.
18. Jalonen J, Hynynen M, Kuitunen A, Heikkilä H, Perttilä J, Salmenperä M, et al. Dexmedetomidine as an anesthetic adjuvant in coronary artery bypass grafting. Anesthesiology 1997; 86:331-45.
19. Bloor BC, Ward DS, Belleville JP, Maze M. Effects of intravenous dexmedetomidine in humans. II. Haemodynamic changes. Anaesthesiology 1992:77; 1134-42.
20. Talke P, Li J, Jain U, Leung J, Drasner K, Hollenberg M, et al. Effects of perioperative dexmedetomidine infusion in patients undergoing vascular surgery. The Study of Perioperative Ischemia Research Group. Anaesthesiology 1995; 82:620-33.
21. Sulaiman S, Karthekeyan RB, Vakamudi M, Sundar AS, Ravullapalli H, Gandham R. The effects of dexmedetomidine on attenuation of stress response to endotracheal intubation in patients undergoing elective off-pump coronary artery bypass grafting. Ann Card Anaesth 2012; 15:39-43.