Original Article

Hemodynamic Stability and Analgesic Effects of Intravenous Dexmedetomidine Premedication in Adult Patients Undergoing Coronary Artery Bypass Graft Surgery

Zahra Faritus[1], Ali Sadeghi[1], Mohsen Ziaiifard[1], Manijeh Yousefi Moghaddam[2], Ali Sadeghpour Tabaei[1], Farhad Gorjipour[1]

[1]Rajaei Cardiovascular Medical And Research Center, Iran University of Medical Sciences, Tehran, [2]Department of Anesthesiology, School of Medicine, Sabzevar University of Medical Sciences, Sabzevar, Iran

Abstract

Background: Sternotomy for coronary artery bypass surgery operation is associated with neuropathic pain, hypertension, tachycardia, agitation, and several other complications. In severe cases, the neuropathic pain may result in arrhythmia which is an important concern in cardiopulmonary bypass surgeries. Premedication for reducing the risk of hemodynamic instability, neuropathic pain, and other adverse associated consequences is very important. **Objectives:** We Scrutinized the effects of dexmedetomidine intravenous infusions on hemodynamic parameters and postsurgical pain in coronary artery bypass patients. **Patients and Methods:** A total of 60 coronary artery bypass surgery patients were recruited and were randomly allocated into two groups. 31 patients received placebo, and 29 received 1 μg/kg of dexmedetomidine 10 min before anesthesia and then 0.4 μg/kg/h of dexmedetomidine until the end of the operation. Heart rate, blood pressure, and postsurgical pain score according to the numerical rating scale were measured and recorded after recovery from anesthesia. **Results:** Blood pressure significantly decreased after bolus administration of dexmedetomidine which remained lower at the end of screening in most of the times. No remarkable adverse effects were observed, and its consumption was associated with significant reduction in the postsurgical pain scores as measured in 2, 4, and 6 h after surgery as well as the time of extubation. **Conclusions:** Infusion with 1 μg/kg of dexmedetomidine 10 min before anesthesia and 0.4 μg/kg/h of dexmedetomidine from the time of sternum closure until the extubation time appears to be effective for the maintenance of hemodynamics in coronary artery bypass surgery without remarkable adverse outcomes.

Keywords: Cardiopulmonary bypass, dexmedetomidine, hemodynamics, pain, premedication

Introduction

Coronary artery stenosis and occlusion are common complications of the cardiac arteries in adults and comprise the leading cause of mortality and morbidity worldwide. Pathologies included in the disease onset include atherosclerosis due to a wide variety of genetic or environmental factors.[1-4] Although nonsurgical management approaches are getting popular, coronary artery bypass surgery (CABG) is yet the gold standard of care in high-risk patients such as those with left main, severe 3-vessel, or diffuse disease, severe ventricular dysfunction, or diabetes mellitus.[5] Sternotomy for coronary artery bypass surgery operation is associated with neuropathic pain, hypertension, tachycardia, agitation, and several other complications.[6] Postsurgical pain from visceral, musculoskeletal, or neurogenic origins is common in CABG surgery and its management along with hemodynamic stability maintenance is an important part of anesthesia practice in CABG surgery.[7] Despite the transitional nature of the reaction, severe cases of it can result in cardiac ischemia and arrhythmias. Thus, premedication for prevention of acute postsurgical pain and hemodynamic instabilities is required. The α-2 receptor agonist, dexmedetomidine, is in use for reducing postsurgical pain and related complications in various settings. Intravenous infusion of dexmedetomidine, 1 μg/L of blood concentration

Address for correspondence: Dr. Manijeh Yousefi Moghaddam, Department of Anesthesiology, Rajaei School of Medicine, Sabzevar University of Medical Sciences, Sabzevar, Iran.
E-mail: ymanijeh@gmail.com

Access this article online

Quick Response Code:

Website: http://www.rcvmonline.com/

DOI: 10.4103/rcm.rcm_6_18

How to cite this article: Faritus Z, Sadeghi A, Ziaiifard M, Moghaddam MY, Tabaei AS, Gorjipour F. Hemodynamic stability and analgesic effects of intravenous dexmedetomidine premedication in adult patients undergoing coronary artery bypass graft surgery. Res Cardiovasc Med 2018;7:87-91.

of the drug, has been revealed to transiently elevate the mean arterial blood pressure (MAP) and systemic vascular resistance through α-1 and β-2 receptor's activity stimulation in the cells of the vascular muscle. Therefore, it has been used along with anesthetics on anesthesia induction to antagonize the hypotensive action of vasodilatory anesthetics.[8] It ameliorates the sympathetic reactions to laryngoscopy, intubation, surgical incision and sternotomy through sympatholytic actions and reducing the release of norepinephrine. During the surgery, it inhibits the release of epinephrine, reduces the heart rate and blood pressure, and improves the endocardial perfusion which, in turn, lowers the myocardial oxygen consumption.[8-10] Furthermore, dexmedetomidine induces the release of substance-P from posterior gray column of the spinal cord and prevents analgesia without respiratory depression making it a good option for use as an agent to induce analgesia and sedation without respiratory depression, disorientation, confusion, lethargy, and delay of the extubation time in the Intensive Care Unit (ICU). We have revealed anxiolytic properties of pretreatment with dexmedetomidine in children.[10] It is now well established that α-2 agonists ameliorate postoperative cardiovascular complications, including hemodynamic alterations and sympathetic adverse reactions.[11] Dexmedetomidine administration has been proved to reduce mortality and the incidence of myocardial ischemia in adult cardiac surgery practice.[12] Since administration of vasodilators is presumably effective in preventing postsurgical high blood pressure, we speculated that administration of dexmedetomidine, as an α-2 agonist,[13] would be beneficial in postoperative hemodynamic stabilization and pain control after CABG in adults in our setting.

Objectives

In the present study, we investigated the hemodynamic alterations and analgesic effects of intravenous dexmedetomidine (1 μg/kg of intravenous infusion of dexmedetomidine for 10 min and then maintenance dose of 0.5 μg/kg/h until the end of operation) in adult patients undergoing CABG.

Patients and Methods

Study design

Sixty patients indicated for elective coronary artery bypass surgery were recruited in this randomized controlled double-blinded trial. The flow of the study according to the Consolidated Standards of Reporting Trials (CONSORT) is depicted in Figure 1. Patients were randomly allocated into two groups: one group was set as control and the second group received dexmedetomidine. Simple randomization was performed using MS Excel software (Microsoft Inc., Washington, United States) as previously described.[14] In brief, each patient received a value between 0 and 1 using MS Excel (randbetween) function. Patients receiving a score above 0.5 were assigned to the control group, and those receiving values below or equal to this score were assigned into the treatment group. Patients over 20 years old indicated for elective coronary artery bypass surgery with the laryngeal view grade from 1 to 3 according to the American Society of Anesthesiologists guidelines on the management of the difficult airway[15] were included in this study. Patients suffering from liver or renal dysfunction, metabolic disorders and left bundle branch block were excluded from the study. Furthermore, patients indicated for emergency surgical operation, history of opioids addiction or drug sensitivity or seizures, smokers, and patients with ejection fraction below 35% were excluded from the study. The study protocol was approved by the Institutional Review Board of the Rajaei Cardiovascular Medical and Research Center with the registration number of 92/1. Protocol of the study was in compliance with Helsinki Declaration on ethical principles for medical research involving human subjects.[16]

Patients in the dexmedetomidine group received a bolus dose of 1 μg/kg of intravenous infusion of Precedex (Hospira, Inc., Illinois, United States) for 10 min and then, maintenance dose (0.4 μg/kg/h) was used until the end of operation. The control group received normal saline in a similar volume and timing of administration as placebo. The study was performed in double-blinded manner. The outcome assessor physician and nurse as well as the patient were not aware of the allocation group for blinding purpose. Then, anesthesia was induced in patients of either of two groups by administration of 0.15–0.2 mg/kg of midazolam, 5 μg/kg phentanyl and 0.1 mg/kg Pavulon (Merck and Co., Inc., New Jersey, United States) and 1 mg/kg of lidocaine. Visual analog scale was used for assessment of severity of pain on 2, 4, and 6 h after transfer to ICU as well as the time of extubation.[17] Hemodynamic parameters were measured and recorded at the time of admission to the operation room (T0), after bolus administration of dexmedetomidine (T1), after anesthesia induction (T2), 1 min after intubation (T3), after incision (T4),

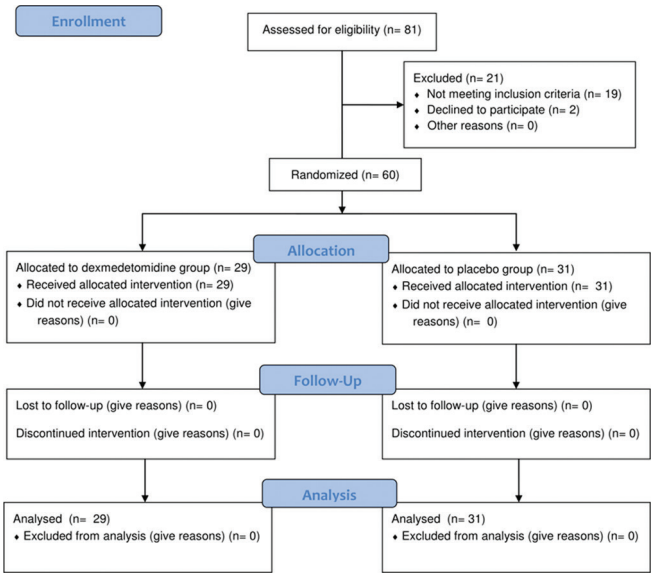

Figure 1: The Consolidated Standards of Reporting Trials flow diagram of the study

and after sternotomy (T5). Arterial blood pressure, central venous pressure, heart rate, temperature, and time of extubation were recorded in the times mentioned above.

Statistical analysis

Data analysis was performed using SPSS software version 19 (IBM, New York, NY, USA) and MS Excel software (Microsoft Inc., Washington, USA) was used for generating allocation sequence and drawing the graphs. Numerical data was inspected with Kolmogorov–Smirnov test to see whether its distribution is normal. Numerical data with normal distribution were expressed as mean ± standard deviation. If the distribution was not normal median (interquartile range) was used for presentation of data. Between groups comparisons were carried out by the Student's *t*-test for normally distributed data and Mann–Whitney U-test for data with nonnormal distribution. Repeated measures analysis of variance (RM-ANOVA) was used for inspecting the changes in quantitative variables over time. Chi-square test was used to examine differences between qualitative data. In all comparisons, statistical significance levels were considered as $P < 0.05$.

Results

In sum, 60 patients were recruited for this study. CONSORT flow diagram of the study is presented in Figure 1 and reveals the flow of study conduct. Demographic information including age, sex, height, and weight of the study groups are presented in Table 1. There were no significant differences between two groups in these parameters ($P > 0.05$). Furthermore, no statistically significant differences between two groups in case of perioperative parameters including cardiopulmonary bypass time, pump time, and other critical factors as well as previous history of drug or alcohol abuse and blood chemistry parameters was observed [Table 2]. Comparison of the data from hemodynamics observations revealed slight change in blood pressure and heart rate in most of the times which were statistically significant [Figure 2]. Heart rate and systolic and diastolic blood pressure were lower in this time ($P < 0.05$) [Figure 2]. Repeated measures analysis of variance revealed no interaction between time and dexmedetomidine administration in modifying heart rate ($P = 0.597$), systolic blood pressure ($P = 0.186$), diastolic blood pressure ($P = 0.205$), and MAP ($P = 0.222$). In case of postsurgical pain, a slight decrease in pain score 2 h postoperation was observed in dexmedetomidine group which was not statistically significant [Figure 3]. There were no significant differences between two groups in pain score in 4 and 6 h after transfer to ICU as well as the time of extubation [Table 3 and Figure 3] ($P > 0.05$). Pain score significantly increased in both groups in 4 and 6 h after transfer to ICU compared to 2 h post-ICU. Then, it did not significantly change in the time of extubation. Analysis of the hemodynamic parameters revealed significantly lower blood pressure (systolic and diastolic and mean arterial pressure) in the dexmedetomidine group compared to control group ($P < 0.05$). Hemodynamic parameters did not significantly differ between groups in 4 and 6 h after transfer to ICU as well as the time of extubation.

Table 1: Demographic information of the patients recruited for this study

Variables	Dexmedetomidine	Control	*P*
Age (years)	59.93±8.56	62.29±6.18	0.224
Height (cm)	167.72±8.67	170.0±8.587	0.312
Weight (kg)	74.86±11.08	73.07±14.15	0.323
Gender (female percentage)	34.48	32.26	0.855

Data included age, sex, height and weight of the patients in the time of study. Dexmedetomidine group received 1 μg/kg of intravenous infusion of Precedex for 10 min and then maintenance dose (0.4 μg/kg/h) was used until the end of operation. Control group received normal saline

Table 2: Some preoperative and perioperative characteristics of the two groups: Dexmedetomidine (received 1 μg/kg of intravenous infusion of Precedex for 10 min and then maintenance dose (0.4 μg/kg/h) until the end of operation) and control (placebo)

Variable	Dexmedetomidine	Control	*P*
Aortic cross-clamping time	62.41±21.68	63.81±21.82	0.805
Duration of circulation by pump	111.17±36.96	109.97±25.39	0.884
Duration of surgical operation	311.38±59.70	318.81±63.84	0.644
Preoperative EF	46.72±8.27	46.68±9.23	0.984
Preoperative hemoglobin value	13.79±1.40	13.50±1.81	0.483
Preoperative hematocrit value	41.31±4.68	40.26±4.73	0.389
Preoperative blood urea nitrogen	20.82±6.19	20.58±7.82	0.895
Preoperative creatinine	0.96±0.27	1.13±0.58	0.165
Preoperative fasting blood sugar	148.24±46.39	132.97±43.43	0.193
Hypertension history (%)	60.71	70.97	0.426
Cigarette smoking (%)	29.63	25.81	0.776
Addiction history (%)	24.14	16.13	0.527
History of alcohol abuse (%)	6.90	6.45	0.945
Diabetes history (%)	42.86	22.58	0.162
History of thyroid disease (%)	3.57	10.35	0.612
History of beta blockers use (%)	68.97	48.39	0.124
ACE inhibitors use history (%)	37.93	51.61	0.312
History of calcium channel blockers (%)	28.57	19.36	0.542
History of diuretics consumption (%)	11.11	6.45	0.656

ACE: Angiotensin converting enzyme, EF: Ejection fraction

Discussion

In the present study, the effectiveness of dexmedetomidine versus control group for the management of acute pain after coronary artery bypass surgery, and hemodynamic stability

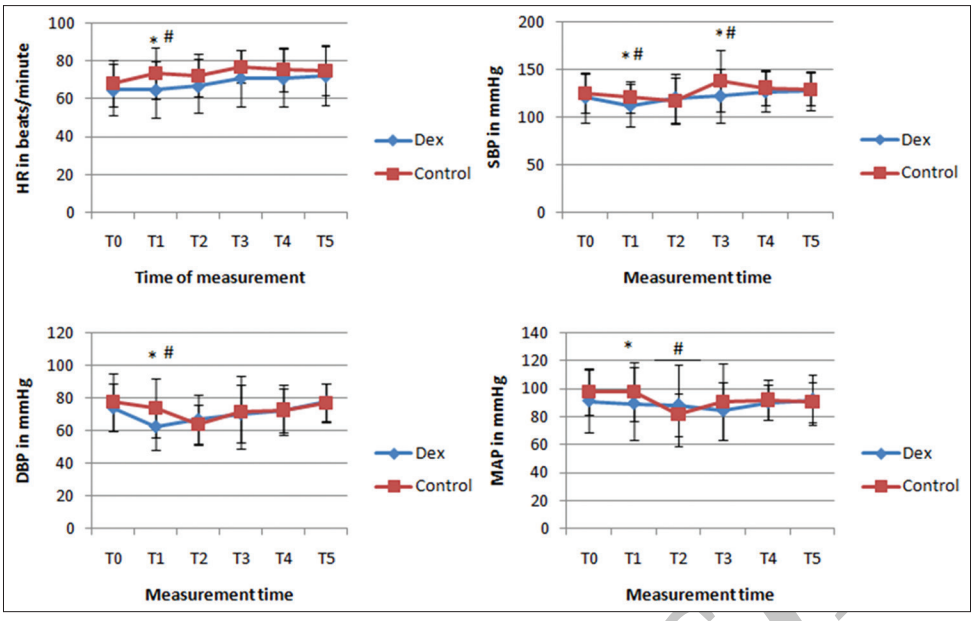

Figure 2: Graphs represent the changes in hemodynamic parameters in two groups: dexmedetomidine (received 1 μg/kg of intravenous infusion of Precedex for 10 min and then maintenance dose (0.5 μg/kg/h) until the end of operation) and control (saline) from admission to the operating room until the end of operation. Comparisons are made with repeated measures analysis of variance and unpaired *t*-test. HR: heart rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, MAP: mean arterial pressure. Hemodynamic parameters were measured and recorded at the time of admission to the operation room (T0), after bolus administration of dexmedetomidine (T1), after anesthesia induction (T2), 1 min after intubation (T3), after incision (T4) and after sternotomy (T5). $^{*}P < 0.05$ for comparison between groups at the same time; $^{\#}P < 0.05$ for comparison of the values with the first measurement

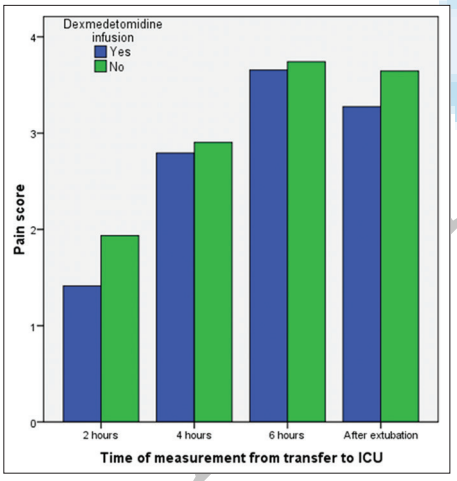

Figure 3: Graph represents the changes in pain score in two groups: dexmedetomidine (received 1 μg/kg of intravenous infusion of Precedex for 10 min and then maintenance dose (0.5 μg/kg/h) until the end of operation) and control (placebo) from admission to the operating room until after sternotomy. Comparisons are made with Mann–Whitney U-test. There were no significant differences between two groups at similar times, however pain score was significantly elevated in 4 and 6 h after transfer to Intensive Care Unit and the time of extubation compared to the time 2 h post-Intensive Care Unit ($P < 0.05$)

Table 3: Pain score following transfer to Intensive Care Unit in two groups: Dexmedetomidine (received 1 μg/kg of intravenous infusion of Precedex for 10 min and then maintenance dose (0.4 μg/kg/h) until the end of operation) and control (placebo) from admission to the operating room until after sternotomy

Time of measurement	Dexmedetomidine	Placebo	*P*
2 h post-ICU	1.41±0.83	1.94±1.41	0.194
4 h post-ICU	2.79±1.74	2.90±1.64	0.778
6 h post-ICU	3.66±1.80	3.74±1.69	0.332
Extubation time	3.28±1.44	3.65±1.40	0.885

Data is presented as mean±SD. SD: Standard deviation, ICU: Intensive Care Unit

was investigated. Findings of the study revealed significant differences in the hemodynamic parameters between two groups. Furthermore, pain score after transfer to ICU between groups was slightly different, which lacked statistical significance. There were decreases in systolic, diastolic, arterial, and central venous blood pressures in dexmedetomidine group after bolus administration of dexmedetomidine and time of intubation, which were statistically significant. Furthermore, administration of dexmedetomidine resulted in a significant decrease of the blood pressure as measured 2 h after transfer to ICU.

There is some evidence from previous studies that administration of dexmedetomidine before anesthesia induction improves the hemodynamic state in response to intubation and anesthesia induction stress. A study by Menda *et al*. revealed that administration of dexmedetomidine (1 μg/kg) before the anesthesia induction in coronary artery bypass surgery patients receiving beta-blockers improves hemodynamic stability.[8] A meta-analysis of published studies on the application of dexmedetomidine for cardiac protection in

noncardiac surgeries revealed potential favorable outcomes of dexmedetomidine administration regarding cardiac protection; however, the study revealed high odds of bradycardia and hypotension after the use of dexmedetomidine.[12] Another study by Ji *et al*. revealed the beneficial effects of postbypass administration of dexmedetomidine on renal function in patients undergoing cardiac surgery.[18] Another study by But *et al*., revealed the effects of dexmedetomidine infusion before anesthesia induction on the MAP, mean pulmonary arterial pressure (MPAP) and pulmonary capillary wedge pressure.[9] Its administration included 1 μg/kg of intravenous infusion for 10 min and then maintenance dose (0.4 μg/kg/h) until the end of cardiopulmonary bypass.[9] Tosun *et al*. revealed that dexmedetomidine administration (started by a loading dose of 0.4 μg/kg/h, followed by a continuous infusion of 0.4 μg/kg/h) resulted in reduced MPAP and improved cardiac index in CABG patients with cardiopulmonary bypass.[19] There exist evidence from many other studies, which have demonstrated the favorable hemodynamic stability in patients receiving dexmedetomidine as an adjunct to anesthetics.[20] We have previously revealed the anxiolytic properties of oral dexmedetomidine for reducing the children struggling against mask acceptance on anesthesia in pediatric surgery for congenital heart disease.[10] The patients experienced hemodynamic stability and sedation like those receiving oral midazolam.[10] The current study replicates the findings from previous studies, which provide evidence that dexmedetomidine decreased blood pressure after administration and resulted in improved hemodynamics during and after the operation. The study is the first of its kind examining the effects of dexmedetomidine on hemodynamics stability and postsurgical pain in CABG patients. Our trial revealed a slight decrease in pain scores between placebo and dexmedetomidine (1 μg/kg of intravenous infusion of Precedex for 10 min and then a maintenance dose of 0.5 μg/kg/h until the transfer to ICU) which was not statistically significant.

Conclusions

In sum, considering the findings of the current study along with the findings of previous studies and safety profile of the drug, it could be recommended to use dexmedetomidine to reduce blood pressure and hemodynamic instabilities in CABG operations. However, further studies in larger populations, different doses and treatment schedules to define if it can be used for management of postoperative pain in these patients.

Acknowledgment

We would like to acknowledge the staff at the RHC for their collaboration during this research.

Financial support and sponsorship

This research was supported by a research grant from Rajaei Cardiovascular Medical and Research Center.

Conflicts of interest

There are no conflicts of interest.

References

1. Franzén O, Ermel R, Cohain A, Akers NK, Di Narzo A, Talukdar HA, *et al.* Cardiometabolic risk loci share downstream cis- and trans-gene regulation across tissues and diseases. Science 2016;353:827-30.
2. Gorjipour F, Asadi Y, Osguei N, Effatkhah M, Samadikuchaksaraei A. Serum level of homocysteine, folate and Vitamin-B12 in epileptic patients under carbamazepine and sodium valproate treatment: A systematic review and meta-analysis. Iran Red Crescent Med J 2013;15:249-53.
3. Pordal AH, Hajmiresmail SJ, Assadpoor-Piranfar M, Hedayati M, Ajami M. Plasma oxysterol level in patients with coronary artery stenosis and its changes in response to the treatment with atorvastatin. Med J Islam Repub Iran 2015;29:192.
4. Wanitschek MM, Dörler J, Alber HF. Chronic stable angina. N Engl J Med 2016;375:292.
5. Rihal CS, Raco DL, Gersh BJ, Yusuf S. Indications for coronary artery bypass surgery and percutaneous coronary intervention in chronic stable angina: Review of the evidence and methodological considerations. Circulation 2003;108:2439-45.
6. Cogan J. Pain management after cardiac surgery. Semin Cardiothorac Vasc Anesth 2010;14:201-4.
7. Lahtinen P, Kokki H, Hynynen M. Pain after cardiac surgery: A prospective cohort study of 1-year incidence and intensity. Anesthesiology 2006;105:794-800.
8. Menda F, Köner O, Sayin M, Türe H, Imer P, Aykaç B, *et al.* Dexmedetomidine as an adjunct to anesthetic induction to attenuate hemodynamic response to endotracheal intubation in patients undergoing fast-track CABG. Ann Card Anaesth 2010;13:16-21.
9. But AK, Ozgul U, Erdil F, Gulhas N, Toprak HI, Durmus M, *et al.* The effects of pre-operative dexmedetomidine infusion on hemodynamics in patients with pulmonary hypertension undergoing mitral valve replacement surgery. Acta Anaesthesiol Scand 2006;50:1207-12.
10. Faritus SZ, Khazaee-Koohpar M, Ziyaeifard M, Mehrabanian MJ. Oral dexmedetomidine versus midazolam as anesthetic premedication in children undergoing congenital heart surgery. Anesth Pain Med 2015;5:e25032.
11. Wijeysundera DN, Naik JS, Beattie WS. Alpha-2 adrenergic agonists to prevent perioperative cardiovascular complications: A meta-analysis. Am J Med 2003;114:742-52.
12. Biccard BM, Goga S, de Beurs J. Dexmedetomidine and cardiac protection for non-cardiac surgery: A meta-analysis of randomised controlled trials. Anaesthesia 2008;63:4-14.
13. Chiba S, Tsukada M. Pharmacological analysis of vasodilator responses to alpha 2-adrenoceptor agonists in isolated rat common carotid arteries. Jpn J Pharmacol 1990;53:135-43.
14. Gorjipour F, Dehaki MG, Totonchi Z, Hajimiresmaiel SJ, Azarfarin R, Pazoki-Toroudi H, *et al.* Inflammatory cytokine response and cardiac troponin I changes in cardiopulmonary bypass using two cardioplegia solutions; del Nido and modified St. Thomas': A randomized controlled trial. Perfusion 2017;32:394-402.
15. Apfelbaum JL, Hagberg CA, Caplan RA, Blitt CD, Connis RT, Nickinovich DG, *et al.* Practice guidelines for management of the difficult airway: An updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Anesthesiology 2013;118:251-70.
16. Mellin-Olsen J, Staender S, Whitaker DK, Smith AF. The Helsinki declaration on patient safety in anaesthesiology. Eur J Anaesthesiol 2010;27:592-7.
17. Huskisson EC. Measurement of pain. J Rheumatol 1982;9:768-9.
18. Ji F, Li Z, Young JN, Yeranossian A, Liu H. Post-bypass dexmedetomidine use and postoperative acute kidney injury in patients undergoing cardiac surgery with cardiopulmonary bypass. PLoS One 2013;8:e77446.
19. Tosun Z, Baktir M, Kahraman HC, Baskol G, Guler G, Boyaci A, *et al.* Does dexmedetomidine provide cardioprotection in coronary artery bypass grafting with cardiopulmonary bypass? A pilot study. J Cardiothorac Vasc Anesth 2013;27:710-5.
20. Mondal S, Ghosh S, Bhattacharya S, Choudhury B, Mallick S, Prasad A, *et al.* Comparison between dexmedetomidine and fentanyl on intubation conditions during awake fiberoptic bronchoscopy: A randomized double-blind prospective study. J Anaesthesiol Clin Pharmacol 2015;31:212-6.