Original Article

The Preconditioning Effect of Sevoflurane on Coronary Artery Bypass Surgery Patients

Abdorasoul Anvaripour[1], Houshang Shahryari[1], Sayed Mehran Marashian[2], Alireza Jahangirifard[3]*

Abstract

Background: One of the most important issues in the field of surgery is ischemic preconditioning (IPC) of the myocardium during the coronary artery bypass grafting (CABG). The current study attempted to reevaluate the issue to find a potential approach to diminish morbidity, inotrope administration, ischemia and possibly intensive care unit stay after CABG in adult patients.

Materials and Methods: Through randomized single-blind clinical trial, all elective coronary bypass surgeries in 40 to 80 years-old patients enrolled the study. Atrioventricular (AV) block (mobitz2); complete heart block; left bundle branch block (LBBB); acute heart failure (ejection fraction (EF) <30%); re-exploration due to surgical complications and MI cases in the last 7 days were excluded. In all patients, induction (sufentanil, cis-atracurium and etomidate) and maintenance phase (sufentanil, midazolam, cis-atracurium) of anesthesia were done following the same protocol. After cross-clamp of aorta in intervention group, the patients received oxygen (2Lit/min) and sevoflurane (4%) during coronary bypass surgery. After rewarming of the patients, sevoflurane was discontinued. Main outcome measures were troponin 4, 8, 24, 48 hours after surgery with charting the electrocardiogram (ECG) changes, need for inotrope agents and hemodynamic indices during and after CABG in ICU.

Results: 58 CABG candidates enrolled the current study: 29 in intervention group and 29 in control group. There were no statistical differences between the groups concerning hemodynamic issues, Central Venous Pressure (CVP), hematocrit (HCT), ECG changes, demands for inotrope, or ICU stay between the groups.

Conclusion: No significant relationship between application of 4% sevoflurane and IPC was found in adult CABG patients. However, the effect of Sevoflurane on IPC might be dose-related.

Keywords: Ischemic preconditioning (IPC); Sevoflurane; Coronary Artery Bypass Surgery (CABG)

Please cite this article as: Anvaripour AR, Shahryari H, Marashian SM, Jahangirifard AR. The preconditioning effect of sevoflurane on coronary artery bypass surgery patients. J Cell Mol Anesth. 2018;3(2):66-73.

1. Anesthesiology department, Bushehr University of Medical sciences, Bushehr, Iran
2. Chronic Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Lung Transplantation Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

Corresponding Author: Alireza Jahangirifard, MD, Masih Daneshvari Hospital, Darabad, Tehran, Iran. Tel: (+98) 21 27122537, Fax: (+98) 21 26109644.
Email: alirezajahangiri@sbmu.ac.ir

Introduction

Ischemic preconditioning (IPC) is a protective way to lessen the ischemia of myocardium. IPC is a natural defensive mechanism that helps the heart tolerate ischemic condition that firstly raised by Murry et al, in the 1986 (1, 2). In this process, many mechanisms are involved such as myocardial G-protein paired receptors, adenosine A1 receptors and α_1 adrenergic receptors. Protein Kinase-C is another mediator involved as a cardiac potassium channel activator (1).

Sevoflurane is one of the liquid general anesthetic medications affecting on ion channels, especially on receptors of acetylcholine, gamma-aminobutyric acid (GABA) and glutamate. This anesthetic has several side effects such as malignant hyperthermia, dose-dependent hypotension, bradycardia, tachycardia, nausea and vomiting (3). Sevoflurane role has been shown as an inhaled anesthetic medication in protection through ischemic preconditioning (IPC) as well. Adenosine administration may induct IPC through previous experiences either before Coronary Artery Bypass Graft (CABG) or before being used along with cardioplegic solutions. IPC facilitates myocardial recovery after surgery via lower myocardial damage and decreased inotrope administration need.

Through a meta-analysis in 2007, clinical trials to compare Sevoflurane and Desflurane were studied concerning mortality and morbidity after CABG to conclude protective effects of halogen-containing anesthetic medicinal diet on heart (4). In addition, a drop in hemodynamic side effects was shown by Annecke et al, using sevoflurane in pigs through general anesthesia compared to propofol as well as a decrease in cellular markers regularly released because of myocardial damage (5).

Measuring Troponin-I four hours after surgery, as a marker of myocardial tissue damage, Frabdorf et al, found that two 5-min cycles of minimum dose of sevoflurane, 10-minute before external blood flow, obviously resulted in less myocardial damage comparing to intravenous Sufentanil and Propofol (6). They confirmed that Sevoflurane inducted strongly dose-dependent IPC.

A comparison between interrupted and continuous administration of Sevoflurane and Propofol was carried out in 2008 by Bein et al, through CABG to realize that interrupted sevoflurane could prominently reduce myocardial damage based on a drop in Troponin-I and creatine phosphokinase-MB (CK-MB) (7). Later in 2014, Kortekaas et al, observed that cardio-specific Sevoflurane administration strongly reduced systemic inflammation without attenuating cell damage markers when used during mitral value repair surgery (8).

Kawamura et al, in 2006 had assessed the effects of sevoflurane and Propofol on interleukin (IL)-10, IL-8, IL-6 and IL-1 receptor antagonist (IL-1ra) in 23 patients to know that Sevoflurane suppressed IL-6 and IL-8 release but had no obvious effect on IL-10 and IL-1ra. They also raised the doubt that its protective role for myocardium may be resulted by a change in the balance between pre-inflammatory and anti-inflammatory cytokines (9).

Finally, two separate studies by Bouwman et al, and Lorsonradee et al, showed the key protective role of sevoflurane on cardiac contracture, kidney, and liver to get better recovery results (10, 11).

In detail, Sevoflurane involves ca-dependent PKC-α channel to protect myocardium during IPC in addition to keeping serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), lactate dehydrogenase (LDH) and serum creatinine better than Propofol.

Few studies have focused on the effects of Sevoflurane on cardiac preconditioning through CABG among which the optimal administration dose to get optimal protection was not precisely available. Therefore, the current study attempted to reevaluate the issue to find better way of diminish in morbidity, inotrope administration, and ischemia and consequently ICU stay after CABG.

Methods

Patients and sample size

Through a randomized clinical trial, 58 patients of CABG were participated to be divided to two groups of intervention and control each containing 29 regarding inclusion criteria. The participants were 40-80 years of age who were candidates for elective CABG referred to a university hospital in Bushehr, Iran, between 2016 and 2017. Background information such as age, sex, ejection fraction, history of

myocardial infarction, cardiomegaly, angiotensin-converting enzyme (ACE) inhibitors administration an also diabetes mellitus types I and II were basically recorded for all the participants.

Simple randomization was done using random numbers to enter the patients into the named groups of this study. The sample size was calculated 30 patients based on previous studies and the following formula:

$$n = \frac{2\left(z1 - \frac{\alpha}{2} + z1 - \beta\right)^2 s}{d2}$$

α=0.05 β=0.8 d=0.04 Tn-I plasma level SD=4.5ng/ml

Two patients had some lost information and were excluded from the study.

Procedure process

Premedication was done night before surgery as well as early morning at surgery date with Lorazepam and intramuscular injection of morphine regarding systolic blood pressure more than 100 mmHg, 30 minutes before entering operation room. All cardiac medications except ACE inhibitors and anticoagulants (like Plavix®) continued until procedure date. Arterial line was inserted left radial or brachial arteries under local anesthesia with lidocaine immediately after entering the operation room. Tracheal intubation, pulse-oximetry, V_2 and V_5-lead ECG and capnography were carried out. All the participants experienced similar protocol of general anesthesia with 1-1.5 μg/kg Sufentanil , 0.1 mg/kg Midazolam, 0.15-0.2 mg/kg Cis-atracurium and 0.2 mg/kg Etomidate followed by maintenance with 2μg/kg/hour Sufentanil+ 1μg/kg/min Midazolam+2μg/kg/min Cis-atracurium. Revascularization was done via left internal mammary artery (LIMA) and saphenous vein. Cannulation of aorta and right atrium was then conducted after 300 U/kg Heparin administration via central venous catheter while activated clotting time (ACT)>400 seconds. Cardioplegic solution was cold liquid plasmalight (6°C) containing 165 mEq sodium chloride, 25 mEq sodium bicarbonate, 45 mEq potassium, 138 mEq chloride with 1800 cc prime volume.

For the group of intervention, participants were administered sevoflurane 4% via vaporizer along with 2 liters oxygen during bypass pump while oxygen was the only thing administered in the control group. Sevoflurane was withdrawn after rewarming. The patients were admitted in ICU after the procedure ended by closing sternum. Analgesia was done using an intravenous pump containing a mixture of 10 mg morphine 2 g Apotel, and 4 mg Ondansetron.

Any changes in ECG showing ischemia as well as any ventricular arrhythmia, which needed medications (such as ventricular fibrillation (VF), ventricular tachycardia verotoxin (VT), or premature ventricular contractions (PVC)) beside atrial fibrillation atrial flutter amniotic fluid (AF) or atrial flutter, were recorded carefully. Ischemic changes of ECG follows:

1- Q-wave myocardial infarction (MI) evidenced by the appearance of new persistent (<24 hours) Q waves >0.04 seconds in greater than or equal to 2 contiguous leads of the same vascular territory or equivalent R-wave increments (R/S ratio >1 in leads V1and V2).

2- A non–Q-wave MI was diagnosed by ST-segment elevation or depression >1 mV 0.08 seconds after the J-point or T-wave inversion of 1 to 2 mV 0.08 seconds after the J-point in 2 contiguous leads of the same vascular territory.

Needed inotropes including Epinephrine, Norepinephrine, Milrinone and Vasopressin at the time of cardiopulmonary bypass (CPB) emerging was recorded as well. ECG changes were recorded at ICU admission time, 24 and 48 hours later. Serum troponin level was also recorded at 4, 8, 24 and 48 hours following operation. Systolic and diastolic blood pressure in addition to mean arterial pressure and heart rate were other parameters to record before anesthesia induction as well as 10 minutes, 60 minutes and 8 and 24 hours after end of CPB.

The current study was approved by the local ethics committee under the code: IR.BPUMS.REC1395.23 and finally by the ministry of health of Iran through approval number: IRCT2016061528477N1.

Regarding 95% confidence interval and significance of 0.05, frequency, mean, standard deviation and range of changes were analyzed using Chi-Square test, Mann-Whitney U test, ANCOVA and Friedman by SPSS 24 for windows.

The current study chiefly faced challenges such

as shortness in Sevoflurane stock as well as patient exclusion due to postoperative uncontrolled bleeding.

Results

Totally, 58 CABG candidates enrolled the current study including 29 in intervention group and 29 in control group. The mean age was 56.24 ± 8.80 (45-70 years) in the former group and 59.59±10.76 (31-81 years) in the latter with no significant difference (Mann-Whitney U: P value=0.348)**.**

Sex wise, no difference was found between the groups as can be seen in table 1 ($X^2_{(1)}$ = 0.672; P value=0.585 by Fisher Exact test). There was no statistical difference between the groups concerning ejection fraction as checked with Mann-Whitney U (P value=0.177).

Table 1 summarizes some key demographic as well as medical history of the participants regarding their groups. History of cardiomegaly (P =0.431), ACE-inhibitors (P =0.065) and diabetes mellitus type Iand II (P =0.248) was not statistically different at all.

The serum level of troponin was the first concern, which showed similar results in intervention and control groups 4, 8, 24 and 48 hours after the surgery (Table 2).

Another factor to be assessed was ECG changes after surgery including Q and non-Q-wave-MI which were similar in the studied groups as observed in table 3.

Similar results were found for the need of Inotropes during on-pump process (P>0.089) and continued during off-pump (P=0.412) (Table3).

Inotropes were similarly needed through postoperative ICU stay as can be checked in table 3. (P=0.506) Inotrope need during intra-aortic balloon pump (IABP) did not differ between the groups (P=0.492).

Concerning hemodynamic factors, no item but systolic blood pressure (P=0.020) and the mean arterial blood pressure (P=0.002) differed statistically when compared the groups preoperatively. After 60 minutes of pump phase, like what happened 7 hours later, statistically similar hemodynamic parameters were obviously found between the groups as can be seen in table 4 as well. This similarity was showed 24 hours after the pump phase (Table 4).

In terms of hematocrit, findings shown no

Table 1: Demographics and some histories of diseases and medications.

		Group	Number	Frequency
Sex	**Male**	Intervention	17	58.6
		Control	20	69
	Female	Intervention	12	41.4
		Control	9	31
Recent MI	**Yes**	Intervention	5	17.2
		Control	5	82.8
	No	Intervention	24	17.2
		Control	24	82.8
Cardiomegaly	**Yes**	Intervention	16	55.2
		Control	12	41.4
	No	Intervention	13	44.8
		Control	17	58.6
ACE-I	**Yes**	Intervention	10	34.5
		Control	18	62.1
	No	Intervention	19	65.5
		Control	11	37.9
History of type 1 Diabetes Mellitus	**Yes**	Intervention	3	10.3
		Control	26	97.7
	No	Intervention	3	10.3
		Control	26	97.7
History of type 2 Diabetes Mellitus	**Yes**	Intervention	11	37.9
		Control	6	20/7
	No	Intervention	18	62.1
		Control	23	97.3

Table 2: Serum troponin levels at evaluating times.

Troponin	Group	Mean	SD	Min	Max	P-value
4 hours afterwards	Intervention	3.56	2.73	0.50	12.12	0.859
	Control	3.81	3.27	0.06	15.55	
8 hours afterwards	Intervention	5.58	7.28	0.43	32.00	0.446
	Control	5.17	5.28	0.62	50.25	
24 hours afterwards	Intervention	3.72	4.21	0.15	18.00	0.525
	Control	5.24	10.12	0.30	56.00	
48 hours afterwards	Intervention	2.15	2.63	0.00	8.80	0.294
	Control	3.74	8.79	0.12	48.70	

Table 3: ECG changes at different times of the study.

MI	Group	N (%)	P-value
Q wave MI	Intervention	0(0.00)	>0.05
	Control	1(3.30)	
Non-Q wave MI	Intervention	6(20.00)	0.761
	Control	8(26.70)	
On-Pump Inotrope Need	Intervention	7(23.3)	>0.05
	Control	8(26.7)	
Off-Pump Inotrope Need	Intervention	18(60.0)	0.412
	Control	22(73.3)	
ICU Inotrope Need	Intervention	4(13.3)	0.506
	Control	7(23.3)	

statistical discrepancy between the studied groups at basic time and 15 mins and 30 mins later like at the end point of pump phase (Table 5). Likely, basic CVP (central vein pressure) and post-pump CVP were statistically similar in the groups (Table 6).

Graft number showed the means of 3±0.13 (±SE) and 3±0.18 in the groups of intervention and control respectively with no statistical difference reported by Mann-Whitney U (P value=0.950).

Two complications including ventricular fibrillation (VF) and ventricular tachycardia (VT) were assessed for occurrence to find similar frequency in the groups (P value>0.05).

Discussion

The current study attempted to find positive effect of Sevoflurane on general anesthesia among 58 CABG surgeries with less hemodynamic and ECG changes finally to confirm similar responses compared to regular techniques of intravenous anesthesia.

Lemoine et al, in 2017 investigated cardio protective effects of sevoflurane through elective on-pump CABG surgery compared with no halogenated volatile anesthesia to conclude that sevoflurane could half the cardiac troponin I in serum of what seen in controls as well as less need to inotropic support (12). At the same time, Wang et al, tried to reveal the biological mechanism involving in sevoflurane-induced anesthesia in CABG surgery based on gene expression features to realize that neuroactive ligand-receptor interaction may play the main role in cardio protective effects of sevoflurane through regulating the pathway (13).

Zhang et al, in 2016 tried to compare the effects of Sevoflurane and regular method of general anesthesia only with inhaled oxygen regarding cardiac enzymes and hemodynamic features to find that Sevoflurane provided lower mean of arterial pressure, heart rate and left ventricle ejection fraction (LVEF) as well as significantly lower plasma level of CK-MB. Additionally, they studied respiratory parameters like tidal volume and vital capacity, respiratory rate and P_aO_2/Fio_2 to get fluctuated data not enough to assess sevoflurane-related improvements. However they realized that Sevoflurane, despite lower LVEF, may contribute to Stabilization of cardiopulmonary function and prevention of myocardial injury (14).

Table 4: Hemodynamics at different points of the study regarding the groups*

Hemodynamics	Group	Mean	SD	Min	Max	P-value
SBP	**Intervention**	152.71	26.53	100.00	200.00	0.020
	Control	169.54	23.08	120.00	220.00	
DBP	**Intervention**	73.27	11.41	50.00	100.00	0.620
	Control	74.61	10.56	50.00	100.00	
MAP	**Intervention**	96.27	13.42	72.00	115.00	0.002
	Control	110.24	16.25	80.00	153.00	
HR	**Intervention**	79.84	15.67	47.00	115.00	0.982
	Control	80.74	15.89	50.00	113.00	
MAP15	**Intervention**	60.74	9.13	45.00	76.00	0.849
	Control	62.04	9.25	40.00	76.00	
MAP30	**Intervention**	65.17	7.75	52.00	81.00	0.812
	Control	66.00	9.53	48.00	85.00	
End-Pump	**Intervention**	54.94	10.74	36.00	72.00	0.538
	Control	58.14	11.21	40.00	85.00	
SBP after 10 min	**Intervention**	119.31	11.21	99.00	141.00	0.140
	Control	114.27	9.96	90.00	133.00	
DBP after 10 min	**Intervention**	56.81	6.08	45.00	70.00	0.941
	Control	56.81	6.39	45.00	70.00	
MAP after 10 min	**Intervention**	73.07	6.32	65.00	85.00	0.486
	Control	74.14	6.65	58.00	86.00	
HR after 10 min	**Intervention**	100.27	8.31	80.00	116.00	0.554
	Control	98.44	9.77	78.00	116.00	
SBP60min	**Intervention**	127.91	13.49	100.00	160.00	0.351
	Control	124.34	13.41	100.00	145.00	
DBP60min	**Intervention**	62.74	9.09	46.00	80.00	0.599
	Control	63.81	8.85	48.00	80.00	
MAP60min	**Intervention**	81.77	11.98	67.00	111.00	0.545
	Control	109.27	153.65	65.00	921.00	
HR60min	**Intervention**	94.27	9.87	75.00	117.00	0.841
	Control	92.54	18.57	10.00	115.00	
SBP8hrs	**Intervention**	138.57	19.56	90.00	180.00	0.116
	Control	140.11	18.94	101.00	190.00	
DBP8hrs	**Intervention**	75.71	12.02	54.00	105.00	0.491
	Control	72.91	10.18	50.00	89.00	
MAP8hrs	**Intervention**	95.24	16.72	68.00	138.00	0.637
	Control	91.21	16.51	62.00	128.00	
HR8hrs	**Intervention**	95.07	14.22	67.00	121.00	0.894
	Control	96.17	10.66	75.00	118.00	
SBP24hrs	**Intervention**	133.91	16.93	103.00	167.00	0.220
	Control	137.84	17.86	107.00	170.00	
DBP24hrs	**Intervention**	72.17	11.32	53.00	100.00	0.801
	Control	72.54	11.21	51.00	91.00	
MAP24hrs	**Intervention**	88.51	17.33	58.00	132.00	0.674
	Control	89.34	14.19	60.00	129.00	
HR24hrs	**Intervention**	91.47	11.13	73.00	110.00	0.599
	Control	90.11	12.17	69.00	117.00	

*SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MAP: Mean Arterial Pressure

A meta-analysis showed in 2016 demonstrated no statistical difference between data about postoperative CK-MB levels among total 384 patients undergoing on-pump CABG with Sevoflurane; though postoperative myocardial troponin levels were significantly lower in sevoflurane group (15).

Table 5: Hematocrit at on-pump and off-pump phases (HCT: Hematocrit)

	Group	Mean	SD	Min	Max	P-value
Base HCT	**Intervention**	39.31	5.21	25.00	48.00	0.563
	Control	38.74	5.15	28.00	54.00	
HCT pump1	**Intervention**	24.64	4.23	17.00	32.00	0.108
	Control	22.74	4.21	16.00	32.00	
HCT pump2	**Intervention**	26.04	4.38	19.00	36.00	0.238
	Control	24.24	4.65	16.00	32.00	
HCT: off-pump	**Intervention**	28.37	6.34	5.00	36.00	0.232
	Control	27.67	3.81	21.00	35.00	

Table 6: Central Venous Pressure (CVP) in two groups at the times of on- and off-pump (SD: Standard Deviation).

	Group	Mean	SD	Min	Max	P-value
CVP: base value	**Intervention**	9.64	2.36	5.00	15.00	0.549
	Control	9.94	2.41	4.00	15.00	
CVP: off-pump	**Intervention**	9.74	3.28	2.00	17.00	0.153
	Control	11.10	2.73	6.00	16.00	

The current study showed reduced length of ICU stay among patients who took Sevoflurane during surgery which was previously pointed out by Likhrantsev et al, in 2016 (16). The named study also confirmed reduced serum levels of cardiac biomarkers like troponin T and N- terminal pro-brain natriuretic peptide as well as mortality.

Sirvinskas et al, raised mitochondrial function involvement in 2015 to explain the effects of Sevoflurane on clinical parameters in CABG surgery to believe that Sevoflurane could slightly protect the mitochondrial outer membrane from ischemia-reperfusion injury and the loss of cytochrome C in addition to its significantly lower postoperative serum troponin levels when compared to Propofol. (17) However, little changes in hemodynamics through the current study were probably due to low dose of Sevoflurane to use; and higher doses may strengthen the protective features.

Regarding clinical and basic studies on the effects of harm reduction of CABG surgery, there are many aspects of studies to perform to get enough reliable documents about protective role of sevoflurane in cardiac safety during and after the named surgery.

Conclusion

The current study could not find significant clinical effect and additional benefit of sevoflurane on ischemic preconditioning with the used dosage in on-pump CABG surgeries. The effect of sevoflurane is probably dose-dependent which would be, in turn, a hypothesis to assess through more future trials as we believe.

Acknowledgment

The authors would like to acknowledge the kind efforts of all physicians and nurses in the operating room that was the research location.

Conflicts of Interest

The authors declare that they have no conflict of interest.

References

1. Shvedova M, Anfinogenova Y, Popov SV, Atochin DN. Connexins and Nitric Oxide Inside and Outside Mitochondria: Significance for Cardiac Protection and Adaptation. Front Physiol. 2018;9:479.

2. Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium. Circulation. 1986;74(5):1124-36.

3. Miller RD. Miller's anesthesia. 8th ed, 2014, Saunders, Philadelphia.ISBN: 9780702052835.

4. El Dib R, Guimarães Pereira JE, Agarwal A, Gomaa H, Ayala AP, Botan AG, Braz LG, de Oliveira LD, Lopes LC, Mathew PJ. Inhalation versus intravenous anaesthesia for adults undergoing on-pump or off-pump coronary artery bypass grafting: A systematic review and meta-analysis of randomized controlled trials. J Clin Anesth. 2017;40:127-138.

5. Annecke T, Kubitz JC, Kahr S, et al. Effects of sevoflurane and

propofol on ischaemia–reperfusion,injury after thoracic-aortic occlusion in pigs. Br J Anaesth. 2007;98(5):581-90.
6. Fräßdorf J, Borowski A, Ebel D, et al. Impact of preconditioning protocol on anesthetic-induced cardioprotection in patients having coronary artery bypass surgery. J ThoracCardiovasc Surg. 2009;137(6):1436-42.
7. Bein B, Renner J, Caliebe D, et al. The effects of interrupted or continuous administration of sevoflurane on preconditioning before cardio-pulmonary bypass in coronary artery surgery: comparison with continuous propofol. Anaesthesia. 2008;63(10):1046-55
8. Kortekaas KA, van der Baan A, Aarts LP, et al. Cardiospecific sevoflurane treatment quenches inflammation but does not attenuate myocardial cell damage markers: a proof-of-concept study in patients undergoing mitral valve repair. British Journal of Anaesthesia. 2014;112(6):1005-14.
9. Kawamura T, Kadosaki M, Nara N, et al. Effects of sevoflurane on cytokine balance in patients undergoing coronary artery bypass graft surgery. J CardiothoracVascAnesth. 2006;20(4):503-8
10. Bouwman R A, Musters R J P, van Beek-Harmsen B J, et al. Sevoflurane-induced cardioprotection depends on PKC-α activation via production of reactive oxygen species. British Journal of Anaesthesia. 2007;99(5):639-45.
11. Lorsomradee S, Cromheecke S, Lorsomradee S, De Hert SG. Effects of sevoflurane on biomechanical markers of hepatic and renal dysfunction after coronary artery surgery. J CardiothoracVascAnesth. 2006; 20(5):684-90
12. Lemoine S, Zhu L, Gérard JL, Hanouz JL. Sevoflurane-induced cardioprotection in coronary artery bypass graft surgery: Randomised trial with clinical and ex-vivo endpoints. Anaesth Crit Care Pain Med. 2018;37(3):217-23.
13. Wang J, Cheng J, Zhang C, Li X. Cardioprotection Effects of Sevoflurane by Regulating the Pathway of Neuroactive Ligand-Receptor Interaction in Patients Undergoing Coronary Artery Bypass Graft Surgery.Computational and Mathematical Methods in Medicine. 2017:7.
14. Zhang J, Wang S. Effects of sevoflurane on cardiopulmonary function in patients undergoing coronary artery bypass.J BiolRegulHomeost Agents. 2016;30(4):1079-83
15. Lu Y, Wang L, Liu N, Dong T, Li R. Sevoflurane preconditioning in on-pump coronary artery bypass grafting: a meta-analysis of randomized controlled trials.J Anesth. 2016;30(6):977-86.
16. Likhvantsev VV, Landoni G, Levikov DI, Grebenchikov OA, Skripkin YV, Cherpakov RA. Sevoflurane Versus Total Intravenous Anesthesia for Isolated Coronary Artery Bypass Surgery With Cardiopulmonary Bypass: A Randomized Trial.J CardiothoracVascAnesth. 2016;30(5):1221-7.
17. Sirvinskas E, Kinderyte A, Trumbeckaite S. Effects of sevoflurane vs. propofol on mitochondrial functional activity after ischemia-reperfusion injury and the influence on clinical parameters in patients undergoing CABG surgery with cardiopulmonary bypass.Perfusion. 2015;30(7):590-5.