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Changes in blood oxygen transport function and body energy expenditure during anaesthesia during coronary artery bypass grafting in adults: A randomized clinical study

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Abstract

Introduction: Cardiac surgery is a dangerous and complex field of medicine with significant morbidity and mortality. Quality anesthetic care with specific attention to detail can greatly enhance patient safety and outcome.

Objectives: Comparison of the effects of anesthetics on oxygen consumption, transport and energy expenditure during coronary artery bypass grafting in adults.

Material and methods: A total of 90 patients were assigned randomly into three groups according to the type of anaesthesia: the first group with propofol (P), the second group with sevoflurane, and the last one was with isoflurane. All patients underwent coronary artery bypass grafting under cardiopulmonary bypass. To determine oxygen delivery and oxygen consumption were determined using the formulas ((DO_2 = CI* CaO_2), (VO_2 = Cardiac index (CI)) and a spirometric device during anaesthesia.

Results: the cardiac index remained at the same level in the propofol and sevoflurane groups (2.5±0.6 l/min/m2 and 2.3±0.5 l/min/m2), while in the isoflurane group it was decreased to 2.3±0.5 l/min/m2. The oxygen transport index was 421.6±57.0 ml/min/m2 in the propofol group, 396.4±63.2 ml/min/m2 in the sevoflurane group, and 376.7±68.0 ml/min/m2 in the isoflurane group. Propofol reduced oxygen consumption to 101.5±23.5 ml/min/m2, while sevoflurane and isoflurane anesthesia reduced it to 106.6±22.3 ml/min/m2 and 116.4±21.4 ml/min/ m2. All anaesthetics reduced energy expenditure, but propofol anaesthesia significantly reduced it from 1491.4 to 1188.3 kcal/day.

Conclusion: In conclusion, isoflurane significantly reduced cardiac index compared to propofol and sevoflurane. Oxygen transport was higher in the propofol group than volatile anesthetics, and propofol reduced oxygen consumption more than inhalational anesthetics. In addition, energy expenditure was lowest in the propofol group than in the other anesthetics.

Keywords: oxygen consumption, energy expenditure, sevoflurane, isoflurane, propofol, oxygen transport, metabolic status

Introduction

Cardiac surgery is done under general anaesthesia, which means the patient is in a state of carefully controlled, medication-induced unconsciousness and will not respond to pain. Anesthesia of patients undergoing cardiac surgery is challenging and requires responsibility. The goals of anesthesia for cardiac surgery include avoidance of perioperative cardiac ischemia, tight hemodynamic control, early extubation. General anesthesia in cardiac surgery should also attempt to preserve myocardial function, prevent ischemia, and maintain stable hemodynamics.

Indirect calorimetry can be an indicator of homeostatic changes during surgery. Stress increases oxygen consumption (VO2) and during anaesthesia there is a decrease in VO_2 [1].

Resting oxygen consumption is influenced by several factors including the consumption and digestion of food, environmental temperature, the performance of muscular work, pregnancy, and hormones [2,3]. Increased

post-operative oxygen consumption is driven by a systemic inflammatory response to tissue trauma sustained during surgery [4-8]. The primary goal of the cardiorespiratory system is to deliver adequate oxygen to the tissues to meet their metabolic demands [9].

Tissues vary considerably in their sensitivity to hypoxia. Neurons tolerate hypoxia for only a few minutes, whereas the smooth muscles of the bladder go several days without oxygen. This has important implications for oxygen transport and monitoring of tissue hypoxia in patients [10]. Increased oxygen extraction, the ratio of consumption to transport, has been associated with poor outcome after surgery [11]. Researchers [12,13] found that surgery and anaesthesia did not significantly affect oxygen consumption and energy expenditure during anaesthesia. General anaesthesia reduced VO_2 by approximately a third in elderly patients undergoing major abdominal surgery. The relevance of these changes needs future assessment in relation to outcomes and haemodynamic interventions. [14]. Oxygen delivery (DO_2) is an important marker of O_2 transport than arterial blood oxygen saturation (SaO_2). Anaesthetics (propofol or sevoflurane) had no significant effect on DO_2. In addition, no correlation was found between SaO_2 and DO_2. DO_2 data may provide useful additional information about the patient's condition, especially with low SaO_2 [15]. Progressive hypothermia in anesthetized patients reduces metabolic rate but does not change DO_2. The significant decrease in oxygen extraction ratio may partly be related to a leftward shift of the oxyhemoglobin dissociation curve, as evidenced by the decrease in P50 [16]. Oxygen consumption during general anaesthesia was independent of the type of anaesthetics. General anaesthesia leads to a marked decrease in oxygen consumption, but during recovery the O_2 uptake can increase dramatically [17]. Indirect calorimetry can be an indicator of homeostatic changes during surgery. Stress increases oxygen consumption and during anaesthesia there is a decrease in VO_2 due to lack of kinetic energy as a cellular metabolic response to surgical trauma and anaesthesia. More research is needed to find out which oxygen consumption measurement system is the most appropriate for anaesthesia and what the VO_2 limit values might be [18].

Objectives: Comparison of the effects of anesthetics on oxygen consumption, transport and energy expenditure during coronary artery bypass grafting in adults.

Material and methods

Study design: Single-centre prospective randomized controlled clinical study.

This study was approved by NJSC "Astana Medical University" No. 3, Session No. 10. Republic of Kazakhstan, Astana. And written informed consent was obtained from all subjects. This manuscript adheres to the applicable CONSORT guidelines. The study includes data from 90 patients operated on at the Medical Center Hospital of the President's Affairs Administration of the Republic of Kazakhstan. All patients underwent coronary artery bypass grafting under cardiopulmonary bypass (CPB). This research work was conducted between 2021 and 2022. To calculate the sample size, we used the formula n=t2*D*N/confidence interval*N+t2*α, which will allow to identify the statistical significance of the study. Clinicaltrials.gov. NCT05693428, first trial registration date 22/01/2022.

Inclusion criteria for the main study phase

- The age is between 40-60 years old.
- coronary revascularization or >50% stenosis on coronary angiography
- CHD. Multivessel coronary lesions.
- Participants of both sexes will be included in the study
- Signed informed consent

Exclusion criteria

- pregnancy (risk to the baby and the mother)
- allergenic patients (anaphylactic shock).
- vulnerable groups.
- current congestive heart failure;
- current unstable angina pectoris;
- preoperative hemodynamic instability, defined as the use of vasopressors;

All patients were divided into 3 groups: 1 (control group) (n=30) consisted of patients who underwent anaesthesia with propofol (P). The second group (n=30) were patients who received sevoflurane inhalation anaesthesia (S). Group 3 (n=30) with isoflurane (I).

The study was conducted in 5 stages:

1) determined the patient's baseline values before anaesthesia;

2) after tracheal intubation;

3) before the cardiopulmonary bypass;

4) after the cardiopulmonary bypass;

5) The post-operative period.

Before induction into anaesthesia, haemodynamic monitoring with Nihon Kohden monitors (Japan) was initiated on admission to the operating theatre. The right radial artery was catheterised for invasive systemic pressure monitoring and arterial blood sampling, then a catheter was inserted into the central jugular vein (under ultrasound machine control) and guided into the right atrium for mixed venous blood sampling.

Cardiac stroke volume was determined by transthoracic echocardiography (CS=end diastolic volume - end systolic volume). Cardiac output (CO=CS x heart rate), cardiac index (CI=CB/body surface area) were determined. Blood oxygen content was determined using the formula CaO_2 (arterial blood gas ABG) and CvO_2 (central mixed venous BG) = [(1.34 × Hb × SO2) + (PO2 × 0.031)] / 100, arteriovenous difference = CaO_2-CvO_2. Oxygen delivery was determined using the formula (DO_2 = CI* CaO_2), oxygen consumption (VO_2 = Cardiac index (CI)*AVD or VO_2 = CB × (CaO_2 - CvO_2) ~ CB × Hb × 1.34 × (SaO_2 - SvO_2) / 100).

In the second stage, GE Datex Ohmeda Aisys CS2 (USA) machine was used for anesthesia, after tracheal intubation, indirect calorimetry was used to determine VO2, energy expenditure during anaesthesia, using a "Spirometry" (GE DATEX OHMEDA E-CAiOV USA), which was connected to an endotracheal tube and continuously showed oxygen demand and energy expenditure. Additionally, cardiac output was determined using Fick's formula. In the third and fourth stages of anaesthesia the same tests (cardiac output, cardiac index, consumption, oxygen delivery and energy expenditure) were determined. In the last stage to assess the pharmaco-efficiency of anaesthetics, the consumption of muscle relaxants and opioid analgesics was calculated. The time of extubation and the time of transfer of the patient to the specialist department were determined.

All patients were given the same type of premedication: 30-40 minutes before surgery, 0.3 mg/kg promedol was administered intramuscularly. Patients continued to take their usual baseline drugs both before and on the day of surgery to prevent withdrawal syndrome and to reduce the risk of myocardial ischaemia in the perioperative period.

All patients in both groups were given fentanyl in a dose of 5-7 μg/kg, ketamine 1.5-2 mg/kg, and propofol 1-1.5 mg/kg intravenously fractionally. Pipecuronium bromide 0.04-

0.07 mg/kg was used as muscle relaxant in all patients. To maintain anaesthesia in Group 1 P, propofol was used as an anaesthetic in a dose of 5 mg/kg/h intravenously on a perfusor (BBRAUN). In Group 2, sevoflurane was used as an anaesthetic in a dose of - 1.7-1.9 MAC. In Group 3 isoflurane was used as anaesthetic in a dose of - 1.1-1.2 MAC. In all groups fentanyl 100 µg intravenously was administered fractionally to increase heart rate and blood pressure, also pipecuronium bromide 2 mg intravenously for muscle relaxation. During CPB in all patients in all groups, propofol was used at a dose of 4-5 mg/kg/h intravenously via perfusion, analgesic regimen: fentanyl 100 µg intravenously every 30 min; myorelaxant piperonium bromide 2 mg every 40-60 min. Norepinephrine solution was administered at a dose of 0.05 µg/kg/min intravenously on perfusor after CPB in all patients at the same dosages in all groups.

Aim to use cardiotonic drugs:

1. In order to maintain mean arterial perfusion pressure (CPB causes cytokine storm and vasodilation).

2. For inotropic support (for reperfusion syndrome, resulting in a lower ejection fraction).

The depth of anaesthesia was monitored with a processed electroencephalogram, such as a BIS.

Statistical analysis was performed using IBM SPSS Statistics 20 package using one-factor analysis of variance for independent samples and nonparametric Kraskel Wallis test. The Kraskel-Wallis test was applied only to myorelaxant consumption, as the distribution was non-normal on this parameter. A Pearson and Spearman correlation analysis was also performed to determine the significance of the association between cardiac index and oxygen consumption, as well as energy expenditure.

Results

Patients in the study subgroups were comparable at baseline, with tables showing demographic, anthropometric, operative volume, cardiac index, consumption, oxygen delivery (Table 1).

Table 1 Demographic, anthropometric, operative volume, cardiac index, consumption, oxygen delivery. Parameters.

Indicator	Propofol (n=30)	Sevoflurane (n=30)	Isoflurane (n=30)
Sex M F	 25 (83,3%) 5 (16,7%)	 27 (90%) 3 (10%)	 22 (73,3%) 8 (26,7%)
Age, years	62,4 ± 7,7	61,5 ± 8,4	62,5 ±8,1
Weight, kilograms	81,5 ± 10,8	86 ± 9,6	81,4 ± 10,9
Height, centimetre	169,8±9,6	168,4±7,9	167,6±9,9
Duration Operation, hour	3,8±0,5	3,7±0,4	3,9±0,5
Cardiac index, l/min/m2	2,5 ± 0,6	2,4 ± 0,5	2,5 ± 0,6
Oxygen consumption, ml/min/m2	125,0±34,4	118,2 ± 38,3	114,9 ± 37,4
Oxygen delivery, ml/min/m2	415,4±62,2	403,9±76,2	398,7±70,4
Oxygen recovery, %	27,4±7,0	26,4±6,6	28,1±6,9
Note: P>0.05.			

At the beginning, before the start of anesthesia, the heart index was almost the same in all 3 groups, there was no statistical difference. But after tracheal intubation, it was observed that the cardiac index increased by 2.6±0.5 L/min/m2 in the propofol group and decreased by 2.3±0.5 L/min/m2 in the sevoflurane and isoflurane groups. However, propofol decreased the cardiac index by 2.5±0.5 l/min/m2 before entering the artificial circulatory system, while inhalation anesthetics remained almost at the same level in the sevoflurane and isoflurane groups (2.3±0.5 l/min/m2 and 2.3±0.6 l/min/m2) (p=0.4). There was no statistical difference. After weaning from the artificial circulation device, the cardiac index remained at the same level in the propofol and sevoflurane groups (2.5±0.6 l/min/m2 and 2.3±0.5 l/min/m2), while in the isoflurane group it was decreased to 2.3±0.5 l/min/m2 (p=0.04) (Figure 1).

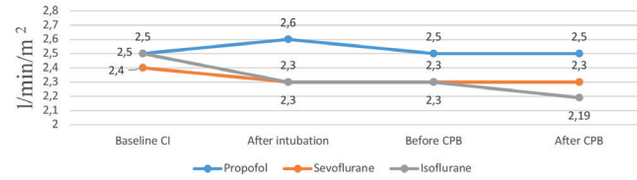

Figure 1 - Changes in cardiac index during surgery.

There was no significant difference between groups in terms of oxygen transport before induction of anesthesia. After tracheal intubation, oxygen transport increased slightly to 429.0±83.4 ml/min/m2 in the propofol group, on the contrary, inhaled anesthetics slightly decreased it (398.6±74.0 ml/min/m2 and 395.1±82, 4 ml/min/m2) (p=0.2). However, it was observed that propofol reduced oxygen transport by 425.0±68.4 ml/min/m2 before entering the artificial blood circulation machine, while oxygen transport in the sevoflurane and isoflurane groups was 397.5±69.6 ml/min/m2 and 387.7±60.6 ml/min/m2 (p=0,096). After leaving the artificial blood circulation device, the oxygen transport index was 421.6±57.0 ml/min/m2 in the propofol group, 396.4±63.2 ml/min/m2 in the sevoflurane group, and 376.7±68.0 ml/min/m2 in the isoflurane group (p=0,025) (Figure 2).

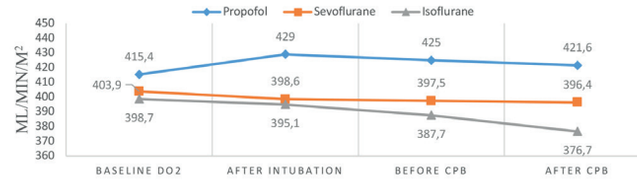

Figure 2 - Changes in oxygen transport during surgery.

There was no difference between groups in terms of oxygen consumption before the onset of anesthesia. After induction of anesthesia, oxygen consumption decreased in all groups, with propofol decreasing oxygen consumption by 111.7±23.7 ml/min/m2, sevoflurane by 109.2±35.6 ml/min/m2, and isoflurane by 121.0±26.4 ml/min/m2 (p=0.2). Before weaning, propofol reduced oxygen consumption by 109.5±23.6 ml/min/m2, while sevoflurane and isoflurane anesthesia reduced it by 108.3±23.8 ml/min/m2 and 118.3±26.9 ml/min/m2 (p=0.2). At the end of surgery, propofol reduced oxygen consumption to 101.5±23.5 ml/min/m2, while sevoflurane and isoflurane anesthesia reduced it to 106.6±22.3 ml/min/m2 and 116.4±21.4 ml/min/ m2 (p=0.037) (Figure 3).

After intubation and connection of a spirometer (UK, Oxford) to the intubation tube, energy expenditure (EE) was found to be 1491.4±199.7 kcal/day in the propofol group, 1497.1±196.6 kcal/day in the sevoflurane group and 1453.5±207.2

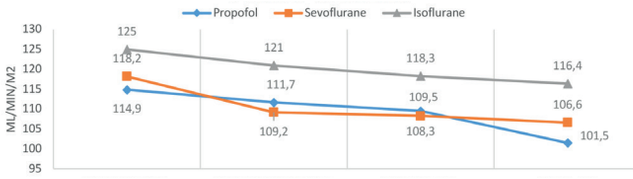

Figure 3 - Changes in oxygen consumption during surgery.

kcal/day in the isoflurane group. All anaesthetics reduced energy expenditure, but propofol anaesthesia significantly reduced it from 1491.4 to 1188.3 kcal/day. However, anaesthesia with sevoflurane did not significantly reduce energy expenditure, energy consumption was decreased to 1389.2 kcal. However, in anesthesia with isoflurane the decrease of energy expenditure was noticeable after CPB, i.e. before CPB it was 1414.9 kcal, and after CPB it decreased to 1289.6 kcal (Figure 4).

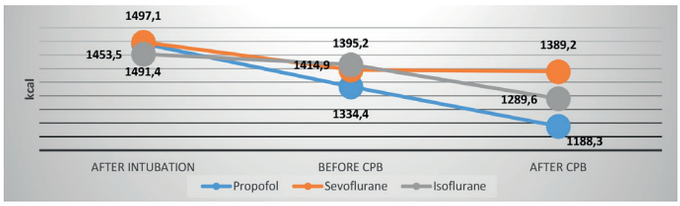

Figure 4 - Changes in energy expenditure during surgery.

Discussion

Traditionally, TIVA and inhalation anaesthesia are used for anaesthesia. The choice of anaesthesia method often depends on the possession of a particular ward tradition, etc. However, there are few studies which have comparatively evaluated their advantages and disadvantages, especially there are no indicators such as O transport2, its utilisation, consumption, energy expenditure.

Anaesthesia has a significant effect on blood circulation and oxidative metabolism, which are closely linked. During prolonged anaesthesia, increased oxygen demand can have adverse effects on haemodynamics. There is an ongoing controversial debate in the literature about the role of different types of anaesthesia in relation to blood oxygen-transport function, O2 uptake and utilisation.

In the immediate postoperative period, the use of sevoflurane prevents the occurrence of bradycardia and a decrease in cardiac index [19]. Increases in propofol blood concentrations decrease vascular stressed volume without a change in cardiac output. The absence of an effect of propofol on cardiac output can be explained by the balance between the decrease in effective, or stressed, volume, the decrease in resistance for venous return, and slightly improved heart function [20]. Anesthesia and surgery have a wide range of effects on the cardiovascular system. Even in healthy patients having minor operations, anesthetic agents can cause significant cardiac depression and hemodynamic instability [21]. Sevoflurane appears to be similar to isoflurane and desflurane with a few exceptions. Sevoflurane was not associated with increases in heart rate in adult patients and volunteers, whereas higher MACs of isoflurane and desflurane and rapid increases in the inspired concentrations of these two anesthetics have been associated with tachycardia. Increasing concentrations of sevoflurane progressively decrease blood pressure in a manner similar to the other volatile anesthetics, and in unstimulated volunteers this decrease may be slightly less than with isoflurane at a higher MAC [22]. Anesthetics have cardiac depressant effects that decrease myocardial oxygen demand and may have a beneficial role on myocardial oxygen balance during ischaemia [23].

According to the results of our research, the effect of anesthetics on cardiac index during coronary artery bypass graft surgery, anesthesia with propofol in a dose 5-6 mg/kg/h increased the cardiac index after tracheal intubation, while inhalational anesthetics decreased it. However, after cardiopulmonary bypass, the heart index was lowered to the initial level and kept at the same level until the end of the operation. And sevoflurane in a dose of - 1.7-1.9 MAC slightly lowered the cardiac index and kept it at the same level until the end of the operation. In anesthesia with isoflurane in a dose of - 1.1-1.2 MAC, after tracheal intubation, the heart index was slightly reduced and it was at the same level after leaving cardiopulmonary bypass, but when we recalculated the cardiac index at the end of the operation, we noticed that its level decreased again.

According to the authors [24] DO_2 did not significantly differ between sevoflurane and propofol. But other researchers [25] observed sevoflurane and propofol had similar effect on PaO_2 during one-lung ventilation when their administration is titrated to maintain BIS between 40 and 60.

Although oxygen transport was initially the same in all groups, after tracheal intubation, its increase was observed in the propofol group, but at this time, on the other hand volatile anesthetics sevoflurane and isoflurane slightly reduced oxygen transport. Also we observed a decrease in oxygen transport in the propofol group before entering cardiopulmonary bypass, while no significant change was observed in the sevoflurane group. However, we noticed that isoflurane further reduced oxygen transport. At the end of the operation, oxygen transport was reduced by propofol to baseline, and sevoflurane had almost no effect on it. Anesthesia with isoflurane significantly reduced DO_2.

The author [17] states that oxygen consumption is independent of the type of anaesthetic. In addition, the researchers [13] argue that further investigation is necessary. VO2 decreased after anaesthesia induction by – 65 ml/min [10].

After induction of anesthesia, oxygen consumption decreased in all anesthetic groups, but sevoflurane reduced oxygen consumption significantly more than the other anesthetics. Isoflurane steadily reduced oxygen consumption from the beginning to the end of the operation. However, sevoflurane had almost no effect on oxygen consumption after tracheal intubation.

A significant decrease in oxygen consumption under propofol anesthesia was observed after cardiopulmonary bypass.

Median energy expenditure under general anesthesia is about one-quarter lower than preoperative awake resting energy expenditure in patients having noncardiac surgery [26].

Energy expenditure was decreased significantly before entering the cardiopulmonary bypass under sevoflurane anesthesia, but its decrease slowed down towards the end of the operation. However, isoflurane significantly reduced energy expenditure from the beginning to the end of anesthesia. In addition, compared to inhalation anesthetics, propofol significantly reduced energy expenditure.

Limitations of the study

This study has 2 limitations. The first limitation is that it was a single-center study. The second limit of our study is the sample size. Because the sample size affects the statistical significance of the study. But we believe that randomized controlled trials with a large number of patients are needed.

Conclusion

In conclusion, isoflurane significantly reduced cardiac index compared to propofol and sevoflurane. Oxygen transport was higher in the propofol group than volatile anesthetics, and propofol reduced oxygen consumption more than inhalational anesthetics. In addition, energy expenditure was the lowest in the propofol group than in the other anesthetics.

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