



Impact of General Anesthesia on the Activity of Lipids Peroxidase Oxidation During Cardiac Surgery for Elderly Patients

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Abstract

This paper examines lipid peroxidation (LPO) dynamics and antioxidant system (AOS) values in 43 patients (aged $69,11 \pm 1,99$, with the weight of 83.7 ± 1.15 kg) during coronary artery bypass graft (CABG) surgery with cardiopulmonary bypass (CPB).

The use of propofol resulted in the increase of diene conjugates number (DC) by $17.1 \pm 0,40\%$ on the background of higher values of malondialdehyde (MDA) $18.4 \pm 1,08\%$ relative to previous values. While with the use of sevoflurane an increase of DC level by $30.1 \pm 1,88\%$ on the background of MDA decrease by $19,03 \pm 1,01\%$ was noticed.

By the end of the operation propofol group showed a decrease in DC values by $20,14 \pm 1,93\%$ compared to the previous values and MDA level decrease by $42.8 \pm 1,99\%$ on the background of a questionable increase of ceruloplasmin level (CP). While with the use of sevoflurane we could observe DC decrease by $39.1 \pm 1,84\%$ compared to the previous values on the background of CP level increase by $28.8 \pm 1,82\%$.

Thus, the anesthetics under study showed differently directed effect on prooxidant and antioxidant systems of the body and a more distinctive effect on the increase of ceruloplasmin antioxidant level was determined with the use of sevoflurane.

Keywords: Elderly Age; Coronary Bypass Surgery; Lipid Peroxidation; Sevoflurane; Propofol.

1. Introduction

Studies conducted over the past 15 years (W. B. Batchelor, 2000 [7]) have proved efficiency of myocardial revascularization among elderly patients. However, elderly patients (older than 60) are at high risk because of the frequency of polymorbidly states occurrence. Moreover, changes of the body's response to surgical stress and cardiopulmonary bypass among elderly patients require special attention to the choice of anesthetics and, in particular, to their effect on pro-oxidant and antioxidant systems of the body.

2. Literature review

LPO is the oxidation of lipids by molecular oxygen which is implemented through the stage of formation of peroxides and hydroperoxides [1, 2]. During the lipid peroxidation the joining of molecular oxygen to the molecules of unsaturated fatty acids occurs, phospholipids of cell membranes join lipoproteins of blood plasma [2, 3].

In anesthetic practice it is believed that LPO activation is initiated by operational stress, which includes factors of surgical aggression, influence of general anaesthesia, etc [4]. Thus, in the works by H. Türkan et al. (2011) the facts of prooxidant activity of sevoflurane, izofluran and halothane [5] are given. Kobayashi K. et al. (2008) describe antioxidant and cytoprotective properties of propofol and fentanyl combination [6].

However, until now in studies conducted in cardiac surgical practice none of the anaesthetics has shown its clear advantages as to its influence on AOS [5,6].

3. Methodology

The purpose of the study was to evaluate the influence of different types of anesthesia on the dynamics of prooxidants and antioxidants at different stages of CABG surgery among patients of elderly and senile age.

The study included 43 patients with coronary heart disease (CHD), which on the basis of the state institution 'Institute of heart of the Ministry of health of Ukraine' (Kyiv) underwent CABG with the superimposition of three coronary anastomoses under the conditions of artificial blood circulation. The age of patients ranged from 62 to 78 years (average $69,11 \pm 1,99$ years). The average weight of patients was $83,7 \pm 1,15$ (from 69 to 114 kg).

For the study we selected the patients whose somatic state corresponded to 3 - 5 points of the European system of estimation of operative intervention risk among patients with coronary artery disease.

Depending on the type of anesthesia used the patients were divided into 2 groups. The first group (n = 22) consisted of patients for whom sevoflurane was used as hypnotics (1.5 to 2.5 MAC).

In the second group of patients (n = 21) anesthesia was performed using continuous infusion of propofol at a target concentration of $2.08 \pm 0,44$ mg/kg/hour.

For analgesia fentanyl ($25 \mu\text{g/kg}$ during all the surgery process) was used in both groups. Relaxation was provided with pipercuronium bromide.

CPB was performed under the conditions of moderate hypothermia (central temperature from $+28^\circ\text{C}$ to $+30^\circ\text{C}$). The performance of heart-lung machine during the perfusion period was 2.5 l/min/m^2 .

On the main stage of operation artificial electric cardiac fibrillation was used for local cardiac protection. It was carried out using the apparatus of the alternating current ("Shtocer", Germany). At this there was a natural perfusion of the coronary arteries due to blood circulation by the heart and lung machine.

Through the process DC, MDA, serum lipids oxidation degree (OD) were defined to determine the activity of oxidative stress. The content of primary peroxidation products LPO was determined by their extraction from the plasma using heptane-isopropanolamine mixture with the subsequent measurement of optical density at the wavelength of 233 and 218 nm, and expressed in DD233 and DD218 per 1 ml of plasma.

The state of antioxidant system in blood serum was measured by the level of extracellular adaptive antioxidant enzyme CP, which was determined spectrophotometrically.

Samples of patients blood serum for the study were taken three days before the surgery (stage I), at the beginning of surgery (stage II), before CPB (III stage), after CPB and restore coronary blood flow (stage IV) and at the end of the operation (stage V).

The analysis of obtained results was performed on a personal computer with use of applied programs "Excel 2007" and "Statistica 6". For all comparisons, p less than 0.05 is considered statistically significant.

4. Data Analysis

Data presented in Table 1, indicate that all the patients with ischemic heart disease had DC and MDA concentrations increased almost twice at their admission to the clinic.

During the period of anesthesia and before the beginning of CPB the dynamics of free radical oxidation indicators and changes in the antioxidant system were not observed.

However, at the fourth stage of the study there was an increase of DC level. Moreover, in the group where anesthesia was performed using propofol the increase of DC values was $17.1 \pm 0,40\%$ compared to the previous values. It was by $22.9 \pm 1,12\%$ greater compared to the baseline values.

In the group of patients for whom sevoflurane was used the rise of the DC values compared to the previous indicators amounted to $30,1 \pm 1,88\%$.

At the V stage of the study the propofol group showed a decline in the values of DC by $20,14 \pm 1,93\%$ compared to the previous ones, which reached almost to the original level. At the fifth stage of the research in the sevoflurane group of patients DC values decreased by $39.1 \pm 1,84\%$ compared to the previous values.

The level of DC in this group was 7.6% less compared to similar values which were obtained in propofol group.

In the process of MDA dynamics study statistical intergroup differences were not observed before the III stage in both groups. But in postperfusion period (stage IV of the studies) in propofol anesthesia group MDA increased by $40,2 \pm 1,01\%$ compared to the baseline indicators and by $18,4 \pm 1,08\%$ compared to previous values.

In the group of patients for whom anesthesia with sevoflurane was used after the restoration of natural blood flow (stage IV) the values of MDA decreased compared to the previous values by $19,03 \pm 1,01\%$.

By the end of the operation the trend of MDA decrease acquired a reverse pattern: in the group of patients for whom propofol was used as hypnotic the percentage of reduced compared to the previous values and amounted to $42,8 \pm 1,99\%$. At the same time in sevoflurane group the percentage of MDA level reduction compared to the previous values was only $9,83 \pm 0,15\%$.

In the process of antioxidant system activity study which we tracked according to CP level it was noted that its value was changing unidirectionally decreasing significantly in both groups.

The greatest changes of CP values were observed at the fourth stage when in anesthetic propofol group they decreased by $17,2 \pm 1,01\%$ compared to the previous values and by $23,3 \pm 1,89\%$ compared to the baseline indicators. At that CP reduction was less noticeable in the group with sevoflurane anesthesia: compared to the previous values they decreased by $6,6 \pm 0,51\%$, and in comparison with the baseline indicators by $11,4 \pm 1,01\%$.

That is the lowest percentage of CP level decrease compared to previous values was observed in the group using sevoflurane as a hypnotic.

In this group by the end of the operation (V stage of the research) we could observe a bigger percentage increase of CP values, the increase of which towards the end of the surgery totaled $28,8 \pm 1,82\%$ compared to the previous values and $19,6 \pm 1,02\%$ compared to the baseline indicators.

Whereas in the group using propofol the increase of CP level at the fifth stage of the research amounted to $8,1 \pm 1,04\%$ compared to the previous values.

Dynamics of Lipid Peroxidation is the AS, Depending on the Type and Stage of Anesthesia (N=43)							
Indicators	Norm	Type of Anesthesia	Etap Study				
			I Stage	II Stage	III Stage	IV Stage	V Stage
DC ($\Delta D233(\text{ml} \cdot \text{mg})$)	0,62±0,03	Propofol	1,15 ± 0,11 ¹	1,20 ± 0,04 ¹	1,24 ± 0,18 ¹	1,49 ± 0,40 ^{1,2}	1,19 ± 0,12 ¹
		Sevoflurane	1,20 ± 0,08 ¹	1,21 ± 0,19 ¹	1,27 ± 0,14 ¹	1,81 ± 0,04 ^{1,2}	1,10 ± 0,02 ¹
MDA (nmol / ml)	1,24±0,07	Propofol	2,15 ± 0,09 ¹	2,23 ± 0,21 ¹	2,93±0,22 ^{1,2}	3,59±0,08 ^{1,2}	2,05 ± 0,19 ^{1,2}
		Sevoflurane	2,28 ± 0,41 ¹	2,32 ± 0,09 ¹	2,89±0,01 ^{1,2}	2,34±0,11 ^{1,2}	2,11 ± 0,04 ^{1,2}
Ox ($\Delta D233/\Delta D218$)	0,54±0,02	Propofol	0,38 ± 0,12 ¹	0,40 ± 0,09 ¹	0,44±0,07	0,36±0,06	0,39 ± 0,03
		Sevoflurane	0,34 ± 0,02 ¹	0,38 ± 0,11 ¹	0,43±0,02	0,33±0,11	0,37 ± 0,08 ²
CP (mg/100 ml)	31,8±2,1	Propofol	31,4 ± 1,12	31,0 ± 1,07	29,1±1,09	24,1±1,88 ^{1,2}	26,2 ± 2,77 ¹
		Sevoflurane	30,8 ± 1,03	29,9 ± 1,02	29,2±1,01	27,3±0,99 ¹	38,3 ± 0,64 ²

Notes: ¹ – p <0,05 rules regarding state; ² – p <0,05 relatively preliminary stage.

DC – diene conjugates; MDA – malonic dialdehyde; Ox – the degree of lipid serum; CP – ceruloplasmin.

Stage I - initial (three days before the surgery); Stage II - the beginning of surgery; Stage III - before cardiopulmonary bypass; Stage IV - after cardiopulmonary bypass and restore coronary blood flow; Stage V - the end of the operation.

5. Results

In the study of DC dynamics under different types of anesthesia the following tendencies were observed:

- In postperfusion period an increase of DC values was observed and a smaller percentage increase compared to previous values was observed in the group with the use of propofol;
- By the end of the operation there was a decrease of DC values which was especially significant in sevoflurane group.

In MDA dynamics at different schemes of anesthesia we noted that at the stage of heart and lung machine switching off in propofol group there was a more significant growth of MDA, whereas in sevoflurane group there was a decline in these values. And at the stage of the surgery finishing in propofol group there was a more significant decrease of MDA values compared to the previous values if to compare with sevoflurane group.

The study of CP values dynamics showed that:

- CP value changed unidirectionally, decreasing significantly in both groups;
- The greatest percentage of these values reduction was observed in propofol group;
- The largest percentage of CP values increase by the end of surgery was observed when using sevoflurane.

In the dynamics of CO values there was no statistical difference in the inter-group values, although there were firm intergroup differences. At all the stages of the research CO level in both groups was below the normal values by $27.7 \pm 2,38\%$ in average.

6. Discussion

Further research will be focused on the study of therapy methods at lipid peroxidation onset during surgery with artificial blood circulation among patients of elderly and senile age with coronary heart disease.

7. Conclusion

- Studied hypnotics (propofol and sevoflurane) had a differently directed effect on the prooxidant and antioxidant body systems of elderly and senile age patients.
- When using propofol in the scheme of anesthesia provision in postperfusion period there was a less significant increase of diene conjugates values on the background of a more significant increase of malondialdehyde level compared to the previous values. While with the use of sevoflurane in this period there was a more significant increase in the level of diene conjugates on the background of malonic dialdehyde decrease.
- When using propofol in the scheme of anesthesia provision by the end of the surgery there was a more significant decrease of malondialdehyde compared to previous values on the background of uncertain increase of ceruloplasmin level.
- When using sevoflurane as hypnotics by the end of the surgery there was a decrease of diene conjugates values on the background of a significant percentage increase of ceruloplasmin level.

8. List of Abbreviations

LPO - Lipid Peroxidation

AOS - Antioxidant System

CABG - Coronary Artery Bypass Graft

CPB – Cardiopulmonary Bypass

DC - Diene Conjugates Number

MDA - Malondialdehyde

CP - Ceruloplasmin Level

CHD - Coronary Heart Disease

OD - Oxidation Degree

9. References

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