Araştırma Makalesi / Research Article

The effect of lung ventilation on total oxidative condition, total antioxidant capacity and oxidative stress index during cardiopulmonary bypass

Kardiyopulmoner baypas sırasında akciğer ventilasyonunun total oksidatif durum, total antioksidan kapasite ve oksidatif stres indeksine etkisi

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Abstract

Background: The aim of this study was to determine the necessity of lung ventilation during cardiopulmonary bypass by comparing the preoperative and postoperative TAS, TOS, OSI values of the patients who were ventilated with 10% volume during cardiopulmonary bypass and without ventilasyaon.
Methods: Totally 30 patients (14 M+ 16 F) that had cardiopulmonary bypass surgery in Thoracic and Cardiovascular Surgery Department for various reasons, were chosen. The patients were seperated into 2 groups (as pulmonary respiration was stopped completely and pulmonary respiration was started by 10% cc volume). Before carrdiopulmonary bypass working group was formed among patients seperated into 2 groups by taking totally 4 tubes of blood before cardiopulmonary bypass, at pump inlet, pump outlet and after operation. After eluting taken blood in centrifuge, they were kept at -80 °C. Then TAS, TOS and OSİ were studied by using Erel method.
Results: Patients were divided into two groups before the cardiopulmonary bypass, at the time of entry to the pump, during the exit from the pump and postoperatively. There was no significant difference between the patients who were ventilated with 10% and non-ventilated patients with TAS values (1.0945 ± 0.25 vs. 1.1514 ± 0.24, p> 0.05). However, in patients who were ventilated at 10%, the value of TOS (15.38 ± 6.10 vs. 25.73 ± 9.25 p <0.05) and OSi value 1.4827 ± 0.67 etc. 2.993 ± 0.85, p <0.05).
Conclusions: In patients who were ventilated at 10% during CPB, TOS and OSI values were significantly lower than non-ventilated patients. This situation shows us that the oxidative stress parameters in the patients who were ventilated 10% during CPB decreased.

Keywords: Cardiopulmonary Bypass, Antioxidants, Oxidative stress.

Öz.

Amaç: Bu çalışmadaki amaç kardiyopulmoner baypas sırasında %10 volüm ile ventile edilen hastalar ile ventilasyon yapılmadan ameliyat edilen hastaların preop ve postop TAS, TOS, OSİ değerlerini karşılaştırarak akciğer ventilasyonunun kardiyopulmoner baypas sırasında gerekliliğini belirlemektir.
Materyal ve Metod: Göğüs Kalp Damar Cerrahisi bölümünde çeşitli sebeplerden dolayı kardiyopulmoner baypas cerrahisi ile ameliyat olan toplam 30 (14 E + 16 K) hasta seçildi. Hastalar 2 gruba (akciğer ventilasyonu tamamen durdurulan grup ve akciğer %10 cc volum ile çalıştırılan grup) ayrıldı. İki gruba ayrılan hastalardan kardiyopulmoner baypas öncesinde, pompaya giriş sırasında, pompadan çıkış sırasında ve ameliyat sonrası olmak üzere toplam 4 jelsiz tüpe kan alınarak bir çalışma grubu oluşturuldu. Alınan kanlar santrifüjde ayrıştırıldıktan sonra plazmaları -80 °C'de saklanarak numunelerin çalışma gününde Erel yöntemiyle total oksidatif stress, total antioksidan kapasite ve oksidatif stres indeks çalışıldı.
Bulgular: İki gruba ayrılan hastalardan kardiyopulmoner baypas öncesinde, pompaya giriş sırasında, pompadan çıkış sırasında ve ameliyat sonrası olmak üzere toplam 4 farklı zamanda kan alındı. %10 ventile edilen hastalar ile ventile edilmeyen hastalar arasındaTAS değerleri açısından anlamlı bir farklılık saptanmadı (1,0945±0,25 vs. 1,1514±0,24, p>0.05). Ancak %10 ventile edilen hastalarda, TOS değeri (15,38±6,10 vs. 25,73±9,25 p<0.05) ve OSi değeri 1,4827±0,67 vs. 2,2993±0,85, p<0.05) anlamlı olarak düşük idi.
Sonuç: KPB sırasında%10 ventile edilen hastalarda, ventile edilmeyen hastalara göreTOS ve OSİ değerleri anlamlı olarak daha düşüktür. Bu durum bize KPB sırasında%10 ventile edilenhastalardaki oksidatif stres parametrelerinin azaldığını göstermektedir.

Anahtar sözcükler: Kardiyopulmoner baypas, Antioksidanlar, Oksidatif stres

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Introduction

In the past in order to provide gas exchange extracorporeally Disc Oxygenerators were used however since they made more blood damage, lately Bubble Oxygenerators that works with a principle of mixing gas bubbles to blood stream was used. Today, however, Membrane Oxygenerators in which blood and fresh gas stream are seperated from eachother by filters having 0,2 µ'luk pores, are widely used (1,2).

Besides great advantages of Cardiopulmonary bypass, there are also many side effects on many organs such as respiratory, circulatory due to preoperative and nonphysiological processes. Disruption of erythrocytes, disorders in coagulation, serious negativenesses on kidney functions and lungs are among these side effects. These side effects are effective on postoperative morbidity and mortality (3,4). The most important postoperative complication after cardiac surgeries is inhibition in gas Exchange due to pulmonary disfunction. Many factors affect decrease of postoperative pulmonary functions. These are preoperative factors, median sternotomy, suffocate lungs with periods, blood transfusion, opening of pleura and excretion of internal mammarian artery (IMA).

In CPB the integrity and mechanism of thoracic wall disorders due to surgical incision. The thickness of respiratory membranes are 6 micron. As pumping period extends, the possibility of lung disorder that may occur in pulmonary functions increases. The lungs are also activated via alternatively by contact of blood with extracorporeal cycles (C3a, C5a) or via classically by protamine antagonization (C4a, C3a) and with endotoxine oscillation to circulation it is exposed to inflammatory responses in blood by stimulating both classical and alternative ways. Complement activation of C3a and C5a causes activation of leucocytes (5,6,7). After cardiac surgery atelectasis and collapsed lung are some of the common situations. During CPB the heart is motionless on left lower lobe of lung. As pleural space is opened, the lung is compressed with entering of blood and fluid. In patients having Coronary revascularization laft pleural space can be entered with LİMA dissection. With these factors after CPB left lower lobe atelectasis of 60 – 70 % can be seen (8). It was reported that icy water used during Cardiopulmonary Bypass (CPB) to provide topical hypothermia to myocard causes hemidiaphragm elevation due to hypothermic phrenic nerve injury, as a result this situation causes atelectasis (9,10).

The lungs are under extreme risk during extracorporal circulation due to activation of blood compounds. These risks can be capillar leak syndrome or acute respiratory insufficiency and can develop as a result of a situation generating from the functions of extracorporal circulation with metabolic functions of bypass (11).

During cardiopulmonary bypass respiration is completely stopped and ventilation is started as cardiopulmonary bypass is ended. The aim in this study is to research the necessity of lung ventilation during bypass by starting respiration of a group of patients with 10% volume and the other group stopping respiration totally as well as by examining Total Antioxidant Status (TAS), Total Oxidant Status (TOS) and Oxidative Stress Index (OSİ= TOS/TAS) values in pre-op and after bypass.

Materials and Methods

Totally 30 patients (14 M+ 16 F) that had cardiopulmonary bypass surgery in Thoracic and Cardiovascular Surgery Department for various reasons, were chosen. The patients were seperated into 2 groups (as pulmonary respiration was stopped completely and pulmonary respiration was started by 10% cc volume). Before cardiopulmonary bypass working group was formed among patients seperated into 2 groups by taking totally 4 tubes of blood before cardiopulmonary bypass, at pump inlet, pump outlet and after operation. Approval of the Ethics Committee of Clinical Investigations for the study was approved with the decision no 12/03/33 on 18.05.2012. All patients were informed about the treatment to be applied in accordance with the Helsinki Declaration and the informed consent form was obtained from the patients.

Adult patients apart from age below 18, ones having cronical kidney failure, tuberculosis endocarditis malign disease and pregnants that will be taken to open heart surgery, were taken to study. Standart anesthesia protocole, venous and coronary sinus blood were taken. In the patients taken to study operations after sternotomy following aortic and venous cannulation at 28-32 °C cardiopulmonary bypass and under cross clamp operations were completed. The first blood samples were taken from patients without having any intervention. The second samples were taken at pump inlet, the third samples at pump outlet andthe fourt samples were taken just after sternum was closed. The obtained heparin containing blood samples were centrifuged at 4000 rpm and were kept at -80 °C in Medical Faculty Biochemistry Lab. Then Total oxidative stress, Total antioxidant capacity and oxidative stress index were studied by using Erel method (12,13). This study was done on 30 patients that were applied elective open heart surgery (coronary artery grafting, cover replacement- repair) by using CPB. Clinical Researches Ethics Committee Approval was taken for this study. All the patients were informed about treatment suitable to Helsinki Decleration and informed consent form were taken from patients as well.

Patients needing urgent surgical treatment, before operation having blood creatine value >1.3 mg/dl, hematocrit value <%30, ejection fraction ≤%35, patients unable to apply extracorporeal circulation, patients having multi operations, ones having applied synchronous noncardiac surgical operations, patients having high CRP and WBC values before operation, were excluded. All the patients were applied median sternotomy. Following systematic heparinization (300 IU/kg, Roche Pharmaceutical, Mannheim, Germany) arterial from aort, from right atrium with venous cannulation CPB was applied. Activated clotting time was kept over 480 seconds. In all patients standart CPB, surgical and perfussion technics were used. Surgical operations were done at 28º-32 ºC.

The age average of participant patients was calculated as 60,83. TAS value was calculated as µmol Trolox Eq/L olarak, TOS value as µmol H2O2 Eq/L and OSİ value was calculated as TOS (µmol H2O2 Eq/L)/TAS (µmol Trolox Eq/L).

Statistical Analysis

Statistical analysis SPSS (SPSS Inc. Chicago, Illinois, USA) 16.0 version statistical software programme was used. p<0.05 values were accepted significant. Datas of patients were given as average ± standart deviation. The comparison between two groups were done by Student's t-test. For evaluation of comorbidity distribution in all groups Chi-square test was used. In order to evaluate significancy of differences between values, two way variance analysis was done.

Results

There was no significant difference between the patients who were ventilated with 10% and non-ventilated patients with TAS values (1.0945 ± 0.25 vs. 1.1514 ± 0.24, p> 0.05). However, in patients who were ventilated at 10%, the value of TOS (15.38 ± 6.10 vs. 25.73 ± 9.25 p <0.05) and OSi value 1.4827 ± 0.67 etc. 2.993 ± 0.85, p <0.05).

The first blood samples were taken from patients without having any intervention, the second samples were taken at pump inlet, the third samples at pump outlet andthe fourt samples were taken just after sternum was closed.In the patients in working group that were ventilated with %10 volume, TAS value was found as 1,0945±0,25, TOS value as 15,38±6,10 and OSi value was found as 1,4827±0,67. In unventilated patients TAS value was found as 1,1514±0,24, TOS value as 25,73±9,25 and OSi value was found as 2,2993±0,85. As a result of statistical evaluations TOS and OSİ values were found as p<0,05 and this was accepted as significant. TAS, TOS and OSİ averages regarding patient groups were given in Table 1. %10 TAS change in ventilated and unventilated patients was presented in Figure 1, TOS change was presented in Figure 2 and OSi change was presented in Figure 3.

Table 1. The oxidative stress index averages of 10% ventilated and non-ventilated patient groups.

	TAS **µmol** Trolox Eq/L	TOS **µmol H2O2 Eq/L**	**OSİ µmol H2O2 Eq/L/ µmol** Trolox Eq/L
10% ventilation	1,0945±0,25	15,38±6,10	1,4827±0,67
Non-ventilated	1,1514±0,24	25,73±9,25	2,2993±0,85
p-value	*p>0,05*	*p<0,05*	*p<0,05*

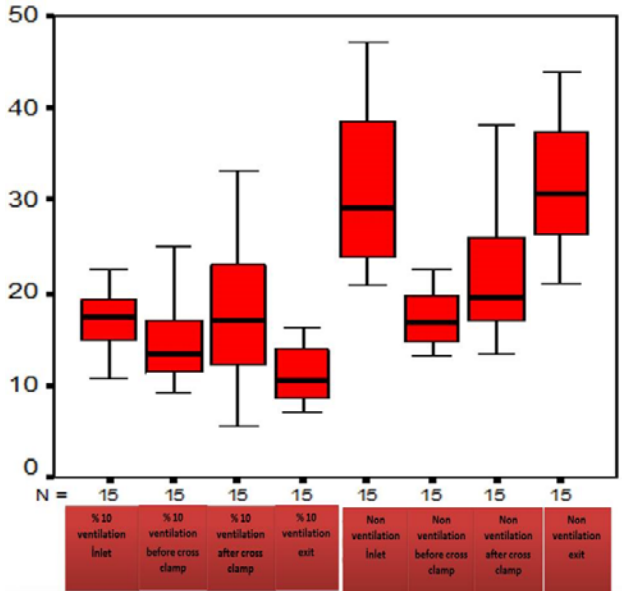

Figure 1. TOS change in 10% ventilated and non-ventilated patients.

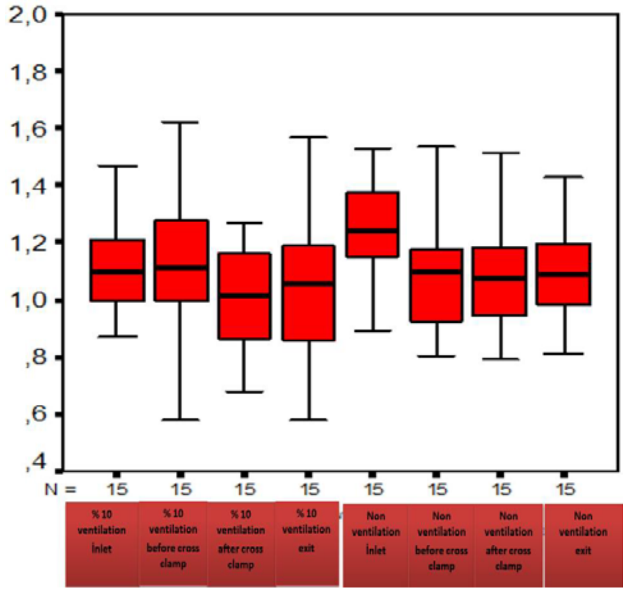

Figure 2. TAS change in 10% ventilated and non-ventilated

patients.

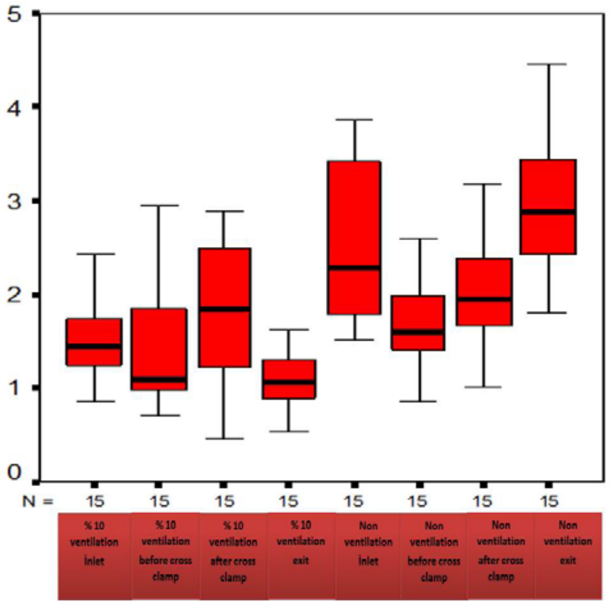

Figure 3. OSI change in 10% ventilated and non-ventilated patients.

Discussion

Today the mortality rate due to cardiac diseases places in the first rank among all mortality reasons. The age of the heart patients is even lower and surgical treatment of most of these patients is performed by cardiopulmonary bypass (CPB).CPB has an important place in cardiac surgery application. These surgical applications can be done by means of Heart and Lung Machine (HLM) that provides heart and respiratory functions temporarily. Although HLM does not give clinical finding in all the patients, it causes morbidity at cellular and molecular level (14). CPB is a system that pumping function of heart and gas exchange function of lungs are connected to venous and arterial vein system of patient temporarily with a pump and an oxigenerator. Heart and Lung Machine should perform the duty of lungs for gas exchange as well as the duty of heart for blood circulation.

In this system that is also named as Extracorporeal Circulation, the blood gathered in venous reservuar via two cannulas placed on superior vena cava and inferior vena cava or via single cannula placed on right atrium, is directed to oxigenerator via pump head and from there it is given back to patient with an arterial cannula placed on aort by filtering and changing the heat of blood via heating and cooling. Accordingly venous blood gathers around CPB without entering heart and from there is sent back to larger artery by taking out carbondioxide and adding oxygen via oxigenerator.

Although the reliability of CPB technology has incresed considerably from its first usage up today, postoperative pulmonary complications still come out as an important problem (15). Some of the studies showing the existence of pulmonary damage during CPB indicate that leucocyte filtration decreases extracellular pulmonary fluid, decreases pulmonary vascular resistence (PVR) compared to control group (8) and reduces postoperative oxygen requirement (8-9). Bando et. al in their histological examination of lungs after CPB, they found that there are intravascular leucocyte aggregation, perivascular hemorrhage and focal alveole damage; there is not any or at minimal level in leucocyte filtration applied patients (16). Kirklin et. al reported pulmonary complication rate after CPB as 30% however they used non specific methods such as trakeal secretion measuring in their studies (17). As Hammermaister et. al reported the rate of patients applied ventilation more than 48 hours after CPB for more than 8000 patient group as 8% (18), Taggart et. al in their study done in 129 patients reported this rate as 7 patients or 5% (19).

John and Ervin (20) in their study during CPB they ventilated 12 patients with 5 ml kg-1 tidal volüme whereas 11 patients did their respiration. As working group was examined, they reported that they found extubation period statistically significantly short and continuous ventilation has a positive effect on pulmonary functions during CPB. It has been shown that pulmonary dysfunction after cardiac surgery may decrease with mechanical ventilator strategies applied during CPB (21-23).

During cardiopulmonary bypass myocardium cannot be perfused in a specific period and accordingly myocardium is exposed to global ischemic damage. The reason of this damage in myocardium is generally free oxygen radicals occured during reperfusion and oxidative stress. As a result of our study when two groups are compared, there does not occur a significant difference in TAS value, there comes out a significant result in terms of TOS and OSİ values. During CPB TOS and OSİ values of unventilated patients were found significantly high compared to 10% ventilated patients. This situation shows us that during CPB oxidative stress parameters reduces in 10% ventilated patients.

Lung dysfunction after open heart surgery is an important problem that extends the duration of stay in extubation and intensive care unit (24,25). Failed extubation and reintubation increase the duration of mechanical ventilation, intensive care stay and discharge time, morbidity and mortality (26,27). In a study conducted by Gilbert and colleagues (28) in 18 patients, CPAP was administered to 9 patients during CPB, 9 patients were left on atmos- phere, and CPR was not posi- tively positive on compliance since measurements were made after sternotomy. Patients taken 10% lung ventilation are seen to have positive effects on oxidative stress and this situation made a positive effect on intubate period in intensive care during postoperative period, stability of respiratory functions in a short term and accordingly staying in intensive care unit.

As a result of our study when two groups are compared, there does not occur a significant difference in TAS value, there comes out a significant result in terms of TOS and OSİ values. During CPB TOS and OSİ values of unventilated patients were found significantly high compared to 10% ventilated patients. This situation shows us that during CPB oxidative stress parameters reduces in 10% ventilated patients.

Patients taken 10% lung ventilation are seen to have positive effects on oxidative stress and this situation made a positive effect on intubate period in intensive care during postoperative period, stability of respiratory functions in a short term and accordingly staying in intensive care unit.

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