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Total antioxidant stress and total oxidant stress levels in geriatric patients with open heart surgery

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Abstract

The aim at this study is to compare the association with oxidative stress with the patients over and below the age of 65, who underwent an open heart surgery. In our prospective and a single-center study, 45 patients, undergoing an elective isolated on-pump CABG and heart-valve surgery, were included. The patients were divided into two groups, including Group I (at the age of 65 over) and Group II (at the age of 65 and below). The serum total oxidant status (TOS) and total antioxidant status (TAS) values were assessed in the patients, by taking blood at the first hour before and after the pump. There is no statistically significant differences between preoperative and postoperative TAS and TOS values within the groups. However, the postoperative TOS value in Group I is statistically greater than Group II. TAS and TOS in organism is affected by many factors. Further controlled studies are needed on this topic.

Keywords: Heart surgery, total antioxidant stress, total oxidant stress, oxidative stress

Introduction

Oxidative stress has been reported to increase in the elderly subjects, possibly arising from an uncontrolled production of the free radicals by aging mitochondria and decreased antioxidant defenses [1-3]. There is abundant experimental and observational evidence supporting the idea that aging is the sum of all free radical reactions throughout all cells and tissues. However, the results of studies investigating oxidative stress in aging are still controversial. In humans, there are Elderliness begins with the age of 65 according to World Health Organization (WHO). Aging is the irremediable structural and functional changes, occurring in our body's molecules, cells, tissues, and organs, and revealing the progression of time [4]. The functional and anatomical changes occur in the molecular, cellular, tissular and organal structures with aging. The incidence of coronary artery disease and degenerative cardiovascular diseases shows an increase with advanced age.

Oxygen, fat, protein and lipids are necessary to have energy in the metabolism. However, they may transform into the reactive and detrimental substances, also called as oxygen free radical (FR). The damages created by FR are known that they have important contributions to the disorders in aging, cardiovascular diseases,

immune disorders, and cancer and brain functions [1]. While

a certain part of the antioxidants, trying to prevent the damages created by free radicals, was the enzyme; another certain part of them composed of the non-enzyme molecules. Although the body's antioxidant/oxidant situation may be evaluated by separately measuring the antioxidant enzymes' activity and antioxidant/oxidant molecules' concentration, the general antioxidant/oxidant situation may be easily evaluated by measurement of the total antioxidant situation (TAS) and total oxidant situation [5,6].

The aim at this study is to compare the association with oxidative stress with the patients over and below the age of 65, who underwent an open heart surgery.

We searched the changes of oxidative stress by comparing the serum TAS (Total Antioxidative Stress) and TOS (Total Oxidative Stress) levels in the patients over and below the age of 65 geriatric patients, undergone an open heart surgery.

Material and Methods

The TAS and TOS levels were measured by taking blood at the first hour before and after pumping for the patients, divided into Group I (n=20) and Group II (below the age of 65, n=25). The patients having chronic kidney failure and liver disease were not included in the study.

A standard anesthesia protocol is performed for all patients. After 0.1 mg/kg midazolam premedication a radial artery cannulation was made for the hemodynamic follow-up. All subjects were breathed with 100% O₂ and intubated with 5-7 mg/kg thiopental, 5 mcg/kg fentanyl and 0.6 mg/kg rocuronium bromide during the anesthesia induction. In the maintenance, 5-6% desflurane, 50% O₂ and 50% dry air, rocuronium bromide and fentanyl were used. The rectal body temperature and urination were followed-up by applying a 3-lumen central catheter from the right internal jugular vein during the surgery.

Body Mass Index (BMI), left ventricular ejection fraction (LVEF), pump time, cross-clamp time, surgery and anesthesia times of the patients were recorded. Cigarette habits, associated diseases and perioperative inotropic uses of the patients were recorded. The study was approved by Ethics Committee of Antalya Education and Research Hospital.

The blood samples were taken within 1-hour of the preoperative (before the anesthesia induction) and postoperative time period. Then, the serum samples were separated from cells for 10 minutes with a centrifuge working in 3000 revolutions a minute (rpm). The lipid parameters and other routine parameters were immediately measured. The remaining sections were kept at -80°C and used to analyze the TOS and TAS.

The data was statistically analyzed by using the statistica 20 for Windows software. The Wilcoxon paired test was used to compare the mean values at each stage of the experiment. The Mann Whitney test was used to compare the differences in TAS and TOS activity between the groups according to their clinical features. The p values less than 0.05 were considered statistically significant.

Results

45 patients, who were included in the study and whose 58% was male, were divided into two groups according to their ages (over and below the age of 65). While the mean age of 20 patients over the age of 65 was 72.35±6.05 in Group I, mean age of 25 patients was found as 46.60±10.50 in Group II (below the age of 65).

While smoking histories of the patients were 30% in Group I, it was 28% in Group II. While the hypertension (HT), diabetes mellitus (DM) and COPD (Chronic Obstructive Pulmonary Disease) between associated diseases were 75%, 45%, and 10%, respectively in Group I; the HT and DM were 52% and 32%, respectively in Group II. There was not a patient having a COPD in Group II. The HT, DM, COPD and smoking history were not significant intergroup between associated diseases (p=0.114, p=0.371, p=0.192 and p=0.883). (Table I).

The information, belonging to operations performed for the patients, takes part in Table II.

While the anesthesia time and surgery time were 202.75±32.54 and 172.25±26.82, respectively in Group I; the anesthesia time and surgery time could not be statistically found significant, when measured them as 188.20±48.60 and 160.60±42.31, respectively in Group II (p>0.05, p=0.25, p=0.29).

The BMI was found as 27.71±4.12 in Group I and as 27.16±5.20 in Group II (p=0.706).

There was not a significant difference statistically in LVEF of the patients in both groups (58.20±7.78 in Group I and 58±9.51 in Group II, p=0.94). Not any significant difference was statistically determined, when compared the pump and cross-clamp times of both groups. While the pump times were found as 68.45±14.06 and 58.44±19.51, respectively p=0.06; the cross-clamp times were found as 38.40±11.33 in Group I and as 33.16±11.93 in Group II p=0.14 (Table I).

While the inotropic medicine was used by 100% of patients in Group I, it was used by 68% of patients in Group II (p=0.005). A significant difference was found intergroup in the perioperative inotropic medicine use (Table I).

While the preoperative TAS values were 2.05±0.28 in Group I in which the geriatric patients took part; not any change was seen in the postoperative period (2.08±0.39). The preoperative and postoperative TOS values were similar in the geriatric patient group. The preoperative and post-operative TAS and TOS values were also recorded as similar in Group II. However, the TAS values were seen high in the postoperative period and the difference could not be statistically found significant (1.92±0.21, 2.02±0.24) (p: 0.52, p>0.05). While the preoperative TOS value was 3.97±4.58 in Group II, it was seen as 1.93±2.27 by decreasing it to the postoperative period.

Not any significant difference was statistically found by the preoperative and postoperative TAS and preoperative TOS, when compared in terms of the preoperative and postoperative TAS and TOS values in both study groups. However, while the postoperative TOS value was 4.30±4.88 in Group I, it was specifically seen as low with 1.93±2.27 values in Group II. This difference was statistically found significant (p=0.03).

Table 1. Comparison of preoperative and intraoperative clinical characteristics between the two groups

	Group I (n=20)		Group II (n=25)		P
	n	%	n	%	
Women	6	30	0,138	52	0,138
Smokers	6	30	0,883	28	0,883
Hypertension	15	75	0,114	52	0,114
Diabetes Mellitus	9	45	P	32	0,371
Inotropic drug use	20	100		68	0,005*
COPD ¹	2	10	0.138 0.883	0	0.192
	Mean±SD		0.114	Mean±SD	
Age (years)	72.35±6.05		P	46.60±10.50	0.001
BMI(kg/m ²)	27.71±4.12			27.16±5.20	0.706
LVEF3	58.20±7.78		0.138	58±9.51	0.940
Pump time(min)	68.45±14.06		0.883	58.44±19.51	0.061
Cross-clamp time(min)	38.40±11.33		0.14	33.16±11.93	0.142
Surgery duration(min)	172.25±26.82		P	160.60±42.31	0.291
Anesthesia duration(min)	202.75±32.54			188.20±48.60	0.258

¹COPD: chronic obstructive pulmonary disease, 2BMI:Body Mass Index, LVEF3: Left ventricular ejection fraction,SD:Standard deviation, *p< 0,05

Table 2. Types of operations performed in groups

	Group I (n=20)	GroupII (n=25)
CABG ¹		
2 greft	2	2
3 greft	10	7
4 greft	2	3
Aort valve replacement	3	4
Mitral valve replacement	3	9
CABG ¹ : Coronary Artery Bypass Greft		

Table 3. TAS and TOS values of groups

	Group I (n=20)	Group II (n=25)	P value
Preoperative TAS ¹	2,05±0,28	1,92±0,212	0,07
Postoperative TAS ¹	2,08±0,39	2,02±0,247	0,52
Preoperative TOS ²	4,43±4,47	3,97±4,58	0,73
Postoperative TOS ²	4,30±4,88	1,93±2,27	0,03*

TAS¹: Total Antioxidative Stress, TOS²: Total Oxidative Stress. *P<0,05

Discussion

It is known that the oxidative stress induces or promotes various diseases such as atherosclerosis and heart diseases, cancer, neurodegenerative diseases (Alzheimer disease, Parkinson's disease), hypertension, diabetes mellitus and aging [7-15]. It is also argued that the oxidative stress constitutes one of the main factors, responsible for the ischemia/reperfusion injury.

It is well-known that various antioxidants in the plasma have an additive effect, protecting the organism from the free radicals [16]. In this respect, the measurement of TAC provides information about the antioxidant capacity of an organism [17]. The previous studies showed that the plasma antioxidant capacity was significantly reduced by the CAD patients. Demirbag et al showed that the TAC is decreased and DNA damage is increased by the CAD patients, when compared with the normal subjects [18]. The DNA damage is negatively correlated by the TAC and it is positively correlated by the severity of CAD. In another study, Demirbag et al found a strong correlation between the TAC level and severity of aortic atherosclerosis [19].

In our study, we searched the changes in oxidative stress by comparing the serum TAS (Total Antioxidative Stress) and TOS (Total Oxidative Stress) levels in the geriatric patients over the age of 65 undergone an open heart surgery and in the patients below the age of 65. We aimed at showing advanced age's changes on the oxidative stress response made to the patients, undergone an open heart surgery.

The oxidative stress occurs as a result of excessive forming into the oxidants, decreasing to the antioxidants or combination of both of them in the body. Although we found the postoperative TOS, a general indicator of the oxidant molecules, high in the geriatric patient group (Group I); we saw a significant difference between them, when compared with Group II (below the age of 65).

Alessandra et al compared the solid gynecologic tumor patients and smoker patients in terms of the oxidative stress. While the

total oxidative stress (TOS) was 8.08±3.43 in smokers, it was statistically found significant as 5.40±2.93 in the gynecologic tumor patients (p=0.0003) (20).

In our study, the TOS values were found high in the preoperative (4.43±4.47) and postoperative (4.30±4.88) periods in the geriatric patient group. The number of smokers is similar in both groups. Therefore, we think that this high level in the TOS value does not have a relationship to the cigarette.

On the other hand, the antioxidant levels may be used as a diagnosis or prognosis indicator in some subjects. Measurement of the whole blood antioxidant capacity of an organism may give us valuable biological information about the status of an organism.

At present, there are no consistent perspectives on an age-associated change of the antioxidant capacity. The certain researchers studied the presentation of catalase, peroxide oxidase, some antioxidant vitamins, lipid peroxidation or protein and DNA oxidation, and they found an increase or decrease of the different factors with the age [21, 22]. In most subjects, a serum Total Antioxidant Capacity (TAC) was observed to increase with the age.

In our study, while the preoperative TAS values were 2.05±0.28 in Group I in which the geriatric patients took part, not any change was seen in the postoperative period (2.08±0.39). The preoperative and postoperative TOS values were similar in the geriatric patient group. The preoperative and postoperative TAS and TOS values were also recorded as similar in Group II (Table III). However, the TAS values were seen as high in the postoperative period and the difference could not be statistically found significant (1.92±0.21, 2.02±0.24) (p: 0.52, p>0.05). While the preoperative TOS value was 3.97±4.58 in Group II, it decreased and was seen as 1.93±2.27 in the postoperative period. The TOS values' decrease was statistically significant in Group II, a geriatric patient group (p<0.05).

Not any difference could be statistically found significant by the preoperative and postoperative TAS and preoperative TOS, when compared in terms of the preoperative and postoperative TAS and TOS values in both study groups.

However, while the postoperative TOS value was 4.30±4.88 in Group I, it was specifically seen as low with 1.93±2.27 values in Group II. This difference was statistically found significant (p: 0.03, Table III)

In most subjects, a serum Total Antioxidant Capacity (TAC) was observed to increase to the age. However, the different measurement methods lead to the different results. For example, measurement of the FRAP method, which may not determine the antioxidants with sulfhydryl groups, showed a decrease in TAC with the age [23, 24]. In other studies, an increase in TAC with the age was found as the second observation for the patients suffering from the cancer disease [25]

Gupta R et al collected the blood samples of 146 volunteers and divided them into three age groups. They showed a substantial increase at the rate of 79% according to the low serum total antioxidant capacity (TAC) in young-aged (18-35 age) individuals when compared with middle-aged and aged individuals, and found that the total serum antioxidant situation increased by the age [23,

24]. In another study, an increase in the TAC and patients suffering from the cancer was observed with the age [25].

In our study, the geriatric patients took part in Group II. The TAS and TOS values in Group II patients were found higher than Group I, in which the patients below the age of 65 took part. However, the difference between two groups was not significant statistically in terms of the TAS and TOS values.

The factors such as gender, stress, physical activity, smoking and diet also affect the total anti-oxidant capacity [26-28]. It was stated that the habits such as cigarette and malnutrition, oxidative stress and diet antioxidant intake might increase the total antioxidant capacity [29,30].

Kunt As et al measured the antioxidative situations and oxidative changes in 79 patients, whose on-pump coronary artery bypass grafting was performed. They evaluated the antioxidant situation by measuring the total antioxidant capacity (TAC) and discussed the oxidative situation by measuring the total peroxide (TP) and OSI. They found a progressive decrease of the TAC and increase in the total peroxide (TP) and OSI values after the surgery begins. They also found a positive correlation between the ejection fraction and TAC [31].

In our study, the TAS and TOS values were compared by the patients, who were applied an on-pump CABG due to the CABG and valve (mitral, aortic) replacement operations. Although not any significant relationship could be established in terms of the TAS and TOS values with advanced age, it is a reality that the TAS and TOS in an organism affected by many factors. In addition, controlled studies and results are insufficient for the relationship between oxidative stresses and aging. Controlled studies, in which broad patient groups take part, are needed on this topic.

Umit Mentese et al divided 23 patients, whose on-pump coronary artery bypass grafting was performed, into two groups according to the cross-clamp times (<42, >42 minutes). They significantly found the TOS levels high ($p<0.015$) at 30th minute according to the patients' preoperative values after the reperfusion and they also found the TAS similar to the preoperative values [32].

Asuman et al researched 70 patients, whose CABG was performed (off-pump and on-pump CABG) and mean age was 64.6 ± 1.2 . They could not find a significant difference in the antioxidant enzyme activities such as TAS, PON and AES and consequently, and they proved that the antioxidant situation did not have a relationship of the CABG technique [33].

Viviana et al measured the urine isoprostane (IPF2-III) excretion and free malondialdehyde (MDA) level in the plasma related to the oxidative stress in 50 patients, whose coronary artery bypass grafting (CABG) and off-pump coronary artery bypass grafting (OPCABG) were performed. They found a lower oxidative stress formation of the OPCABG patients (35).

In our study, our patients were the patients, whose on-pump CABG was applied due to the CABG and valve (mitral and aortic) replacement operations. Not any difference statistically determined significant, when compared the pump and cross-clamp times of both groups. The pump times were found as 68.45 ± 14.06 and 58.44 ± 19.51 , respectively $p=0.06$, and the cross-clamp times were determined as 38.40 ± 11.33 in Group I and as 33.16 ± 11.93

in Group II $p=0.14$. We think that the differences seen in TAS and TOS values do not have a relationship with the pump.

Conclusion

The recent searches show that the oxidative damage to various biomolecules increases to the age, and the calorie restriction lengthening lifetime and delaying aging decreases the increase, depending on the age for the oxidative damage to biomolecules [34].

Competing interests

The authors declare that they have no competing interest.

Financial disclosure

The financial support for this study was provided by the investigators themselves.

Ethical approval

The study was approved by Ethics Committee of Antalya Education and Research Hospital.

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