International Journal of Nutrology
(Official Journal of the ABRAN - Brazilian Association of Nutrology)

Review Article | Artigo de Revisão

Use of Antioxidants in Cardiovascular Surgery

O uso de antioxidantes em cirurgia cardiovascular

Edmo Atique Gabriel[1] Camila Alcalde Mazza[1] Marina Alves Jacintho de Mello[1]

[1] União das Faculdades dos Grandes Lagos- UNILAGO, Brazil

Int J Nutrol 2018;11:80–86.

Address for correspondence Edmo Atique Gabriel, MD, PhD, União das Faculdades dos Grandes Lagos- UNILAGO, Rua Dr. Eduardo Nielsen, 960, Jardim Novo Aeroporto, 15030-070, São José do Rio Preto, SP, Brazil (e-mail: edag@uol.com.br).

Abstract

Morbidity and mortality due to postoperative complications, related to inflammation and systemic oxidative stress, of coronary artery bypass grafting is high and inadmissible. It is suggested that numerous adverse outcomes may be caused by the systemic effect of cardiopulmonary bypass (CPB). One of the most damaging consequences of these events is the formation of reactive oxygen species (ROS) and radicals, which originate from a variety of cellular and enzymatic sources, such as myocardial cells, activated neutrophils, or endothelial xanthine oxidase. Many studies have described the nature of these ROS and the time of their formation during CPB. With the goal of reducing these damages, studies have investigated the use of antioxidant supplements during CPB. The present study focused on the time course of the innate antioxidant activity (antioxidant enzymes and overall antioxidant capacity in plasma) in patients undergoing CABG. The methodology used was the literature review.

Keywords

- coronary artery bypass grafting
- cardiopulmonary bypass (CPB)
- reactive oxygen species (ROS)

Resumo

Embora a cirurgia de revascularização do miocárdio tenha se tornado um procedimento de rotina em todo o mundo, a morbidade e a mortalidade dos pacientes devido a complicações pós-operatórias adversas ainda são inaceitavelmente altas.

Tem sido sugerido que, além de causar dano miocárdico, uma proporção significativa de desfechos adversos também pode ser causada pelos efeitos sistêmicos da circulação extracorpórea (CEC). Além disso, foi demonstrado que o procedimento com circulação extracorpórea dá origem a inflamação sistêmica e estresse oxidativo mais pronunciado que o procedimento sem CEC.

Os mecanismos que explicam essas observações podem estar relacionados a vários eventos deletérios que ocorrem durante a CEC e que são dependentes do material (causado pela exposição do sangue a superfícies e condições não fisiológicas durante a circulação extracorpórea ou independente de material por trauma cirúrgico, isquemia-reperfusão e alterações no corpo temperatura). Uma das conseqüências mais danosas desses eventos é a formação de espécies reativas de oxigênio (ROS) e radicais, que se originam de uma variedade de fontes celulares e enzimáticas, como células miocárdicas, neutrófilos ativados ou xantina oxidase endotelial.

A fim de contrabalançar essa sequência de eventos e reduzir o dano oxidativo, vários estudos têm investigado o uso de suplementos antioxidantes durante a CEC.

Palavras-chave

- cirurgia de revascularização do miocárdio
- circulação extracorpórea (CEC)
- uso de suplementos antioxidantes

received
October 11, 2018
accepted
December 10, 2018

DOI https://doi.org/10.1055/s-0039-1678705.
ISSN 1984-3011.

Com o objetivo de investigar essa questão, o presente estudo enfocou o curso temporal da atividade antioxidante inata (enzimas antioxidantes e capacidade antioxidante total no plasma) em pacientes submetidos à cirurgia de revascularização do miocárdio. A metodologia utilizada foi a revisão de literatura.

Introduction

Although coronary artery bypass grafting has become a routine procedure worldwide, the morbidity and mortality of patients due to adverse postoperative complications are still unacceptably high. Endothelial injury and/or cardiac, renal, hepatic or pulmonary dysfunction associated with myocardial revascularization surgery (CABG) have been related to the inflammatory responses and to the systemic oxidative stress (OS) caused directly by this procedure, but the underlying mechanisms have not yet been fully elucidated.[1]

It has been suggested that, in addition to direct myocardial damage, a significant proportion of adverse outcomes may also be caused by the systemic effects of cardiopulmonary bypass (CPB). In addition, it has been demonstrated that the procedure with extracorporeal circulation gives rise to systemic inflammation and OS more pronounced than the procedure without CPB. The mechanisms explaining these observations may be related to several deleterious events occurring during CPB that are material-dependent (caused by exposure of blood to surfaces and non-physiological conditions during cardiopulmonary bypass or material-independent, by surgery trauma, ischemia-reperfusion and changes in body temperature). One of the most damaging consequences of these events is the formation of reactive oxygen species (ROS) and radicals, which originate from a variety of cellular and enzymatic sources, such as myocardial cells, activated neutrophils, or endothelial xanthine oxidase. These are closely linked to inflammatory responses, including complement activation, cytokine release and leukocyte activation, along with the expression of adhesion molecules. Many studies have described the nature of these ROS and the time of their formation during CPB. The nature of these oxidative events leads to the depletion of plasma antioxidants, increased lipid peroxidation and the formation of other harmful metabolites. To counterbalance this sequence of events and to reduce oxidative damage, several studies have investigated the use of antioxidant supplements during CPB. Less is known about the consequences of extracorporeal circulation (ECC) in the endogenous antioxidant capacity that is derived from the activity of antioxidant enzymes such as glutathione peroxidase (GPx) and superoxide dismutase (SOD), responsible for the clearance of peroxide and superoxide, respectively.[2]

With the objective of investigating this issue, the present study focused on the time course of the innate antioxidant activity (antioxidant enzymes and overall antioxidant capacity in plasma) in patients undergoing myocardial revascularization surgery. The methodology used was the literature review.

Development

Antioxidants

Oxidative stress is an imbalance between the production of reactive oxygen radicals and the ability of the body's natural protective mechanisms to cope with these radicals and prevent adverse effects. The cells of the body are exposed to ROS under normal circumstances, through electron-chain transport of electrons, phagocytic cells and endogenous systems of enzymes. Oxidation of lipids, nucleic acids, or proteins by these ROS is thought to be associated with the etiology of various age-related chronic diseases, including cancer, cardiovascular disease, cataract, and age. These chronic diseases are responsible for a high percentage of morbidity and mortality, and their prevention is one of the main public health priorities.[1]

Defense systems protect the body from the deleterious effects of OS. These include antioxidant enzymes and antioxidants for radical removal. Antioxidant nutrients, such as vitamin E, carotenoids, and fruits and vegetables rich in antioxidants have been associated with a lower risk of diseases caused by OS. Considering that individual actions of antioxidants have been reported, a large number of studies have indicated that there are cooperative/synergistic interactions among antioxidants in plasma. Therefore, studying the overall antioxidant status may be more biologically relevant than studying a single antioxidant. A relatively recent method called total antioxidant performance (TAP), developed by Aldini et al[3] and validated by Beretta et al[3], measures not only the antioxidant capacity in the hydrophilic and lipophilic compartments of the biological system, but also their synergistic/cooperative interactions. Given the potential of nutrients and foods to contribute to the prevention of chronic diseases associated with OS and TAP's unique ability to measure total antioxidant status, the objectives of our study were: 1) to measure serum antioxidant capacity using the TAP assay in a subgroup of participants from the Jackson Heart Study (JHS); 2) to examine associations between dietary and total intakes of α-tocopherol, γ-tocopherol (diet only), β-carotene, vitamin C, vegetable, fruit and nut consumption and TAP levels; and 3) to examine associations between serum levels of α and γ-tocopherol, β-carotene and TAP.[2]

A variety of assays have been developed to measure antioxidant capacity in plasma. These include testing the oxygen radical absorption capacity (ORAC), the antioxidant capacity of Trolox test equivalent to Randox and ferric reducing ability of plasma assay. However, most of these trials use a hydrophilic or lipophilic approach, not capturing, therefore, valuable information about the interactions between the antioxidants of the two compartments.[4]

The TAP assay measures the activity of both hydrophilic and lipophilic antioxidants in serum/plasma, along with their interactions. The results of this study show that in African-Americans, the total α-tocopherol, total vitamin C, and total dietary β-carotene consumption of fruits, vegetables and more vegetables fruits are associated with serum levels of TAP. Serum α-tocopherol was also associated with this measure of total antioxidant status.[5]

Serum α-tocopherol is a potent liposoluble antioxidant. Total antioxidant performance levels did not differ between quartiles of γ-tocopherol ingestion. The inverse association between serum γ-tocopherol and TAP levels for one of the statistical models examined was surprising. A study that examined the effect of smoking and exposure to tobacco in the plasma antioxidant status of smokers, passive smokers and nonsmokers found that while other the concentrations of antioxidants in plasma were significantly lower in smokers and passive smokers compared with non-smokers, the γ-tocopherol levels were elevated even after adjustment for dietary intake. These results merit further investigation on the role of γ-tocopherol in OS.[2]

Both β-carotene intake and total vitamin C intake were associated with serum TAP. Intervention studies have shown that β-carotene and vitamin C supplements, either alone or in combination with other known antioxidants, have been shown to enhance antioxidant capacity or reduce markers of OS. Although we observed significantly higher values of TAP with higher intakes of β-carotene and vitamin C intake (total intake only), the results were not reflected in the serum associations of β-carotene and TAP. As serum vitamin C was not estimated in the cohort, we were not able to examine its associations with serum TAP levels. Considering that TAP was significantly (positively) associated with fruit and vegetable intake and that it remained so after adjustment for dietary intake of β-carotene and vitamin C (data not shown), the association of these food groups with TAP is not just these vitamins well documented antioxidants. Intervention studies have shown increases in overall antioxidant status with increased intake of fruits and vegetables. On the other hand, interventions with a single or combination of antioxidant supplements did not demonstrate improvements in antioxidant status or OS measures. It is interesting to note that observational studies have also suggested that higher intakes of foods that are rich sources of these phytochemicals are associated with a lower risk of morbidity and mortality from chronic diseases.[6]

We are not aware of any other study examining associations between this particular measure of antioxidant status (serum TAP levels) and dietary intake of antioxidants and antioxidant-rich foods. The results of our study are consistent with others that examined the associations between diet, dietary estimates of total antioxidant capacity and other biological estimates of total antioxidant capacity. In a recent study, Rautiainen et al[7] concluded that fruits and vegetables were the main contributors to measures of total antioxidant capacity based on free fatty acid (FFA), such as ORAC, antioxidant parameters of total radical capture and ferric reduction capacity of the plasma assay. These dietary estimates were also positively correlated with the plasma measurements of the antioxidant ORAC and free radical capture parameters. The results of the ATTICA epidemiological study demonstrated that, in an apparently healthy population, total plasma antioxidant capacity was positively associated with fruit and vegetable consumption. Our results disagree with a recent cross-intervention study examining the effects of a diet intervention with high and low total antioxidant capacity on markers of antioxidant status, systemic inflammation and hepatic dysfunction.[8]

In the past, there have been criticisms against the concept of total antioxidant capacity. Most assays use a hydrophilic or lipophilic approach and are unable to capture interactions between antioxidants that are soluble in fat and water or antioxidant enzymes that contribute to the antioxidant defense systems in the body. Studies have recently shown that the TAP assay captures the synergistic protective associations between water soluble and liposoluble antioxidants. However, it is important to note that, similar to the deficiencies of other trials, TAP cannot capture direct reactive oxygen or nitrogen elimination activities.[9]

In recent years, several trials with antioxidant supplements have shown lack of benefit and, in some cases, potential harm. This shifted the focus to general eating patterns and food intake rather than individual nutrient intakes. Although higher total antioxidant status has been associated with the use of antioxidant supplements, our study also clearly demonstrates that modest increases in fruit and vegetable intake (1 serving/day of vegetables or 2 servings/day of fruits and vegetables) were positively associated with status total antioxidant. Antioxidant nutrients that are associated with increased consumption of fruits and vegetables include carotenoids and vitamin C. Beneficial effects of increased consumption of fruits and vegetables have been attributed in part to their antioxidant flavonoids. A review of intervention studies examining the effect of fruits and vegetables on measures of antioxidant capacity attributed to postintervention increases to an increase in serum/plasma concentrations of uric acid. According to the authors, the consumption of fructose (mainly due to fruit consumption) results in the degradation of purine nucleotides from the fructose catabolism, resulting in an increase in uric acid concentrations and, therefore, an increase in antioxidant capacity measurements.[9]

In general, studies found $\sim$ 4% more serum TAP levels in the extreme quartile categories of total α-tocopherol, β-carotene (total and dietary) intake, total vitamin C, fruits and vegetables and serum α-tocopherol measurements This apparently small increase may be due to the fact that components of endogenous serum (such as protein, uric acid, etc.) contribute greatly to overall antioxidant capacity and dietary micronutrients may thus play a relatively small role. The clinical importance of this increase in serum TAP levels is not currently known. More studies measuring TAP in other populations and examining their associations with clinical outcomes are needed.[4]

Oxidant-Antioxidant Balance During Myocardial Revascularization with Extracorporeal Circulation

Coronary artery bypass grafting induces OS. This situation is closely associated with overproduction of ROS. ROS play an important role in the pathophysiology of OS. Reactive oxygen species have toxic effects on cell structures, including lipids, proteins and nucleic acids. Oxidative reaction leads to damage of cellular function and may increase perioperative or postoperative complications after CABG.[8]

However, ROS that have been considered not only as lethal byproducts of cell metabolism but also as important molecules in vascular signaling are normally present in cells. The production of ROS in organisms and their degradation by antioxidants is in equilibrium. When ROS exceeds antioxidant capacity, this results in OS. Thus, the evaluation of oxidants and antioxidants together in patients undergoing myocardial revascularization may provide a more objective view on the change in oxidative balance.[9]

Serum concentrations of different oxidative components can be measured in the laboratory separately, but the measurement of these molecules is cumbersome and time-consuming, with complicated techniques and high cost. Total antioxidant status (TAS), total oxidant status (TOS), and oxidative stress index (OSI) reflect the redox balance between oxidation and antioxidation. Total antioxidant status measurement is an indicator of the activity of all antioxidants, while TOS is an indicator of ROS. Oxidative stress index is the ratio of TOS to TAS and an indicator of OS degree.[1]

There are several obstacles to devising appropriate strategies for optimal perioperative antioxidant therapy. The contribution of the various mechanisms on oxidative-antioxidant balance during on-pumpcoronary artery bypass grafting (ONCABG) has not yet been fully evaluated. In this study, we evaluated changes in oxidative-antioxidant balance and their relationship to time XC by measuring TOS, TAS and calculating OSI in ONCABG patients.[5]

Studies have shown that patients submitted to ONCABG are exposed to potent oxidative imbalance and increase of oxidants in reperfusion that are associated with the duration of XC.[8]

The myocardial revascularization procedure induces the overproduction of ROS (hydroxyl, hydrogen peroxide, hypochlorite and superoxide) that originates from several enzymatic and cellular sources. Determining TOS is more practical than individual ROS measurements. In the present study, the significant increase in TOS levels at 30 minutes shows an increase in ROS production in ONCABG patients.[10]

On the other hand, controversial findings have been reported on the perioperative course of antioxidants in patients with CABG,[2,5,8,11,12] The effects of antioxidant molecules in serum are additives. Serum antioxidant cooperation provides protection to the body against ROS. The body's true antioxidant status may not be reflected by individual antioxidant measurement. The measurement of SAD should be essential in assessing the actual state of the antioxidant. In the present study, patients' perioperative SAD levels were similar to baseline levels.[6]

Oxidative stress is a state of oxidative-antioxidant imbalance due to oxidants that exceed antioxidant capacity. Oxidative stress index is the ratio between TOS and TAS and is an indicator of the degree of OS. It may offer a more accurate comment for the evaluation of the change in the oxidative-antioxidant balance. In the present study, we found a significant increase in IOS values in 30 minutes. This finding suggests the development of oxidative imbalance or increase of OS degree in ONCABG patients.[10]

In ONCABG patients there are many causes of OS, such as surgical damage, CPB and reperfusion injury of ischemia. In our study, we aimed to detect a different finding in terms of oxidative-antioxidant balance evaluation during the ischemia period (20 minutes), and also tried to distinguish the effect of reperfusion. If blood samples for the ischemia period were taken immediately prior to removal of the aortic clamping, the effects of ischemia, as well as the effects of reperfusion due to cardioplegias, could have occurred. Some of the surgical manipulations had been done and CPB had started before that part of the intervention (20 minutes) as well. The presence of an increase in TOS and OSI at 30 minutes, with no increase in 20 minutes, suggests that reperfusion may be an important inducer of oxidative imbalance at ONCABG.[10]

Ischemic period is associated with OS in myocardial revascularization. Authors reported that Cross-Clamping (XC) time is correlated with levels of total peroxide, 8-isoprostane and nitrites/nitrates in patients undergoing myocardial revascularization. Studies also detect a positive correlation between time XC and TOS levels in 30 minutes.[13]

Ferrari et al[14] reported a significant and sustained increase in OS in 10 patients submitted to ONCABG with an average duration of XC of 55.2 minutes, while a discrete and temporary increase of OS in 10 patients submitted to ONCABG with a mean duration of XC of 25.2 minutes. Nowicki et al[15] also reported the absence of significant oxidative damage in myocardial biopsy samples from 8 patients undergoing ONCABG with a mean XC duration of 29.5 minutes. According to our knowledge, this work is the first of the literature that did not report systemic oxidative increase nor systemic oxidative imbalance in patients with a mean duration of XC of 29 minutes (group 1) evaluating OS and OSI. In contrast, a significant increase in systemic oxidant and systemic oxidative imbalance was observed in group 2. The increase in OSA and OSI values of all patients was mainly affected by the increase in OSA and OSI values of group 2 patients.[4]

The alteration in the oxidative balance, which was more significant in group 2, may be affected by the demographic data of the patients. The relationship between hormon therapy (HT) and smoking with changes in oxidative balance was previously reported. In our study, the statistical similarity of these parameters can be caused by the small number of patients. Furthermore, the similarity of the demographic characteristics of the patients dispersed in groups may allow us to isolate the effect of time XC on suggested dietary target (SDT) from other potential effective statuses, such as HT, smoking, any drug use and so on.[10]

The duration of CPB from the groups was also different. But there was no difference in terms of aerobic pump times. The prolongation of CPB time in group 2 was mainly due to the longer duration of XC.[13]

Clinical trials conducted with a variety of antioxidant strategies have been largely disappointing. The ideal design of antioxidant strategies in patients submitted to ONCABG requires a detailed evaluation of the oxidative phenomenon. Studies have shown that oxidant-antioxidant balance was not affected in ONCABG patients with short duration of XC, so we believe that generalized antioxidant therapy may not be necessary. The administration of antioxidants in selected cases may be more effective. Studies to determine the critical XC durations in terms of oxidative imbalance can be projected. Other large-scale prospective studies are needed for precise strategies for this clinical phenomenon. The main limitation of the present study may be the relatively small number of patients.[16]

Antioxidant during Cardiopulmonary Bypass Surgery

The systemic increase of OS during CABG is well documented, but the various components of the oxidative-antioxidant balance and the contribution of the various mechanisms involved have not yet been fully evaluated. In this subtopic we aimed to describe the changes in endogenous antioxidant capacity in patients undergoing myocardial revascularization under procedures that are known to increase the production and release of oxidants. First, the intermittent clamping technique used in CPB is a direct cause of ischemia-reperfusion, with consequent release of superoxide by the xanthine oxidase system. In addition, extracorporeal circulation, by increasing blood contact with foreign substances, will induce systemic inflammatory responses associated with complement activation, cytokine release, and cellular neutrophil activation. These are all sources of ROS production that will eventually lead to the depletion of antioxidants in plasma.[11]

The nature of this increase is not known. Two abundant plasma molecules with antioxidant activity, namely albumin and uric acid, are the main determinants of the value of trolox equivalent antioxidant capacity (TEAC). The plasma albumin concentration, however, did not increase significantly during ECC (data not shown) and could therefore not have contributed to the increase in the value of the TEAC. The contribution of uric acid here could not be assessed due to technical limitations. Another possible cause of the increase in the value of TEAC could have been hemolysis of erythrocytes during or after sampling. Hemoglobin has been shown to interfere with the measurements of TEAC. The activity of enzymatic antioxidants glutathione peroxidase (GPx) and SOD significantly increases the activity of free hemoglobin and uric acid in the plasma in measuring the global antioxidant capacity in future studies[10] during ECC. This could explain the course of GSH depletion time we observed earlier because GPx uses GSH as a cofactor. In addition, when comparing the duration time of GPx activation and the elapsed time of the reactive peroxides to TBA, as described by Davies, we see an approximate match. This parallelism suggests that glutathione peroxidase forms a first barrier against the ROS formed during the operation. Some studies confirm the results obtained by Arduini et al[17], who also found an increase in GPx activity. Other studies, however, observed a decrease in GPx activity, or no change during CPB. Most of these studies, however, were performed on animal models, which may explain part of the discrepancy between our study and those just mentioned.[12]

Superoxidase dismutase, the enzyme responsible for the conversion of superoxide anion to hydrogen peroxide, is also strongly activated, a rather acute response that lasted from the onset of ECC until after the administration of protamine. This can be explained by the fact that the contact of the blood with polymers in the ECC circuit releases cytokines and activates neutrophils, regardless of the heparin coating. Activated neutrophils, through the respiratory burst, generate the superoxide anion, which is detoxified by SOD. These two findings illustrate that GPx and SOD form a strong first line of defense against ROS. In addition, GPx and SOD are enzymatic antioxidants that are not consumed during their detoxification activities. In contrast, antioxidants acting as free radical scavengers are consumed during oxidative processes and time courses of depletion vary depending on the nature of the antioxidant.[18]

Retinol is not considered a very potent antioxidant, although its precursors from the carotenoids group are. Alpha-tocopherol, on the other hand, is well known for its antioxidant capacity. However, its role is rather controversial, as some studies consider supplementation of α-tocopherol patients before beneficial CPB, while several large-scale studies, such as the Heart Outcomes Prevention Evaluation (HOPE) study, clearly demonstrated that supplementation of vitamin E, regardless of surgery, had no apparent effect on cardiovascular outcomes. In addition, the role and consumption of α-tocopherol during CPB are debatable. Some studies claim that the level of α-tocopherol decreases during and after CPB, while others find a slight or non-significant decrease in serum α-tocopherol concentration. Our results, after correction for hemodilution, are similar to those published by Barsacchi et al[19], which found a decrease in Î ± -tocopherol concentration under conditions of ischemia and reoxygenation. However, the decrease observed in our study was significant only after surgery. This course of time suggests that it may be the result of postischemic repair of lipid peroxides (membrane). An additional cause may be vitamin C depletion during CPB. Since vitamin C is able to regenerate vitamin E from its radical intermediate, consumption of α-tocopherol is more likely if vitamin C is depleted. Ballmer et al[20] demonstrated that vitamin C is heavily depleted after CPB. These observations suggest that OS during CPB would initially consume vitamin C along with reduced glutathione, which are the most effective non-enzymatic water-soluble antioxidants under OS conditions. The resulting depletion and, consequently, that of a-tocopherol, can seriously alter the rest of the antioxidant cascade and result in systemic inflammation of the whole body, which increases the risk of postischemic damage.[9]

To elucidate the relationship between changes in antioxidant status and the activation of inflammatory cells during

myocardial revascularization, the markers of leukocyte activation are also monitored. Evidence of neutrophil activation during CPB was provided by other authors. In addition, in a previous study conducted in our institution by Jorens et al[21], the interleukin (IL)-8 response was monitored and found to be significantly increased during CPB, returning to normal values 20 hours after the surgery. In the present study, we found a perioperative increase in serum eosinophil cationic protein (ECP) and tryptase levels. This suggests that both eosinophils and mast cells were activated during or after myocardial revascularization and point to a possible anaphylactoid reaction. However, release of ECP is not only a signal of activation of eosinophils, as it is supposed to be carried by neutrophils. In addition, although ECP is of eosinophilic origin, in some studies in patients with asthma no relationship was found between the number of eosinophils and sputum ECP levels. This observation suggests that ECP sputum concentrations are not merely a function of the number of eosinophils, but may also be an indirect marker of neutrophil activation.[22]

Regarding the activation of mast cells during myocardial revascularization, several underlying mechanisms could explain this observation. Mast cells are highly granulated vaginal cells found in connective tissue and abundant beneath the epithelial surfaces. The release of granule contents (heparin, histamine and many proteases such as tryptase) can be triggered by physical factors (mechanical trauma, temperature changes), toxins, endogenous mediators (proteins, tissue proteases) and immunological mechanisms (IgE-dependent and independent). In addition, complement activation may cause degranulation of mast cells (anaphylatoxins C5a, C3a and C4a are formed during complement activation). All these processes can occur during ischemia-reperfusion and CPB of the CPB procedure and, moreover, may be linked to oxidative activity. For example, activation of C5a receptors in mast cells during CPB can trigger degranulation. In addition, tryptase released by mast cells may further stimulate IL-8 release and positively regulate intercellular adhesion molecule (ICAM-1) in epithelial cells. Based on these facts, the activation of mast cells during CPB is not necessarily a sign of allergy, but may be only a consequence of complement activation. There is also a growing body of evidence that mast cells are activated during ischemia-reperfusion. The increase in the influx of oxidants occurring at the onset of reperfusion may therefore also be responsible for the activation of mast cells. It has been reported that superoxide is known to activate these cells, which in turn play a role in neutrophil activation and infiltration in the lung, thus further aggravating the release of ROS.[23,24]

Conclusion

In summary, studies show that there is a strong innate antioxidant response under conditions of acute OS that occur during myocardial revascularization. However, it is well documented that postischemic oxidative damage still occurs. This indicates that this antioxidant response is not sufficient to neutralize the heavy oxidizing burden of these surgical procedures. It would be interesting to investigate whether supplementation with antioxidant mixtures such as vitamin C and glutathione could, at first, prevent its depletion during CPB and, secondarily, suppress postischemic inflammatory response.

This study also shows that there is a significant and parallel release of anaphylaxis markers. The role played by the activation of mast cells and eosinophils needs further investigation. The information collected in such studies will aid in the search for effective systemic measures to prevent postischemic damage and, thus, guarantee a better outcome for patients undergoing cardiac surgery.

References

1 Prasad AS. Clinical, immunological, anti-inflammatory and antioxidant roles of zinc. Exp Gerontol 2008;43(05):370–377
2 Valko M, Leibfritz D, Moncol J, Cronin MT, Mazur M, Telser J. Free radicals and antioxidants in normal physiological functions and human disease. Int J Biochem Cell Biol 2007;39(01):44–84
3 Beretta G, Aldini G, Facino RM, Russell RM, Krinsky NI, Yeum KJ. Total antioxidant performance: a validated fluorescence assay for the measurement of plasma oxidizability. Anal Biochem 2006; 354:290–298
4 Penckofer S, Schwertz D, Florczak K. Oxidative stress and cardiovascular disease in type 2 diabetes: the role of antioxidants and pro-oxidants. J Cardiovasc Nurs 2002;16(02):68–85
5 Callegaro GD, Koerich C, Lanzoni Gde M, Baggio MA, Erdmann AL. Significance of myocardial revascularization surgery: changes in lifestyle. Rev Gauch Nurs 2012;33(04):149–156
6 Koerich C, Baggio MA, Erdmann AL, Lanzoni Gde M, Higashi GDC. Myocardial revascularization: strategies for coping with the disease and the surgical process. Acta Paul Nurs 2013;26(01):8–13
7 Susanne Rautiainen Emily B, Levitan Murray A, Mittleman Alicja Wolk. Fruit and vegetable intake and rate of heart failure: a population?based prospective cohort of women First published: 08 November 2014 https://doi.org/10.1002/ejhf.191 Cited by: 18
8 Quintana JF, Kalil RAK. Cardiac surgery: psychological manifestations of the patient in the pre and postoperative period. Psicol Hosp (Sao Paulo) 2012;10(02):17–32
9 COSTA. Rui Pedro. Surgery of bypass coronary artery without extracorporeal circulation: evolution and application. 2016. Available at: https://repositorio-aberto.up.pt/bitstream/10216/90705/2/173221.pdf. Accessed on June 2, 2018.
10 Couto MAL, Canniatti-Brazaca SG. Quantification of vitamin C and antioxidant capacity of citrus varieties. Food Sci Tech 2010;30 (01):15–19
11 CHORILLI. Marlus. Free radicals and antioxidants: fundamental concepts for application in pharmaceutical and cosmetic formulations. 2007. Available at: http://rbfarma.org.br/files/PAG_113a118_RADICAIS.pdf. Accessed on June 2, 2018
12 Stahl W, Sies H. Antioxidant defense: vitamins E and C and carotenoids. Diabetes 1997;46(02, Suppl 2):S14–S18
13 Diaz MN, Frei B, Vita JA, Keaney JF Jr. Antioxidants and atherosclerotic heart disease. N Engl J Med 1997;337(06):408–416
14 Ferrari R, Alfieri O, Curello S, et al. Occurrence of oxidative stress during reperfusion of the human heart. Circulation 1990;81(01): 201–211
15 Nowicki R, Saczko J, Kulbacka J, et al. The estimation of oxidative stress markers and apoptosis in right atrium auricles cardiomyocytes of patients undergoing surgical heart revascularization with the use of warm blood cardioplegia. Folia Histochemica et Cytobiologica 2010;48(02):202–207
16 SARMENTO. Roberta Aguiar. Micronutrients Antioxidants and Cardiovascular Risk in Patients with Diabetes: A Systematic Review. Brazilian Archives of Cardiology, 2013

17 Arduini A, Mezzet A, Porecca E, Lapenna D, DeJulia J, Marzio L, Polidoro G, Cuccurullo F. Effect of ischemia reperfusion on antioxidant enzymes and mitochondrial inner membraneproteins in perfused rat heart. Biochim Biophys Acta 1988;970:113–21
18 MESQUITA. Braulio Fortes et al. Inflammatory response in extracorporeal circulation: therapeutic strategies. 2017. Available at: http://rmmg.org/artigo/detalhes/1027. Accessed on June 2, 2018.
19 Barsacchi R, Pelosi G, Maffei S, Baroni M, Salvatore L, Ursini F, Verunelli F, Biagini A. Myocardial vitamin E is consumed during cardiopulmonary bypass: indirect evidence of free radical generation in human ischemic heart. Int J Cardiol 1992; 37:339–343
20 Ballmer PE, Reinhart WH, Jordan P, Buhler M, Moser UK, Gey KF. Depletion of plasma vit C but not of vit E in response to cardiac operations. J Thorac Cardiovasc Surg 1994;108:311–320
21 Jorens PG, De Jongh RF, De Backer WA, Van Damme J, van Overveld FJ, Bossaert L, Walter P, Herman AG, Rampart M. Interleukin-8 production in patients undergoing cardiopulmonary bypass. The influence of pre-treatment with methylprednisolone. Am Rev Respir Dis 1993;148:890–895
22 Callegaro GD, Koerich C, Lanzoni GM, de M, Baggio MA, Erdmann AL. Significando o processo de viver a cirurgia de revascularização miocárdica: mudanças no estilo de vida. Rev Gauch Enferm 2012; 33(04):149–156
23 Factors that influence the process of living cardiac revascularization. Texto Contexto Enferm 2015; [periodical on the Internet]
24 KNIHS. Neide da Silva. Path traveled to cardiac surgery: needs and expectations in the preoperative period. 2017. Available at: http://www.scielo.org.co/pdf/aven/v35n1/v35n1a04.pdf. Accessed on June 2, 2018