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Short Communication

**THE TOTAL ANTIOXIDANT CAPACITY OF BLOOD PLASMA
DURING CARDIOVASCULAR BYPASS SURGERY IN PATIENTS
WITH CORONARY HEART DISEASE**

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Abstract: We studied the effect of ischemia and reperfusion on the total antioxidant capacity (TAC) of blood plasma during cardiopulmonary bypass surgery employing the modified St. Thomas Hospital cardioplegic solution. TAC was determined using the FRAP method. TAC decreased during surgery, but no further decrease in TAC was observed during reperfusion, indicating that it is a relatively stable parameter of the antioxidative barrier of the body.

Key Words: Antioxidant Capacity, Antioxidants, Coronary Heart Disease, Cardiovascular Bypass

INTRODUCTION

Ischemia-reperfusion is an important pathogenic factor in cardiology and a complication of such surgical interventions as a cardiopulmonary bypass. There is abundant evidence that the mechanism of ischemic-reperfusion injury invokes increased generation of reactive oxygen species, and that both endogenous and exogenous antioxidants and antioxidative enzymes ameliorate the extent of the damage [1, 2]. Ischemia-reperfusion injury was found to increase the level of peroxides and the extent of lipid peroxidation; treatment with antioxidant enzymes, superoxide dismutase plus catalase (the antioxidant enzymes, superoxide dismutase and catalase/antioxidant enzymes and superoxide

dismutase plus catalase/superoxide dismutase together with catalase) protected against these effects [3, 4]. It has recently been demonstrated that reperfusion brings about a depletion of endogenous antioxidant in the ischemic heart and that this change was dependent on the severity of ischemia-reperfusion [5]. Hydrophilic antioxidants such as glutathione and ascorbate were not altered during ischemia, but their concentrations decreased during 40 min of reperfusion, whereas the concentrations of vitamin E and ubiquinol 9 did not change, even during reperfusion. These findings suggest that glutathione and ascorbate act as a first line of defence against oxidative stress during the ischemia-reperfusion cycle [6].

Another important parameter of the antioxidant defense of the body is the Total Antioxidant Capacity (TAC) of the blood plasma; this parameter is studied more and more frequently; this parameter is attracting more and more attention. Representing the functional sum of antioxidants present in the plasma, it is a measure of the of the extracellular antioxidant barrier [7-9]. It is possible that heart surgery, using cardioplegic solutions devoid of antioxidants, may lead to a considerable decrease in TAC, due to blood dilution and the oxidative stress of reperfusion. The aim of this paper was to examine the TAC of blood plasma during coronary bypass surgery employing the St. Thomas Hospital cardioplegic solution.

MATERIALS AND METHODS

Blood was taken from 50 patients with stable angina pectoris, aged 62.1 ± 8.6 (45-79) years, undergoing coronary artery bypass grafting. The surgery consisted of a median sternotomy and emplacement of saphenous vein and left internal mammary artery grafts. A heart-lung machine with a Bentley Univox membrane oxygenator was primed with Ringer's solution (1.5 l), 20% mannitol (3 ml/kg), plasma (600 ml) and 8.4% NaHCO_3 (1 mmol/kg). Moderate hemodilution (down to a hematocrit of 15-34%) and moderate systemic hypothermia (a nasopharyngeal temperature of 28-30°C) were employed. Cardiopulmonary bypass flow rates were maintained between 2.0 and 2.5 l/min/m², and mean arterial pressures were maintained between 60 and 70 mm Hg. A modified St. Thomas solution of the following composition was used: NaCl, 110 mM; KCl, 16 mM; MgCl_2 , 16 mM; CaCl_2 , 1.2 mM, and NaHCO_3 , to pH 7.4 at 40°C. Initially, 1 l of the cardioplegic solution was infused into the aortic root. Samples of aortic blood were obtained from the patients before cardioplegic arrest, at the peak of ischemia and after 10-13 min of reperfusion; these samples were then anticoagulated with heparin. The time of blood sampling during reperfusion was chosen because both literature data [10-12] and our own results point to the most intense alterations occurring at this time, after the onset of reperfusion.

The TAC of blood plasma was estimated using the Ferric Reducing Ability of Plasma (FRAP) method [13, 14]. Briefly, 20 µl of plasma was added to 600 µl of the freshly prepared working solution of: 10 vol of 300 mM acetate buffer, pH

3.6 + 1 vol of 10 mM 2,4,6-tripirydyd-*s*-triazine + 1 vol of 20 mM FeCl₃, prewarmed to 37°C. Then, increase in absorbance at 593 nm was measured after 5-min incubation at 37°C. The results were expressed in mmol Trolox equivalents/l of blood plasma.

RESULTS AND DISCUSSION

The surgery using the cardioplegic solution resulted in a considerable dilution of the blood, as reflected by the decreased hematocrit values. The TAC of the blood plasma was also subject to a decrease during ischemia. However, no further decrease in TAC took place after reperfusion (Tab. 1). Interestingly, the decrease in the TAC of the blood plasma was much lower than what expected considering the blood dilution. The mean dilution of the blood was 1.67 at the peak of ischemia and 1.58 during reperfusion, while TAC decreased by a factor of 1.20 and 1.18, respectively. Looking for possible reasons for the behavior of TAC, it is necessary to take into account the results of Wayner *et al.*, who showed that the antioxidant efficiency of ascorbate is concentration-dependent, increasing with decreasing concentration of ascorbate [15]. However, ascorbate has an only minor contribution to the TAC of the blood plasma [16, 17], and other antioxidants (as well as ascorbate itself in some systems) do not display/show a similar concentration dependence in their free radical-scavenging potency [18]. A more probable explanation for the observed effect is the release of antioxidants from damaged heart cells during the surgery. A/The slight elevation of TAC during ischemia (when the intracellular antioxidants are consumed [5]) is in line with this interpretation.

Tab. 1. The Hematocrit values and Total Antioxidant Capacity of the blood plasma in patients undergoing a cardiopulmonary bypass. Mean \pm SD, n=50.

Parameter	Before ischemia	Peak of ischemia	Reperfusion
Hematocrit	40.8 \pm 4.5	24.5 \pm 4.1*	25.8 \pm 4.0*
TAC [mmol/l]	1.038 \pm 0.169	0.869 \pm 0.138*	0.878 \pm 0.144*

*Statistically significant with respect to values before ischemia ($P < 0.001$) using the Student's "t" test.

Therefore, even the use of a cardioplegic solution devoid of exogenous antioxidants does not bring about a drastic decrease in the TAC of the blood plasma during a cardiopulmonary bypass. While it is difficult to judge what the physiological significance of the observed 16% decrease in TAC can be, the TAC value was not affected further by reperfusion. Therefore, it can be suggested that the cardiopulmonary bypass does not involve a dangerous decrease in TAC. Similarly, no significant decrease in TAC was observed during and after heart infarction [19]. Thus, TAC may be considered as a relatively stable parameter of the antioxidative barrier of the body.

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