

Zinc in Children Undergoing Cardiac Surgery with Cardiopulmonary Bypass

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Introduction

During cardiac surgery with extracorporeal circulation (ECC), a series of immunological and inflammatory alterations occur, which trigger oxidative stress^{1,2}. Under the non-physiological conditions during the ECC and due to the alterations related to ischemia-reperfusion, a large amount of free radicals is formed³. These are responsible for systemic inflammation and considerable structural and functional cellular lesion⁴.

Zinc, an important trace element, has decisive role in several biological processes, including protein synthesis, nucleic acid, carbohydrate and lipid metabolism, among others. Its essential biochemical action is to act as an antioxidant⁴, stabilizing the membranes, preventing lipoperoxidation and protein denaturation⁵. It is an essential component of the dismutase superoxide enzyme, which inactivates the superoxide radicals, turning them into less harmful forms. The protective role of the element in relation to the cardiac cell is well known, decreasing the formation of the hydroxyl radical, which is highly hazardous to the myocardium⁶. The purpose of this study is to investigate the dynamics of zinc in children submitted to cardiac surgery with ECC.

Methods

This study included a total of 21 children with non-cyanotic congenital cardiopathies, electively submitted to cardiac surgery with ECC from May 2005 to December 2006 (Table 1). The investigation protocol was approved by the Medical Ethics Committee of the Federal University of Mato Grosso do Sul University Hospital and parents of each participant signed the free and informed consent form. The patients were submitted to moderate hypothermia. The hemodilution caused by the additional volume of the ECC circuit was evaluated by the hematocrit.

Key words

Zinc; extracorporeal circulation; thoracic surgery; child.

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Tabela 1 - Demographic data of 21 children submitted to cardiac surgery with ECC

Characteristics	Indicators
Age (months)	80.14±9.27 (27 to 170)
Sex	
Female	14
Male	7
Body mass (kg)	24.82±2.94 (12 to 58)

The first blood sample (A), used to establish the basal parameters, was collected through a central venous catheter, right after the anesthesia. The second blood sample (B) was collected from the right atrium, before the perfusion cannulae were inserted. During the ECC, samples were collected from the circuit at the 5th (C) and the 10th minute (D), respectively.

During the reperfusion period, the blood was collected from the coronary sinus (I) and the ECC circuit (J), simultaneously, three minutes after the removal of the aortic clamp. The M sample was collected from the radial artery during the closing of the thorax, and the last sample (N) was collected 24 hours after the surgery. The samples were stored in appropriate flasks at - 18° C, until the measurements were performed.

All plastic or glass materials were previously immersed for a minimum period of 24 hours in a 5% Extran (Merck) solution, rinsed and once again immersed for 24 hours in a 10% nitric acid solution (Merck), for any metal residue decontamination. Subsequently, the materials were washed with Milli-Q type ultrapurified water and dried at 40°C. The analytical curves were constructed with 5 points, between 0.03 and 0.80 mg/l.

The analysis of the samples was carried out by atomic absorption spectrometry⁷. The statistical analyses were carried out using Friedman's and Mann-Whitney's tests, Spearman's correlation and Dunn's post-test. The value of *p* was set at ≤ 0.05.

Results

The zinc concentration in female children at moment A was 0.72±0.10 mg/l, and 0.85±0.13 mg/l for male children, a non-significant difference (*p*=0.43). At the moment A, no

correlation was observed between zinc concentration and age ($p=0.54$, $r=0.14$) or weight ($p=0.65$ and $r=0.10$). There was no correlation between zinc and ECC time (47.8 ± 16.4 min) at moments M ($p=0.28$, $r=-0.25$) and N ($p=0.26$, $r=-0.26$). Similarly, there was no correlation with anoxia time (47.8 ± 16.4 min) at moments M ($p=0.27$, $r=-0.25$) and N ($p=0.35$, $r=-0.21$).

The dynamics of the plasma zinc concentrations is shown in Figure 1. The concentration observed at moment B is higher than that observed at moments C, D, J, I and N ($p < 0.05$). When comparing the measured concentration (circle) and that considering the hemodilution (square), significant difference was observed at moments J and N ($p=0.048$ and $p=0.003$, respectively). At the other moments, there was no difference between the measured concentration and the one expected for the hemodilution ($p > 0.09$).

Discussion

There is no consensus in literature regarding the reference values for zinc in children, with values ranging from 0.6 to 1.2 mg/l^{8,9}.

In the present study, the mean initial zinc concentration, at moment A, which was taken as the basal parameter, was 0.76 ± 0.08 mg/l, which is within the normal range. However, the individual evaluation of the results showed that 10 children (47%) presented zinc concentrations < 0.7 mg/l. It is possible that the decreased plasma concentrations were due to the low intake of the element, as the sources of zinc are of animal origin, and thus, are more costly. Other possibilities are calcium- and phytate-rich diets⁹.

According to Figure 1, the zinc concentrations were not different at moments A and B, the interval between anesthesia and the start of ECC. Thus, it can be inferred that, during this time interval, the anesthetic procedure and the surgical trauma did not trigger considerable inflammatory activity. At the moments C, D and I, the decrease in zinc was caused solely by the hemodilution. However, at moment J, zinc values decreased beyond those expected for hemodilution, demonstrating its antioxidant effect. At the end of the surgical procedure (M), zinc concentrations returned to the initial values; however, at moment (N), there was a significant decrease. This might have been due to the zinc redistribution with its uptake by the liver for protein synthesis and the migration of this ion to the places that underwent surgical trauma. There, it would participate in the processes of

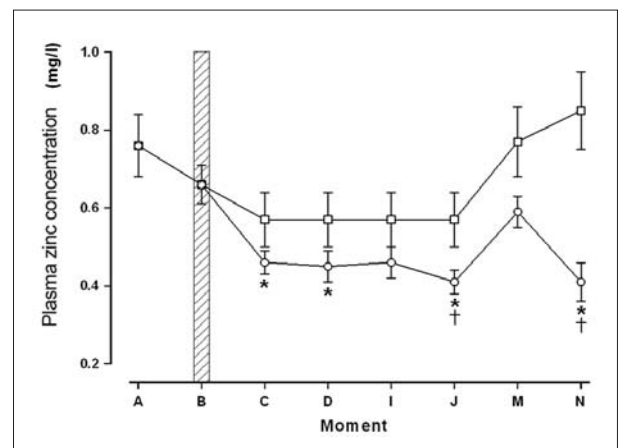


Figure 1 - Measured plasma zinc concentrations and those calculated for hemodilution in 21 children, before and after ECC. The symbols represent the mean values and the bars represent the mean standard error. * Significant difference in relation to moment B ($p < 0.001$). † Significant difference in relation to that calculated at hemodilution, at the same moment ($p < 0.05$).

epithelization and healing¹⁰.

Conclusions

Plasma zinc assessment is indicated in the preoperative period of cardiac surgeries.

The inflammation caused by ECC is neither extremely long-term nor of considerable intensity.

Zinc replacement in the preoperative period is beneficial for the recovery of reperfusion injury.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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References

- Clermont C, Vergely C, Jazayeri S, Lahet JJ, Goudeau JJ, Lecour S, et al. Systemic free radical activation is a major event involved in myocardial oxidative stress related to cardiopulmonary bypass. *Anesthesiology*. 2002; 96: 80-7.
- Christen S, Finckh B, Lykkesfeld J, Gessler P, Frese-Schaper M, Nielsen P, et al. Oxidative stress precedes peak systemic inflammatory response in pediatric patients undergoing cardiopulmonary bypass operation. *Free Radic Biol Med*. 2005; 38: 1323-32.
- Bolli R, Jeroudi MO, Patel BS, Aruoma OI, Halliwell B, Lai EK, et al. Marked reduction of free radical generation and contractile dysfunction by antioxidant therapy begun at the time of reperfusion: evidence that myocardial "stunning" is a manifestation of reperfusion injury. *Circ Res*. 1989; 65: 607-22.
- Valko M, Morris H, Cronin MT. Metals toxicity and oxidative stress. *Curr Med*

Brief Comments

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- Chem. 2005; 12: 1161-208.
5. Bray TM, Bettger WJ. The physiological role of zinc as an antioxidant. *Free Radic Biol Med.* 1990; 8: 281-91.
 6. Powell SR. The antioxidant properties of zinc. *J Nutr.* 2000; 130 (Suppl 5S): S1447-54.
 7. Terres-Martos C, Navarro-Alarcon M, Martín-Lagos F, Lopez de la Serrana GH, Lopez-Martinez MC. Determination of copper levels in serum of healthy subjects by atomic absorption spectrometry. *Sci Total Environ.* 1997; 198: 97-103.
 8. Fávoro RMD, Vannucchi H. Níveis plasmáticos de zinco e antropometria de crianças da periferia de centro urbano no Brasil. *Rev Saúde Publ.* 1990; 24: 5-10.
 9. Organização Mundial De Saúde. Elementos traço na nutrição e saúde humanas. São Paulo: Roca, 1998.
 10. Fraser WD, Taggart DP, Fell GS, Lyon TD, Wheatley D, Garden OJ, et al. Changes in iron, zinc, and copper concentrations in serum and in their binding to transport proteins after cholecystectomy and cardiac surgery. *Clin Chem.* 1989; 35: 2243-7.