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Original article

Plasma concentration of IL-6 and TNF- α and its relationship with zincemia in obese women[☆]

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ABSTRACT

Objective: In obesity, the excessive adipose tissue increases the synthesis of inflammatory cytokines, which appear to alter the metabolism of minerals, such as zinc. However, the mechanisms involved remain unclear. This study investigated whether the concentrations of interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) in plasma can influence biochemical parameters of zinc in obese women.

Methods: Seventy-six pre-menopausal women, aged between 20 and 50 years, were divided into two groups: the case group, composed of obese women (n = 37) and the control group, composed of non-obese women (n = 39). Analysis of the plasmatic and erythrocytary zinc, and plasmatic cytokines were conducted by flame atomic absorption spectrophotometry and by ELISA, respectively.

Results: The plasmatic zinc and concentrations of IL-6 in plasma did not show significant differences between obese women and controls (p > 0.05). The erythrocytary zinc was $36.4 \pm 15.0 \mu\text{g/gHb}$ in the case group, and $45.4 \pm 14.3 \mu\text{g/gHb}$ (p = 0.025) in the control group. The concentrations of TNF- α in plasma were $42.0 \pm 11.9 \text{ pg/mL}$ and $19.0 \pm 1.0 \text{ pg/mL}$ in obese women and in controls, respectively (p < 0.001). The plasmatic zinc had a significant negative correlation with the values of TNF α (r = -0.44, p = 0.015).

Conclusion: Obese women presented lower concentrations of erythrocytary zinc than the control group. The study demonstrated a probable influence of the inflammatory process on metabolism of zinc in obese patients.

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Concentrações plasmáticas de IL-6 e TNF- α e sua relação com a zincemia em mulheres obesas

R E S U M O

Objetivo: Na obesidade, o excesso de tecido adiposo aumenta a síntese de citocinas inflamatórias que parecem alterar o metabolismo de minerais, como o zinco. Entretanto, os mecanismos envolvidos neste processo ainda não estão totalmente esclarecidos. O estudo

Palavras-chave:

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Inflamação
Interleucina-6
Fator de necrose tumoral- α

investigou se as concentrações de interleucina-6 (IL-6) e fator de necrose tumoral- α (TNF- α) no plasma podem influenciar os parâmetros bioquímicos do zinco.

Métodos: Setenta e três mulheres, com idade entre 20 e 50 anos, foram distribuídas em dois grupos: grupo caso, composto de obesas (n=37) e grupo controle, composto de não obesas (n=39). Análises de zinco plasmático e eritrocitário e as citocinas inflamatórias plasmáticas foram realizadas pelo método da espectrofotometria de absorção atômica e pelo ELISA, respectivamente.

Resultados: O zinco plasmático e as concentrações de IL-6 no plasma não mostraram diferenças significativas entre as mulheres obesas e grupo controle ($p > 0,05$). O valor do zinco eritrocitário foi $36,4 \pm 15,0 \mu\text{g/gHb}$ nas mulheres obesas e $45,4 \pm 14,3 \mu\text{g/gHb}$ ($p = 0,025$) no grupo controle. As concentrações de TNF- α no plasma foram $42,0 \pm 11,9 \text{ pg/mL}$ e $19,0 \pm 1,0 \text{ pg/mL}$ nas mulheres obesas e controles, respectivamente ($p < 0,001$). O zinco plasmático apresentou uma correlação negativa significativa com os valores de TNF- α ($r = -0,44$, $p = 0,015$).

Conclusão: As mulheres obesas apresentaram menores concentrações de zinco eritrocitário em relação ao grupo controle. O estudo mostra uma provável influência do processo inflamatório no metabolismo do zinco em pacientes obesos.

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Introduction

Obesity is directly related to changes in the endocrine and metabolic functions of adipose tissue. In obese individuals, this tissue increases the capacity for synthesis of adipocytokines or adipokines with proinflammatory action. Studies have identified that metabolic disturbances in obesity are related to macronutrient levels. Recently, there has been an increased interest on the contribution of minerals in various pathophysiological changes associated with obesity.¹⁻³

Zinc is one of the most important minerals for metabolism. Among its biological functions, this element is a cofactor of over 300 metalloenzymes; it acts in the catalytic activity of several enzymes, such as carbonic anhydrase, alcohol dehydrogenase, alkaline phosphatase, and enzymes involved in the metabolism of carbohydrates, lipids, and proteins.^{4,5}

Tissues of obese animals have low concentrations of micronutrients, such as zinc, copper, iron, and manganese. Kennedy and Failla⁶ observed low concentrations of zinc in the skin, muscle, pancreas, and bone of obese mice. Moreover, the liver, intestine, and adipose tissues had higher zinc concentrations, suggesting a possible change in the distribution of the mineral in the obese.

A relationship between zinc status and cytokine production is reported in disorders associated with chronic inflammation, such as obesity. This process may occur through an increase in the content of hepatic zinc at the expense of plasmatic zinc. Elevated concentrations of glucocorticoids lead to a reduction of plasmatic zinc and an increase in zinc uptake by the liver. These data show the involvement of synergistic participation of interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), and glucocorticoids on the metabolic behavior of zinc; the combination of these elements depend on an adequate zinc content in the liver.^{7,8}

In humans, inflammatory cytokines have been demonstrated to both up- and down-regulate the expression of specific cellular zinc transporters (ZnT's and Zip's), in response to an increasing demand for zinc in inflammation.^{9,10} In these processes, there is an increase of expression of encoding

genes for zinc-transporter protein Zip-14, which promotes the uptake of zinc from the extracellular compartment to the interior of the cells. In obesity, a high concentration of IL-6 in plasma promotes an increase in gene expression of this transporter, which may alter the distribution of zinc in cellular compartments.^{7,11} Studies have demonstrated a rapid decrease in zinc plasma concentration that was preceded by prominent increases in concentration of TNF- α and IL-6 in plasma in humans exposed to inflammation.^{9,12,13}

Considering the importance of obesity as a chronic disease, the secretion of adipocytokines and other proteins in the adipose tissue, and the possible influence of these metabolites on the homeostasis of zinc, this study aimed to investigate the relationship between biochemical parameters of zinc and the concentrations of IL-6 and of TNF- α in the plasma of obese women.

Methods

This was a clinical and case-control study, involving 76 randomly selected adult females, aged between 20 and 50 years, who sought treatment at an endocrinology clinic. This sample derived from the study by Ferro et al.¹⁴ The analysis of concentrations of proinflammatory cytokines in plasma was performed from a biobank of samples arising from the aforementioned research,¹⁴ developed in the Universidade Federal do Piauí (UFPI) by researchers involved in this study.

The obese women (n=37) who presented at the clinic were selected for the study if they met the following criteria: their body mass index (BMI) was higher than 30 kg/m^2 ; they were not taking any vitamin-mineral supplementation and/or other medicines; they did not have any illnesses that could interfere with zinc-related nutritional status and metabolic profile, such as diabetes mellitus, chronic renal insufficiency, chronic diarrhea, and malabsorption syndrome; and were nonsmokers. The control group (n=39) was selected according to the same criteria as the obese women, but had a BMI between 18.5 kg/m^2 and 24.9 kg/m^2 . The study was approved by the

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