Assessment of Copper Status in Pregnant Women

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Deficiencies of iron, iodine, zinc and selenium are recognized public health problems either regionally or globally. Athough probably of lesser public health importance, the identification of adequate biomarkers of copper status also merits attention (1). Recently Pathak et al. have evaluated the copper nutriture in 255 pregnant women from a rural area of India, measuring the dietary intake of copper and serum copper concentration (2). The mean daily intake of copper was 1.6 mg, in accordance with the daily normal intake which is 0.6-2.0 mg (3); however, during pregnancy the need for metabolic micronutrients increases due the requeriments of a growing fetus. The mean serum copper concentration of this pregnant women group was 192.9 ± 60.9 mg/dL, and only 7 cases (2.7% of total) were identified as copper deficients on the basis of a copper level less than 80.0 mg/dL (2). Newertheless, the estrogen induction of hepatic synthesis of ceruloplasmin would mask some cases of possible marginal, or even moderate, copper deficiency.

The ceruloplasmin (ferroxidase I, EC 1.16.3.1) is a multifunctional protein which contains more than 95% of the serum copper, and whose hepatic synthesis depends on an adequate supply of copper. Serum copper and ceruloplasmin concentrations, the most frequently used biomarkers of copper status, are depressed in copper deficiency; however, ceruloplasmin is an acute phase reactant and pathophysiological conditions such as infections and inflammatory reactions may increase the serum levels of ceruloplasmin, and therefore of copper. Likewise, significant increases of serum ceruloplasmin due to hormonal impregnation in pregnant women or taking oral contraceptives is a well-documented issue. These circunstances, which tend to elevate serum copper, may obscure changes in copper status even during copper deprivation (4,5). On the contrary, hepatic ceruloplasmin synthesis may be depressed by protein deficiency and results in low levels of serum copper, that are not caused by a copper deficiency (1). Consequently, in these conditions the lack of sensitivity and specificity may compromise the value of serum copper and ceruloplasmin concentrations for the assessment of copper status.

Marginal or moderate copper deficiency is difficult to study, and several index of copper status have been proposed, however some of these are not suitable for epidemiologic studies (1). The results of Milne suggest that the specific enzymatic activity of ceruloplasmin

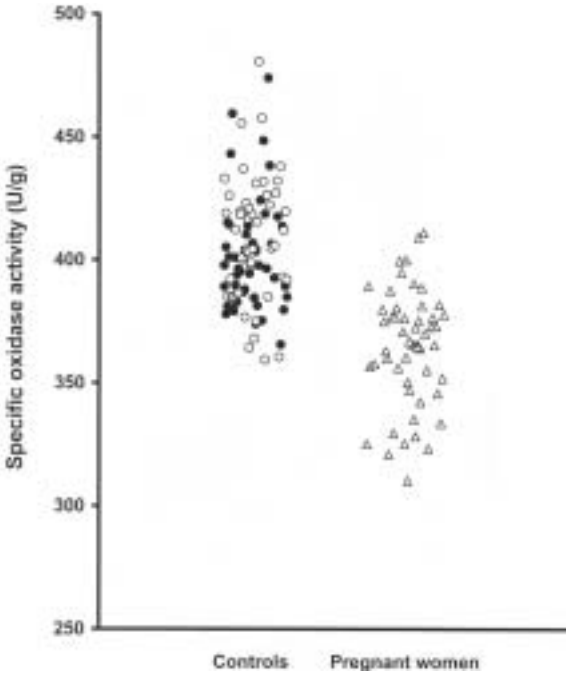

Figure 1. Specific oxidase activity of ceruloplasmin in male (●) and female (❍) controls and in pregnant women (△).

(activity per unit mass of enzyme protein), which in adults is not influenced by factors such as age, gender or hormone use, is a more sensitive indicator of copper status than either serum copper and ceruloplasmin or erythrocyte superoxide dysmutase (4,5). A decrease of the copper reserves, leads to an increase of the relative proportion of ceruloplasmin molecular forms which have a low copper content, and consecuently to a decrease of the specific enzymatic activity of circulating ceruloplasmin.

In a previous paper we have determined serum immunoreactive ceruloplasmin and its oxidase activity using o-dianisidine (which permit the expression of the enzyme activity in International Units) in a group of 52 women in the 3rd trimester of normal pregnancy (6). Although, the serum levels of copper, ceruloplasmin and its oxidase activity were significantly higher ($p<0.001$), the copper/ceruloplasmin ratio and the specific oxidase activity of ceruloplasmin were significantly lower ($p<0.001$) than in a control group of non-pregnant women living in the same geographical area. Likewise, we did not find a statistical significant difference for the specific

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oxidase activity between healthy male and female controls. In all pregnant women studied, the serum levels of copper, ceruloplasmin and oxidase activity were greater than the lower limits of the correspondent reference ranges; however, in 18 cases (35% of total), the ceruloplasmin specific oxidase activity was smaller than the lower limit of the reference range (359 U/g), as it is shown in figure 1.

These results suggest a higher frequency of marginal or moderate copper deficiency during normal pregnancy, at least in the 3rd trimester when supply of copper to the fetus is at great level, than described by Pathak el al (2).

References

1. Hambidge M: Biomarkers of nutritional exposure and nutritional status. J Nutr 133: 948-955, 2003.
2. Pathak P, Kapoor SK, Kapil U, Joshi YK: Copper nutriture amongst pregnant women in a rural area of India. Eastern J Med 8: 15-17, 2003.
3. Gambling L, Danzeisen R, Fosset C, Andersen HS, Dunford S, Srai SKS: Iron and copper interactions in development and the effect on pregnancy out come. J Nutr 133: 1554-1556, 2003.
4. Milne DB: Trace elements. In: Tietz Textbook in Clinical Chemistry.3rd edition. (Eds. Burtis CA and Ashwood ER). Saunders, Philadelphia 1999: 1029-1055.
5. Milne DB: Assessment of copper nutritional status. Clin Chem 40: 1479-1484, 1994.
6. Louro MO, Cocho JA, Tutor JC: Assessment of copper status in pregnancy by means of determining the specific oxidase activity of ceruloplasmin. Clin Chim Acta 312: 123-127, 2001.

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