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Comparison of Direct Versus Indirect Determination of Zinc Concentration in Erythrocytes in Euthyroid and Hyperthyroid Subjects

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Summary: Zinc concentration in erythrocytes is a suitable marker of peripheral tissue response to thyroid hormones. Therefore, the determination of erythrocyte zinc concentration has become an important marker for duration of preexisting hyperthyroidism in the clinical laboratory. We compared a new indirect erythrocyte zinc determination method with a commonly used direct method in 42 euthyroid and 14 hyperthyroid subjects. Zinc concentrations (median and range) obtained by direct and indirect methods were 172.8 (134.4–241.1) and 176.8 (143–243.9) $\mu\text{mol/l}$ erythrocytes in the euthyroid group and 117.1 (71–141.9) and 118.5 (73–137) $\mu\text{mol/l}$ erythrocytes in the hyperthyroid group. Values measured by the indirect method were slightly higher in both groups. Regression analysis showed a good correlation ($r = 0.967$, $p = 0.0001$). The influence of the anticoagulants, potassium EDTA and heparin, on erythrocyte and plasma zinc values was studied, and zinc concentrations in serum and plasma were compared. No statistically significant differences were found. Thus, the indirect determination of erythrocyte zinc concentration is a simple and rapid technique well suited for use in clinical laboratory work, yielding accurate and reliable results. For the indirect method reference concentrations were established in a collective of 102 thyroid healthy subjects. An erythrocyte zinc concentration of $176.3 \pm 23.9 \mu\text{mol/l}$ (mean \pm SD) was found with a cut-off limit of 138 $\mu\text{mol/l}$ to hyperthyroidism.

Introduction

The interaction between thyroid function and zinc metabolism has long been a matter of investigation (1–3). It is a well known fact that during hyperthyroidism the zinc concentration in erythrocytes decreases and serum zinc is increased (4, 5). The reason for the decreased erythrocyte zinc concentration is inhibition of the synthesis of carbonic anhydrase-I isoenzyme in erythrocytes by high thyroid hormone concentrations. The greatest amount of zinc in erythrocytes is bound as a structural part of this enzyme (6–8). Changes in erythrocyte zinc concentration, as a result of changes in thyroid function, take time to develop because of the relatively long half-life of erythrocytes. Therefore, erythrocyte zinc concentration reflects the patient's mean thyroid hormone con-

centration over the previous several weeks and months (9, 10). For this reason it is possible to differentiate short from the long duration hyperthyroidism by determination of the erythrocyte zinc concentration. Lao et al. (11) reported that determination of erythrocyte zinc concentration makes it possible to discriminate between preexisting hyperthyroidism and transient hyperthyroidism in pregnancy due to hyperemesis gravidarum, and so facilitates the choice of therapy.

Erythrocyte zinc concentration is commonly measured directly: erythrocytes are separated from whole blood and the resulting pellet is analysed (10, 12). The separation and washing procedures have to be performed immediately after venous puncture, and they are labour intensive and time consuming. Indirect