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ORIGINAL ARTICLE

Acute inflammatory response does not affect erythrocyte concentrations of copper, zinc and selenium

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Summary
Background & aims: Measuring the nutritional status of trace elements in plasma is invalidated in the presence of a systemic inflammatory response. We examined the potential of erythrocytes to assess copper, zinc and selenium status in such situations.
Methods: Venous blood samples were withdrawn pre-operatively and at 12, 24, 48, 72 and 168 h post-operatively from 11 patients (6 males and 5 females) who were admitted for elective knee arthroplasty. C-reactive protein, albumin, copper, zinc, selenium and iron were measured in plasma and erythrocytes.
Results: Plasma zinc and selenium concentrations fell significantly: 95% confidence intervals (CI) = −32% to −44% and −22% to −36%, respectively. Copper concentrations fell transiently and then increased significantly: CI = 12–43%. No significant changes were seen in trace element concentrations in erythrocytes expressed either as a ratio of haemoglobin or iron concentration. Erythrocyte iron levels correlated significantly with haemoglobin ($r = 0.93$).

Abbreviations: CRP, C-reactive protein; ICP-MS, inductively coupled plasma mass spectrometry.

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Conclusions: Plasma concentrations of copper, zinc and selenium are unreliable markers of status in patients with an acute inflammatory response. Erythrocyte concentrations of these trace elements may provide a more reliable measure in long-term studies of patients with a chronic systemic inflammatory response. Iron can be used instead of haemoglobin as the denominator when expressing erythrocyte concentrations of trace elements.

Introduction

Micronutrient trace elements and vitamins are an integral component of many metabolic processes and are generally required daily in minute quantities from the diet in order to maintain health. Micronutrient deficiencies due to malnutrition are prevalent in the developing world and constitute a major health problem. However, deficiencies also occur in developed countries among elderly people in both hospital and community settings.[1,2] A knowledge of the micronutrient status is important in such individuals, in patients requiring nutritional support,[3] and following bariatric surgery.[4] Post-surgery and trauma patients may also be at risk of inadequate nutrition to cope with their increased metabolic demand and from pre-existing deficits.[3] In routine practice micronutrient status is usually determined by measuring trace elements and vitamins in plasma. However, plasma concentrations of essential trace elements may fluctuate independently of nutritional status[5]: for example, during the acute inflammatory response to injury, plasma zinc and selenium concentrations fall while plasma copper concentrations increase; plasma selenium and zinc are partly albumin-bound and so may be influenced by plasma albumin concentrations. Consequently interpretation of results may be difficult and may occasionally lead to mismanagement of patients.[6,7]

The use of plasma to measure vitamin status is prone to the same interpretation difficulties. Recently we have investigated the effect of acute inflammatory response on vitamin concentrations in plasma and erythrocytes.[8] In this study, we demonstrated that in nutritionally replete patients who were undergoing elective knee arthroplasty, plasma concentrations of vitamins were transiently reduced by 40–50% following the inflammatory insult and were therefore unlikely to be a reliable measure of their status in the presence of a systemic inflammatory response.[9,10] In contrast, vitamin concentrations in erythrocytes remained stable and so may represent a more reliable index of status in such patients. The purpose of the current study was to repeat this work to determine if the same was true for essential trace elements.

Erythrocyte analytes are usually reported with respect to haemoglobin concentration in order to overcome the problems of inaccuracy in pipetting packed red blood cells. All erythrocyte iron is associated with haemoglobin and so in this study we also investigated iron as a potential surrogate marker for haemoglobin. This is an attractive analytical option since iron can be concurrently measured with the other trace elements by inductively coupled plasma mass spectrometry (ICP-MS).

Materials and methods

Patients and study design

Eleven patients (6 males and 5 females with age range 60–83 years) who were admitted for elective knee arthroplasty and were receiving no micronutrient supplementation were studied. All patients had C-reactive protein (CRP) concentrations of less than 10 mg/L and so had no evidence of existing systemic inflammation. No patients had renal dysfunction or electrolyte abnormalities as evidenced by normal serum urea, creatinine, sodium and chloride concentrations. Standard post-operative treatment was provided and the clinical course in all patients was unremarkable. Venous blood samples were collected into heparin trace element tubes pre-operatively and then at 12, 24, 48, 72 and 168 h after surgery. After centrifugation, the plasma was removed for analysis and packed erythrocytes were prepared by carefully removing any residual plasma and the Buffy coat. Samples were stored at $-70\,^{\circ}C$ until analysed. Packed red cells were lysed by a 4-fold dilution with deionised water, mixed and then centrifuged to remove cell debris. The lysate was then diluted ten-fold with a reagent containing 1% ammonia, 0.5 M diammonium EDTA, 8 mmol/L ammonium citrate, 0.1% Triton-X, 1% butanol, 20 μ/L rhodium). Samples from individual patients were analysed in a single batch to reduce inter-batch analytical variation.

The study was approved by the local Ethics Committee. Subjects were informed of the purpose and procedure of the study and all gave informed consent.

Analytical methods

Copper, zinc, selenium and iron in plasma and erythrocytes were analysed simultaneously by ICP-MS on an Elan 6000 (Perkin-Elmer SCIEX, Ontario, Canada); within-batch imprecision was less than 5% for all trace elements. Albumin was measured by a dye-binding method using bromocresol green and CRP was measured by turbidimetry on an Advia 1650 (Bayer Corporation, Tarrytown, NY, USA). Haemoglobin was measured colorimetrically using Drabkin's method on a Cobas Mira (Roche Diagnostics, Lewes, Sussex): within-batch imprecision was 6.8%.

Statistics

Data are presented as mean. Correlation coefficients were calculated using Pearson's correlation test on Excel. Baseline concentrations were compared with peak or trough