Endothelial Dysfunction, Isoprostanes, and Copper Deficiency

To the Editor:

Following the tradition of using animal experiments to clarify and illustrate human pathology, Lavi et al. sought similarities between people with ischemic heart disease and animals fed cholesterol. They detected a decreased effect of acetylcholine on coronary arteries in 8 of 20 angiogram patients with minimal coronary artery disease. F2-isoprostanes were higher and extracellular superoxide dismutase activity was lower in those with impaired dilation. Findings were consonant with decreased superoxide dismutase activity associated with myocardial infarction history and coronary artery disease.

Results were quite similar to those with rats deficient in copper: a 2-fold increase in isoprostanes and decreased superoxide dismutase. Also, arterial relaxation in response to acetylcholine was decreased and was correlated inversely with plasma isoprostanes.

Impaired vasodilation with acetylcholine in animals deficient in copper and in people with angina pectoris, coronary artery disease, hypercholesterolemia, and untreated hypertension has been reviewed. In addition, cholesterol feeding induces copper deficiency; this phenomenon has been confirmed several times since discovery.

Copper deficiency can be diagnosed when copper is decreased in tissues and when activity of enzymes depending on copper, such as superoxide dismutase, is decreased. Low myocardial copper in ischemic heart disease first was found 4 decades ago. Also, coronary atherosclerosis is inversely proportional to leukocyte copper. Data reviewed here and elsewhere reveal that copper deficiency may be important in ischemic heart disease.

The Western diet often is low in copper in comparison with dietary reference intakes according to chemical analysis of more than 900 diets summarized in several articles. Copper deficiency is the only nutritional insult that elevates cholesterol, blood pressure, homocysteine, isoprostanes, and uric acid; has adverse effects on electrocardiograms and arteries; impairs glucose tolerance and paraoxonase activity; promotes thrombosis and oxidative damage; and to which males respond differently than females. More than 80 anatomic, chemical, and physiological similarities between animals deficient in copper and people with ischemic heart disease have been identified.

A third criterion for diagnosing deficiency is improvement from extra copper. Perhaps the researchers can supplement their subjects with copper and re-evaluate measurements in a search for improvement. Witte et al. gave micronutrients, including copper, to people with ischemic heart disease and found both objective and subjective improvement of heart failure. It is likely that the copper in the supplement was contributory.

Disclosures

None.

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