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Tissue levels of iron, copper, zinc and magnesium in iron deficient rats

Temidayo A. OLADIJI

Biochemistry Department, University of Ilorin, Ilorin

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Abstract

The effects of iron deficiency on the levels of iron, copper, zinc and magnesium in the brain, liver, kidney, heart and lungs of albino rats (*Rattus novergicus*) was investigated. Forty rats were divided into two groups and the first group was fed a control diet containing 1.09g iron/kg diet while the test group was fed diet containing 9ppm iron/kg diet. Tissue iron level reduced in all the dietary groups which may be a reflection of the diet fed to the animals. Copper level increased significantly ($p < 0.05$) in all the tissues studied. This may be a consequence of increased absorption or altered metabolism. It could also mean that the copper binding proteins have a greater affinity for copper during iron deficiency. It was observed that iron deficiency caused a significant ($p < 0.05$) increase in zinc concentration in the tissues studied and magnesium level was found to reduce in all the tissues except the liver. It is proposed that magnesium may be utilized more for some processes that require iron during iron deficiency. It is hereby proposed that the complications of iron deficiency are not due to anaemia alone but also due to its effect on the metabolism of some other trace elements especially copper, zinc and magnesium.

Keywords: Iron, copper, zinc, magnesium

E-mail: atoladiji@yahoo.com

INTRODUCTION

Iron is one of the important mineral elements necessary for the effective metabolism of the mammalian body. Although it is present in very small amounts in the body, iron plays an important role in many metabolic processes (Dallman *et al*, 1975; Worwood, 1977). Iron plays a vital role in oxygen transport and energy production. The average adult body contains approximately 4gm of iron, 3gm in active or functional form and about 1gm in storage. The deficiency of iron continues to be a widespread condition affecting millions of people throughout the world. Although poor populations suffer from it most, lack of iron is one of the few nutrition pathologies present in affluent societies with pre-school age children and women of child bearing ages being the most vulnerable groups. Iron deficiency is present when iron supply is inadequate for the normal synthesis of essential iron compounds (Finch, 1977). Most cases of iron deficiency are mild and do not result in symptoms that are recognized as requiring medical attention. Iron deficiency is therefore most commonly detected through routine laboratory assessment of populations that are particularly at risk (WHO, 1996).

Iron deficiency is the most common nutritional deficiency encountered in surveys of diverse populations in industrialized countries (Cook *et al*, 1970) and it is said to be the most common cause of anaemia in the world. A UN report in 1980 on world nutrition quotes a figure of 43% of children between birth and four years as being anaemic, 20% of adult men and 35% of adult women are anaemic with iron deficiency accounting for more than half of the cases. In recent years, iron requirement during early development have been better defined (Vyas and Chandra, 1984) and greater attention is being paid not only to preventing iron deficiency but also to avoid unnecessary supplementation of iron (Dallman *et al,* 1975). Iron needs are greatest during infancy because of rapid growth, expansion of the blood volumes and lack of reserve of iron in infants below 6 months of age (Steckel, 1984). The risk of developing iron deficiency is greatest after the first two months of life for pre-term infants and after four months in full term infants.

Iron deficiency has been associated with various disorders in the human body. There is altered immune response (Vyas and Chandra, 1984), limitation in physical performance (Cook and Lynch, 1986), and neurological dysfunction (Hurrell and Cook, 1990; Rose, 1995). Several studies in our laboratory have also shown that iron deficiency affects the activities of certain enzymes in rat tissues. Such enzymes include alkaline phosphatase (Oloyede *et al*, 1992), adenosine triphosphatases (Oladiji and Oloyede, 1997), hexokinase and lactate dehydrogenase (Oloyede and Folayan, 1995b) as well as peroxidase (Oladiji and Oloyede, 2000). We also observed that iron deficiency affects the biochemical constituents of rat tissues (Oloyede *et al* 1992). However, the effect of iron deficiency on tissue levels of other mineral elements has not been studied.

Biological interactions among trace elements have been reported to alter the metabolism of other nutrients and metabolites (Cook and Lynch, 1986). Mineral elements interact with each other according to their physicochemical properties i.e. valence shell, electronic structure, ionic radius, co-ordination number, geometric configuration, redox potential, spin transition and ligand exchange. Minerals with similarities in some

of these properties can be predicted to develop antagonistic relationships. The antagonism between zinc and copper is being exploited in the treatment of Wilson's disease, a genetic disease in which copper abnormally accumulates in the liver (Shils and Young, 1998).

Trace elements interact with each other and with other nutrients to such an extent that the margin between the levels at which the effects on the organisms are beneficial and toxic may be quite small or even overlap. This is particularly striking between copper and molybdenum; zinc and cadmium and also selenium and mercury (Prasad *et al*, 1971). The interactions that can occur when excessive amounts of minerals are ingested led nutritionists to suggest that mineral supplements of one mineral can upset the delicate balance of other minerals in the body (WHO, 1996). Consumption of a varied, nutrient dence diet has been proposed to be a better choice than supplementation.

Information on the effect of iron deficiency on tissue levels of some mineral elements is scarce. Sharman and Tissue (1987) reported that offsprings of iron deficient rats had altered tissue zinc levels and also that copper deficiency produces anaemia in rats due to impaired iron mobilization

The present study has therefore investigated the tissue levels of iron, copper, zinc and magnesium in the brain, liver, lungs, kidney and heart of rats fed iron deficient diet.

MATERIALS AND METHODS

Forty (40) male albino rats (*Rattus novergicus*) of twenty-one day old and average weight of 31.5g were used in this study. The rats were divided into two groups and were maintained on diets deficient or adequate in iron. The rats maintained on iron deficient diet served as the test group, while those containing diet adequate in iron served as the control. The composition of the diet is shown in Table 1. The various components were thoroughly mixed and made into pellets to ensure that the rats were well fed. The locust beans employed in the feed formulation were treated as described by Oloyede and Folayan (1995a). The diet was digested using perchloric acid and assayed for iron using the atomic absorption spectrophotometer. The diet deficient in iron was found to contain 9ppm iron, a level that was found to be necessary to avoid high mortality rate of animals maintained on lower iron levels in our preliminary studies. The feed was kept in air tight plastic container and refrigerated from where enough quantities were taken to feed the rats.

The rats were fed their respective diets and demineralized water *ad libitum* for a period of ten weeks. At the end of the feeding period (10 weeks), the rats were sacrificed by cervical dislocation. The brain, liver, heart, kidney and lungs were removed, quickly weighed, acid digested and assayed for iron, copper, zinc and magnesium using the atomic absorption spectrophotometer. The data was analyzed using the students t test.

RESULTS AND DISCUSSION

In all the tissues studied, there was a significant reduction ($p < 0.05$) in the iron level of the test compared to the control rats (Figure 1). This is a reflection of the diet fed to the rats. However, in all the tissues studied, the highest level of reduction in iron content was manifested in the liver and the lowest was recorded in the brain. This may mean that the body iron store is being depleted and the liver being one of the

Table 1: Composition of Diets

Component	Quantity (g/kg)
Corn starch	40
Locust beans	750
Corn oil	40
Sucrose	100
Methionine	20
Lysine	10
*Vitamins mix	10
**Mineral mix	30

*Vitamin mix (per Kg diet): Thiamine hydrochloride, 6mg; Pyridoxine hydrochloride, 7mg; nicotinic acid, 30mg; calcium pantothenate, 16mg; folic acid, 2mg; biotin, 0.2mg; cyanocobalamin, 0.01mg; retinal palmitate, 4,000 IU; cholecalciferol, 1,000 IU; α-tocophenol acetate, 50 IU; menadione, 0.05mg; choline chloride, 2g.

**Mineral mix (g/kg diet): $CoCl_2.6H_2O$ (0.001), $CuSO_4.5H_2O$ (0.078), $MnSO_4.2H_2O$ (0.178), KI (0.032), KH_2PO_4 (10.559), NaCl (3.573), $MgSO_4.7H_2O$ (1.292), $Zn(CO_3)_2$ (1.6), $CaSO_4$ (11.61), $FeSO_4.7H_2O$ (1.078).
Iron deficient diet contains no additional $FeSO_4.7H_2O$.

organs involved in iron storage will release its iron content during iron deficiency (Vyas and Chandra, 1984). Also, the relatively low reduction in brain iron content during iron deficiency compared with those of other tissues may be due to the very important role of iron in brain function. Iron in the brain has been associated with myelination process, memory, attention, cognition and behaviour (Cook and Lynch, 1986). The brain may therefore be spared relatively in this respect.

The copper level of the tissues studied increased significantly ($p < 0.05$) when compared with those of control (Figure 2). This may arise due to increased absorption or altered metabolism of copper causing

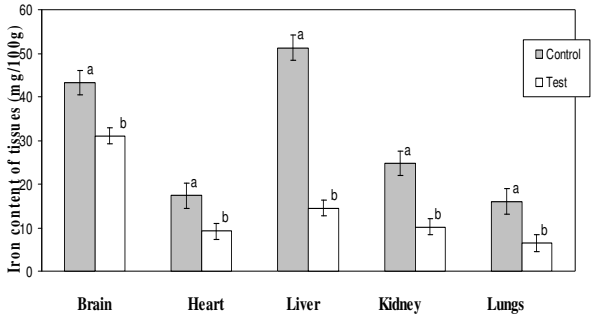

Figure 1: Iron content (mg/100g) of tissues of rats fed iron deficient diet

excessive accumulation of this element in iron deficiency. Also, increased copper level may be as a result of abnormal sequestering of copper and failure of the occurrence of normal mobilization of copper with maturation in iron deficient rats as reported by Sherman and Tissue (1987). One possible factor known to affect the sequestering of copper during iron deficiency is the reduction in the synthesis of cerruloplasmin which is required to accomplish the feroxidase needs which exert a catalytic activity in the plasma to convert Fe^{2+} to Fe^{3+} thereby promoting the rate of incorporation of iron into transferin. If less cerruloplasmin is synthesized, more copper may be stored in tissues. It is also possible that during iron deficiency, copper binding proteins may have a greater affinity for copper than during adequate iron nutrition. This will cause a slow release of copper thereby causing increased tissue concentration of this metal.

Figure 3 shows the level of zinc in the tissue studied. It is observed that there is a significant ($p < 0.05$) increase in the level of zinc in all the tissues studied. Earlier reports have shown that high dietary iron reduces zinc absorption (Prasad, 1983). Low dietary iron therefore may result in an increased rate of zinc absorption. This is because transferin is also essential for zinc transportation and more transferin will be available during iron deficiency (King, 1990). However, the level of magnesium in brain, heart, lungs and kidney reduced significantly ($p < 0.05$) while that of the liver was not significantly ($p > 0.05$) affected (Figure 4). It could be possible that magnesium may be utilized more for some processes that require iron during iron deficiency. This speculation is

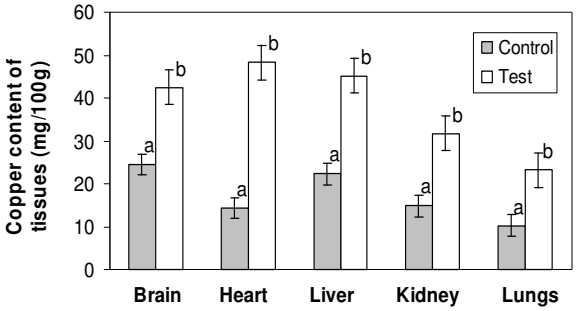

Figure 2: Copper content (mg/100g) of tissues of rats fed diet deficient in iron

further strengthened by the fact that magnesium level in the liver remains unchanged. It is considered that since the liver is one of the storage organs for iron, the liver will have adequate iron from its store for cellular metabolism even during iron deficiency (Steckel, 1984). It is also possible that iron deficiency affects magnesium absorption and transportation causing a reduction in magnesium contents in these tissues.

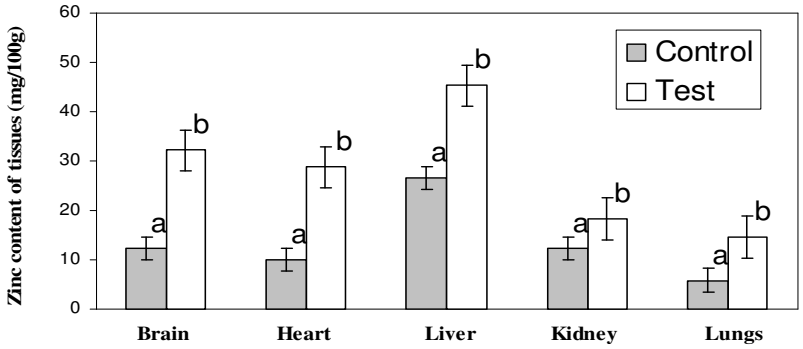

Figure 3: Zinc content (mg/100g) of tissues of rats fed diet deficient in iron.

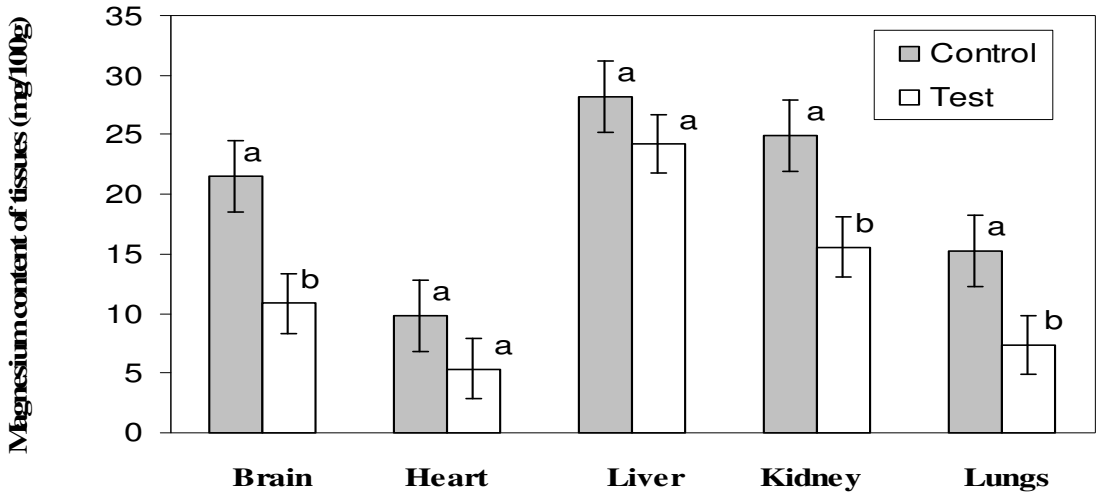

Figure 4: Magnesium content (mg/100g) of tissues of rats fed diet deficient in iron.

The significant interactions that occur during iron deficiency with copper, zinc and magnesium showed that the complication of iron deficiency is not strictly due to anaemia but also due to imbalance in the metabolism of other trace elements especially those that have common absorptive pathway with iron.

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