Indian J Med Res 146, September 2017, pp 430-432
DOI: 10.4103/ijmr.IJMR_246_17

Quick Response Code:

Correspondence

Ocular lesions from copper deficiency

Sir,

Bharathselvi *et al*[1] found negative correlations between plasma copper and homocysteine or homocysteine-thiolactone in patients with age-related macular degeneration (ARMD). They suggest that copper deficiency may play an important role in pathogenesis, partly because the thiolactone inhibits a copper enzyme. Specifically, Cu-Zn superoxide dismutase in human retina may be decreased in ARMD[1].

Some interrelationships among the homocysteine compounds and copper metabolism have been summarized[2,3]. In brief, copper deficiency in rats increases homocysteine and feeding homocysteine to rats disrupts copper utilization. The thiolactone is an irreversible inhibitor of lysyl oxidase, an enzyme dependent on copper for activity has also been noted by the authors. Men supplemented with copper have decreased homocysteine in plasma[2-4].

The epidemic of neuropathy responsive to copper supplementation may be worldwide. It has been called 'human swayback' because of similarity to deficient lambs[5]. Poor balance is the most common complaint. It resembles the neuropathy of pernicious anaemia and may be as prevalent[6]. The neuropathy seems rare enough to be published, but common enough that 10-15 cases can be reported from single clinic[7,8].

Most authors reported myelopathy or peripheral neuropathy with sensory/motor involvement from copper deficiency. Visual complaints were less frequent, perhaps because these were more subtle and thus were less likely to be noticed. Gregg *et al*[9] mentioned optic neuritis briefly. Spinazzi *et al*[10] noticed optic nerve involvement. Naismith *et al*[11] described a woman with an acute onset of blindness. Khaleeli *et al*[12] described a man with reduced visual acuity. Pineles *et al*[13] found progressive optic neuropathy. Decreased myelination of optic nerves has been found in deficient animals[14,15]. These latter experiments and a clinical case[12] revealed that ocular pathology was not peculiar to copper deficiency resulting from gastrointestinal surgery.

None of the studies have addressed the most appropriate dose, duration, route and form of copper supplementation, although Kumar[5] provided some guidelines. Anaemia if present, can be cured rapidly. It has been suggested that supplementation leads to (neurological) stabilization rather than improvement[7]; therapy for 12 months may be necessary for improvement[8]. Plasma copper may be an insensitive test of deficiency; numerous experiments with animals reveal that plasma copper may be normal or increased even though copper in liver or other organs is low[16]. Supplementation with at least 4 mg elemental copper daily (such as gluconate) may be effective[16].

The Age-related Eye Disease Study Research Group[17] observed 3640 people over the age of 55 for more than six years. Three treatment groups and a placebo group were evaluated to determine the effect of dietary supplements on ARMD. Both zinc and antioxidants plus zinc significantly reduced the odds of developing advanced ARMD[17]. Zinc received a major emphasis in the various reports of this study, but no one received zinc without receiving copper as well. Perhaps, copper supplementation rather than zinc was beneficial.

It is not clear whether low cure rates result from insufficient supplementation or severe deficiency. Nerves grow slowly and re-myelination also may be slow. It is clear that copper deficiency leads to neuropathy; eyes should be examined carefully when it is present. Copper deficiency and homocysteine metabolism should receive more attention in studies of ARMD.

***Conflicts of Interest*:** None.

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Received February 9, 2017

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