Movement Disorders
CLINICAL PRACTICE

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Copper Deficiency as a Serious Complication of Anti-Copper Treatment in Wilson's Disease

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We read with great interest the article by Chevalier et al[1] on copper deficiency in patients with Wilson's disease (WD) receiving anti-copper agents. Anti-copper treatment in WD is lifelong, but some patients are overtreated and develop copper deficiency.[2] However, few cases of copper deficiency in WD have been published to date, with no epidemiological data available.[2] Copper deficiency may cause myeloneuropathy and aggravate the neurological symptoms of WD, such as gait disturbances, falls, and weakness.[3] Such clinical worsening may prompt intensification of anti-copper treatment, which will further aggravate the neurological symptoms caused by copper deficiency.[4] Similarly, anemia and neutropenia due to copper deficiency may suggest progressive liver damage or hypersplenism, leading to unnecessary treatments, including splenectomy, which can worsen these hematological complications.[1] Therefore, clinicians must be aware that copper deficiency may worsen both the neurological and hepatic symptoms of WD.[3]

Copper deficiency in WD is diagnosed when urinary copper excretion is markedly reduced: < 20 μg/24 h on zinc salts or <100 μg/24 h on chelators, with low total serum copper and ceruloplasmin.[2] Decreased concentration of non-ceruloplasmin bound copper (NCC) < 5 μg/dl may also indicate copper deficiency in WD, but this method gives false negative results in nearly 20% cases.[2,5] However, high concentrations of NCC (>25 μg/dl) may help differentiate copper deficiency from non-compliance with chelators. In both situations, urinary copper excretion is low, but NCC is high in non-compliant patients and low in those with copper deficiency.[2] Currently, the clinical value of NCC is limited because it is calculated indirectly from serum concentrations of copper and ceruloplasmin. Measuring NCC directly seems promising, but the available methods, such as exchangeable copper, labile bound copper or dNCC need validation in practice.[5] We believe that using such direct measurements of NCC will just help adjust anti-copper treatment and avoid copper deficiency in patients with WD.[5]

Author Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the first draft, B. Review and Critique.

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