

## Is exchangeable copper, a better prognostic tool for assessing treatment control in hepatic Wilson's disease in children?

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### ABSTRACT:

Standard assessment of chelation adequacy in Wilson's Disease (WD) by liver function tests (LFT), non-ceruloplasmin copper (NCC) and 24-hour urine copper (UCu) have fallacies. Exchangeable copper (ExCu) is a newer concept in the diagnosis and management of neurological WD. The aim of the study is to explore the role of ExCu as a prognostic tool for assessment of therapy in liver disease. Hepatic WD patients on  $\geq 1$  y chelation therapy were prospectively enrolled. Newly diagnosed chelation-naive WD children were controls. ExCu in ultrafiltrates was analysed by atomic mass spectrophotometry. Relative exchangeable copper (REC) was defined as percentage ratio of ExCu and total serum copper. Sub-group analysis of ExCu on degree of chelation [well-chelated (UCu 200-500  $\mu\text{g/day}$ ); poorly chelated (UCu  $< 200$  or  $> 500$   $\mu\text{g/day}$ )] and liver disease [stable (normal liver synthetic function and transaminases  $< 2$  times upper limit of normal) and unstable (poor synthetic functions and elevated transaminases)] The authors found that 96 children (n = 61 on chelation, n = 35 controls) aged  $12.5 \pm 4.4$ y were assessed. Chelated WD vs. controls had lower ExCu ( $0.9 \pm 0.6$  vs  $3 \pm 7$   $\mu\text{mol/L}$ ,  $p = 0.03$ ) and higher REC ( $43 \pm 27.4\%$  vs  $30.4 \pm 14.3\%$ ,  $p = 0.01$ ). AUROC of ExCu in chelated vs. controls was 0.8 (cut-off 0.97  $\mu\text{mol/L}$ , sensitivity 80%, specificity of 68%,  $p < 0.01$ ) and stable vs. unstable liver disease was 0.73 (cut-off 0.87  $\mu\text{mol/L}$ , sensitivity 77%, specificity of 65%  $p = 0.01$ ). ExCu had positive correlation with NCC ( $r = 0.92$ ,  $p < 0.001$ ), UCu ( $r = 0.52$ ,  $p < 0.001$ ) and Pediatric end-stage liver disease (PELD) scores ( $r = 0.47$ ,  $p = 0.01$ ). Multivariate analysis of the entire cohort showed Child Turcotte Pugh scores ( $p = 0.002$ ) and duration of treatment ( $> 1$ -year vs  $< 1$ -year) ( $p = 0.002$ ) significantly influences ExCu values. Median follow-up duration was 10 (0-24) months. 14/96 (15%) either died or were referred for liver transplantation. Survival on Kaplan Meier curves were significantly higher ( $p = 0.01$ ) if baseline ExCu was  $\leq 0.87$ .

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The conclusion from the study was Exchangeable copper is an effective monitoring tool to assess chelation. New chelators reduce ExCu levels to  $< 0.97$   $\mu\text{mol/L}$  after 1 year of chelation and thereafter achieve liver stability if values are  $< 0.87$   $\mu\text{mol/L}$ .

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