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Ursodeoxycholic acid improves liver function via phenylalanine/tyrosine pathway and microbiome remodelling in patients with liver dysfunction

Ursodeoxycholic acid (UDCA) is a metabolic by-product of intestinal bacteria, showing hepatoprotective effects. However, its underlying molecular mechanisms remain unclear. The purpose of this study was to elucidate the action mechanisms underlying the protective effects of UDCA and vitamin E against liver dysfunction using metabolomics and metagenomic analysis. In this study, we analysed blood and urine samples from patients with obesity and liver dysfunction. Nine patients were randomly assigned to receive UDCA (300mg twice daily), and 10 subjects received vitamin E (400 IU twice daily) for 8 weeks. UDCA signifcantly improved the liver function scores after 4 weeks of treatment and effectively reduced hepatic deoxycholic acid and serum microRNA-122 levels. To better understand its protective mechanism, a global metabolomics study was conducted, and we found that UDCA regulated uremic toxins (hippuric acid, p-cresol sulphate, and indole-derived metabolites), antioxidants (ascorbate sulphate and N-acetyl-L-cysteine), and the phenylalanine/tyrosine pathway. Furthermore, microbiome involvement, particularly of Lactobacillus and Bifdobacterium, was demonstrated through metagenomic analysis of bacteria-derived extracellular vesicles. Meanwhile, vitamin E treatment did not result in such alterations, except that it reduced uremic toxins and liver dysfunction. Our fndings suggested that both treatments were effective in improving liver function, albeit via diferent mechanisms.

Biography

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