Interventions for patients with primary biliary cirrhosis

Systematic reviews and meta-analyses of randomised clinical trials

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ABSTRACT

This study has been carried out in the Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen University Hospital since 2002.

To assess the effects of ursodeoxycholic acid (UDCA), d-penicillamine, colchicine, methotrexate, azathioprine, and cyclosporin A in patients with primary biliary cirrhosis (PBC).

Six systematic reviews and meta-analyses of relevant randomised clinical trials.

Trials were identified mainly through The Cochrane Hepato-Biliary Group Controlled Trials Register, The Cochrane Library, MEDLINE, and EMBASE. We applied meta-analyses, where appropriate, to determine intervention effects on mortality, mortality or liver transplantation, clinical symptoms, liver biochemistry, liver histology, and adverse events.

Six systematic reviews include a total of 42 trials with 4009 patients with PBC. Two thirds of the trials had low methodological quality regarding generation of the allocation sequence, allocation concealment, blinding, and follow-up. The meta-analyses did not show significant benefits of UDCA, d-penicillamine, colchicine, methotrexate, azathioprine, and cyclosporin A on survival of patients with PBC. UDCA improved biochemical variables and clinical symptoms such as ascites and jaundice, but it was associated with adverse events, mainly weight gain. D-penicillamine had no significant beneficial clinical effects, but significantly increased adverse events. Colchicine may improve pruritus, but it tended to lead to more adverse events (mostly transient diarrhoea), although it is not statistically significant. Methotrexate may improve pruritus and decrease the levels of serum alkaline phosphatases and plasma immunoglobulin M, but the hepatotoxicity could not be ruled out. Patients given azathioprine experienced more adverse events than patients given no intervention or placebo, such as rash, severe diarrhoea and bone marrow depression. Cyclosporin A might improve pruritus, reduce alanine aminotransferase, and increase serum albumin level. But cyclosporin A caused more adverse events, including renal dysfunction and hypertension.

We did not find reliable evidence to support the clinical use of the assessed interventions in patients with PBC. A large proportion of the trials is flawed by low methodological quality, small number of patients, and short trial duration. None of the interventions can be recommended for general use in clinical practice.