BAYESIAN HIERARCHICAL MODELING OF RANDOMIZED AND NON-RANDOMIZED STUDIES COMPARING CICLOSPORIN WITH IMMEDIATE- AND PROLONGED-RELEASE TACROLIMUS IN LIVER TRANSPLANT RECIPIENTS

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OBJECTIVES: Several meta-analyses comparing ciclosporin with immediate-release (IR) tacrolimus have been published. There have been insufficient randomized trials comparing ciclosporin with prolonged-release (PR) tacrolimus. In the present study, a network meta-analysis (NMA) was conducted to compare the efficacy of ciclosporin, IR and PR tacrolimus in liver transplant recipients. METHODS: Systematic literature review of PubMed, EMBASE and the Cochrane Library identified randomized controlled trials and large-scale observational studies (>500 patients) published since January 2000 comparing IR tacrolimus with PR tacrolimus or ciclosporin. A Bayesian NMA was used to conduct a meta-analysis of death, graft loss, and acute rejection (AR) at 12 months. Outcomes were adjusted for recipient gender and age, hepatitis C (HCV) status, hepatocellular carcinoma, mycophenolate mofetil, azathioprine, and steroid use. RESULTS: Head-to-head comparisons of ciclosporin versus IR tacrolimus and PR tacrolimus versus IR tacrolimus (n=2). Relative to ciclosporin, IR and PR tacrolimus were associated with reduced likelihood of death within 12 months of transplant (median odds ratio [OR] of 0.78 and 0.60, respectively). Mortality outcomes were superior with PR versus IR tacrolimus (median OR of 0.76). AR was less common with IR tacrolimus compared with ciclosporin (median OR of 0.69), whereas limited data for PR tacrolimus was evidenced by large credible intervals. There were no significant differences between PR tacrolimus and ciclosporin (median OR of 0.76). There were no significant differences between PR tacrolimus and PR tacrolimus compared with ciclosporin (median OR of 0.69), whereas limited data for PR tacrolimus was evidenced by large credible intervals. There were no significant differences between PR tacrolimus and PR tacrolimus compared with ciclosporin (median OR of 0.76). There were no significant differences between PR tacrolimus and PR tacrolimus compared with ciclosporin (median OR of 0.76). There were no significant differences between PR tacrolimus and PR tacrolimus compared with ciclosporin (median OR of 0.76).

The AMELIORATION OF DOXORUBICIN-INDUCED OXIDATIVE LIVER INJURY BY URSODEOXYCHOLIC ACID

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OBJECTIVE: The overproduction of free radicals is considered as a significant cause regarding the complications of doxorubicin therapy, such as growth inhibition, antiangiogenic effect and increased oxidative stress. The aim of our study was to evaluate the potential hepatoprotective properties of ursodeoxycholic acid (UDCA), its influence on lipid peroxidation (LPO) and expression of glutathione-dependent antioxidative enzymes in the livers of rats treated with DOX. METHODS: Twenty-four male Wistar rats were divided in four groups. Animals were administered either with vehicle (saline i.p. [K1] or saline i.p. with propylene glycol p.o. [K2]), DOX (3 mg/kg i.p. every other day for total 3 doses) or combined UDCA 25 mg/kg p.o. every day for total 3 doses, starting one day before administering DOX. On the 28 days animals were euthanized and the livers were immediately harvested in order to determine the expression of selected parameters of oxidative stress. RESULTS: In the livers of animals administered with DOX, LPO was increased compared to both control groups, whereas in DOX+UDCA group the intensity of LPO was decreased, closely to control values. Treatment with DOX significantly increased the specific activity of glutathione peroxidase (GPx) compared to control groups (p<0.01 vs. K1 and K2). Combined treatment with DOX+UDCA decreased GPx activity. Similarly, the activity of glutathione reductase was highest in group treated with DOX and lowest in group treated with UDCA. Specific activities of catalase and superoxide dismutase were not significantly different between control and experimental groups. The main result was that UDCA decreased the activity of glutathione peroxidase and modulated the expression of glutathione-dependent antioxidative enzymes. CONCLUSIONS: UDCA might be considered as a potential alternative therapy for the treatment of patients with doxorubicin-induced oxidative stress injury. However, further studies are necessary to confirm these findings.

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Randomized clinical trials (RCTs) assessing effectiveness of DT vs TT medications. The present study comprised a systematic review, meta-analysis and indirect treatment comparison of ciclosporin, immediate-release (IR) and prolonged-release (PR) tacrolimus in liver transplant recipients using studies published since January 2000 comparing IR tacrolimus with PR tacrolimus or ciclosporin. A random effects meta-analysis was conducted to compare all three regimens. In intention-to-treat (ITT) analysis, no significant differences were observed between ciclosporin, IR and PR tacrolimus. Relative to ciclosporin, IR and PR tacrolimus were both associated with reduced likelihood of death within 12 months of transplant (median OR of 0.78 and 0.76, respectively). Mortality outcomes were superior with PR versus IR tacrolimus (median OR of 0.76). AR was less common with IR tacrolimus compared with ciclosporin (median OR of 0.69), whereas limited data for PR tacrolimus was evidenced by large credible intervals. There were no significant differences between PR tacrolimus and ciclosporin (median OR of 0.76). There were no significant differences between PR tacrolimus and PR tacrolimus compared with ciclosporin (median OR of 0.76). There were no significant differences between PR tacrolimus and PR tacrolimus compared with ciclosporin (median OR of 0.76). There were no significant differences between PR tacrolimus and PR tacrolimus compared with ciclosporin (median OR of 0.76). There were no significant differences between PR tacrolimus and PR tacrolimus compared with ciclosporin (median OR of 0.76). There were no significant differences between PR tacrolimus and PR tacrolimus compared with ciclosporin (median OR of 0.76).