Effect of Standard Dosage of Paracetamol versus Placebo as Antipyretic Therapy on Transaminitis in Adult Dengue Infection: A Randomized Controlled Trial

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Background: Dengue infection is an important cause of acute liver failure in tropical countries. Paracetamol is recommended as the antipyretic of choice for dengue infection. Previous observational studies have suggested that excessive paracetamol intake can be related to transaminitis. Whether the standard dosage of paracetamol causes transaminitis in dengue infection is uncertain.

Objective: To determine the effect of standard dosage of paracetamol on transaminitis in dengue infection.

Methods: In this multicenter, randomized, double-blinded, placebo-controlled trial, we randomly assigned adult participants who were admitted with laboratory-confirmed dengue infection to receive either paracetamol (500mg) or placebo (500mg) every 4 hours if body temperature exceeded 38°C during hospitalization. The primary outcome was the percentage of participants with transaminitis, defined as a combination of serum aspartate transaminase (AST) and alanine transaminase (ALT) level of more than 3 times of the upper normal limit at the recovery day. Secondary outcomes were mean and maximum daily body temperatures and mean overall pain score during the admission.

Results: A total of 125 participants were randomly assigned to receive either paracetamol (n=63) or placebo (n=62). The mean age ±SD of participants was 27.5±10.5 years and 86.2% were male. There were no significant differences in age, gender, AST and ALT levels between the two groups at baseline. The median total dosage of paracetamol was 2.5 (IQR: 1.1-5) g, and median daily dosage at 1.5 (IQR 0.8-2.0) g. The study was early terminated owing to a significantly higher rate of transaminitis in the paracetamol group than in the placebo group (22.2% VS 10.0%; IRR 3.77, 95%CI 1.36-10.46, p=0.011). The change of AST and ALT levels in paracetamol group was significantly more than in placebo group (mean difference 12.43 U/L/day, p<0.001, and 7.40 U/L/day, p<0.001, respectively). The differences in mean and maximum daily body temperatures, study medication intake, analgesic intake, pain score, duration of fever, and length of hospital stay between the two groups were insignificant. Neither the mortality, nor the liver failure was found.

Conclusion: Use of standard dosage of paracetamol in dengue infection can increase the rate of transaminitis and transaminase level. In addition, paracetamol shows no benefit in term of fever reduction or pain score. (ClinicalTrials.gov, number NCT02833584.)

Keywords: Paracetamol, Dengue, Hepatitis, Transaminitis