Estimate Time to Develop Hepatotoxicity from Anti-Tuberculosis Drugs and Predisposing Factors in Tuberculosis Co-Infection with HIV Patients versus Patients with Tuberculosis Infection Alone in Maharaj Nakorn Chiang Mai Hospital

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Background: The Hepatotoxicity from standard course regimen of anti-tuberculosis drugs remains a common adverse effect among tuberculosis patients, which consequently causes the expansion of treatment duration, extravagant medical resources, risk of treatment failure, and increasing mortality. The predisposing factors of anti-tuberculosis drugs induced liver injury (DILI) and optimal time to follow-up liver function test are still limited.

Objective: To determine the predisposing factors of anti-tuberculosis drugs induced liver injury (DILI) and optimal time to follow-up liver function test.

Methods: We conducted a retrospective cohort study of adult-patients with diagnosed tuberculosis in Maharaj Nakorn Chiang Mai Hospital during January 2010 – January 2017 by reviewing medical records. The primary outcome was to compare the time to develop hepatotoxicity from anti-tuberculosis drugs between tuberculosis patients versus those co-infected with HIV. The secondary outcome was to find the predisposing risk factors and predictive model to predict the probability to develop hepatotoxicity.

Result: A total of 212 tuberculosis patients, who received standard course regimen of anti-tuberculosis drugs, were reviewed. The cumulative incidence of hepatotoxicity during treatment occurred in 30 of 130 patients (23.08%) in tuberculosis alone, and in 15 of 70 patients (21.43 %) with HIV co-infection (RR 0.93, 95%CI, 0.54 - 1.60). There was no significant time to develop hepatotoxicity after initiation therapy (14 (10-21) versus 11 (6-32); p-value 0.42) in both groups. The age ≥ 60 years (HR 2.09, 95%CI 1.04-4.23), percentage of lymphocyte count (HR 0.95; 95%CI 0.92-0.98), aspartate aminotransferase (AST)-to-platelet ratio index (APRI) ≥ 0.7 (HR 2.88; 95%CI 1.42-5.83), and unknown status of hepatitis B or C infection (HR 0.37; 95%CI 0.14-0.94) were significant predisposing factors of developing hepatotoxicity. The combined model of age ≥ 60 years, underlying diabetes mellitus, percentage of lymphocyte count, APRI and status of hepatitis B or C infection could be used as a predictive tool for the probability to develop hepatotoxicity after treatment.

Conclusion: The risk of developing hepatotoxicity from anti-tuberculosis drugs is not statically different between patients with tuberculosis alone compared with HIV co-infection. However, there is an increasing trend of hepatotoxicity in hepatitis C co-infection patients.

Keywords: Anti-tuberculosis drugs, Hepatotoxicity, Drug induced liver injury, HIV-co-infection, Predictive tool