Use of N-acetylcysteine for prevention and treatment of isoniazid induced liver injury during treatment of mycobacterial infections

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Introduction
• Hepatotoxicity is the most common adverse event of anti-tuberculosis therapy.
• Approximately 20% of patients on standard MTB therapy (or INH alone) develop liver enzyme increase leading to drug discontinuation in ~11%.
• N-acetylcysteine (NAC) exerts a hepatoprotective effect by replenishing glutathione stores and enhancing the cellular antioxidant defense mechanism.
• Randomized controlled trials have shown that the use of NAC in humans decreases the risk of hepatotoxicity associated with MTB treatment but there is limited data regarding its utility.

Materials and Methods
• Patients who received NAC from January 2012 to March 2018 for prophylaxis and treatment of increasing liver function tests (LFTs) while on isoniazid (INH) were included.
• A retrospective review of the medical record system was performed.
• Inclusion criteria: patients age >18 who received INH for mycobacterium infections + NAC.
• Exclusion criteria: Follow up labs not available, patient not on INH, or metastatic cancer.

Results
• 19 patients were included. Eleven received NAC for prevention of hepatotoxicity, eight received NAC for treatment.
• Underlying liver issue: 5 liver cirrhosis, 2 hepatic steatosis vs fibrosis, 11 HCV, 1 HBV.
• Site of infection: -10 pulmonary; 3 LTBI, 2 CNS, 3 disseminated, 1 atypical mycobacteria (M. abscessus)
• All patients received the same dose of INH (appropriately dosed according to weight).
• The prophylaxis group had stable LFTs during treatment except for 2 patients (underlying HCV and liver cirrhosis) whose enzymes increased >3x upper limit of normal.
• Only pt 11 required discontinuation of INH.
• The treatment group had a favorable trend of liver enzymes after NAC initiation with levels significantly improving in general by day 14.
• Three patients, 1, 6, and 9, did not require discontinuation of antibiotics.
• No side effects of NAC were documented in any patient.

References