

Drug Safety



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Early Drug Induced Liver Injury After Intensive Phase of Tb Treatment in Indonesia: Primary Care Centers and Lung Hospital Study

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Background: Tuberculosis are still a problem for emerging countries such Indonesia. The program for controlling and eliminations had been addressed on the use of antituberculosis medicines. The safety profile of those drugs, particularly drug-induced liver injury (DILI), has been studied, however, this information on local or Indonesian capture is still minimum.

Objectives: To assess the proportion of early drug-induced liver injury (eDILI) due to tuberculosis treatment (TbT) among Indonesian's TB patients during the intensive phase of treatment.

Methods: Prospective cohort study in 10 primary care centers and 2 lung hospitals based setting from 2 provinces (Yogyakarta and Lampung Provinces, Indonesia) were conducted in TB patients who used standard fixed combination regimens during the intensive phase of treatment. Patients with abnormal baseline AST and ALT level, lower hemoglobin level and HIV positive were excluded. The AST and ALT level were measured before treatment and after two months intensive phase of treatment. Early DILI (eDILI) was defined if the AST/ALT increasing above the upper normal limit.

Results: One hundred and fifteen subjects were followed, 58.3 % were male, age 38.6 years (± 16.6), and 58.3 % were underweight BMI. The baseline of AST and ALT were in normal range value, 20.4 (± 1.4) and 16.7 (± 1.7), respectively. After intensive phase of treatment, 7.5 % patients were considered as eDILI. This group has significantly higher percentage of increase AST and ALT after intensive treatment compared to non-eDILI (63.3 ($\pm 0.22.4$) vs. 39.1 ($\pm .3.8$), $p < 0.001$, respectively for AST, and 191.1 ($\pm .67.6$) vs. 78.1 ($\pm .7.5$), $p < 0.001$, respectively for ALT. This changed has still significantly difference after adjusting of age and BMI.

Conclusions: The incidence of drug-induced liver injury is around 10 % among Indonesian's TB patients who used standard fixed combination regimens. The TB program need to increase awareness on this potential liver injury related to TB drugs. Prospective studies are needed to know the DILI among these after continuation phase of treatment

Autoimmune Disease Induced by Anti-TNF Agents and Tocilizumab: An Analysis of the Italian and English Pharmacovigilance Database

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Introduction: Anti-TNF agents are increasingly being used in the widely expanding number of rheumatic and systemic autoimmune diseases. As a result of this use, and of the longer follow-up period, recently, there are a growing number of reports of autoimmune diseases related to anti-TNF agents and tocilizumab, ranging from mild immunological alteration to life-threatening systemic autoimmune disease.

Aim: The aim of this study was to make a comparison between the Italian and the English pharmacovigilance database on ADR reports of autoimmune disease related to anti-TNF agents: adalimumab, certolizumab, etanercept, golimumab, ustekinumab, infliximab, and tocilizumab.

Methods: We used both the Italian Rete Nazionale di Farmacovigilanza (RNF) and the English MHRA (Medicines and Healthcare Regulatory Agency) databases to extract ADR data. We analyzed reports till March 13th 2013.

Results: Over the study period, the incidence of autoimmune diseases related to those biological agents on the total of ADR is 6.23 % in RNF and 4.06 % in MHRA. System organ class involved in autoimmune ADR are: muscle and tissue disorders (31.97 % RNF, 31.97 % MHRA), skin disorders (35.92 % RNF, 35.92 % MHRA) and nervous system disorders (14.3 % RNF, 10.63 % MHRA). Representative autoimmune ADR reported in RNF are: psoriasis (17.5 %), pustular psoriasis (7.75 %), Lupus erythematosus (7.75 %), Crohn's disease (4.9 %), noninfectious pericarditis, sarcoidosis and uveitis (3.6 %). In the MHRA database, representative autoimmune ADR reported are: rheumatoid arthritis (18.62 %), psoriasis (18.44 %), Crohn's disease (7.18 %), Sjögren's syndrome (6.18 %), pustular psoriasis (5.36 %), vasculitis (5.36 %), Lupus erythematosus (4.45 %). Anti-TNF agents mostly involved in autoimmune disease are adalimumab (7.27 % RNF, 3.96 % MHRA), etanercept (6.49 % RNF, 4.06 % MHRA), infliximab (6.56 % RNF, 3.98 % MHRA), ustekinumab (5.88 % RNF, 11.15 % MHRA). Tocilizumab is involved both in the two databases is the tocilizumab (1.55 % RNF, 2.25 % MHRA).

Conclusion: Data suggest that the type of autoimmune ADR reported is more or less the same in the two databases as the agents.