Drug-induced Liver Injury: An 11-year Experience of 764 Patients From Single Tertiary Academic Center in Thailand

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Background: There is a growing concern about drug-induced liver injury (DILI).

Objective: To investigate the significance of DILI in a tertiary medical center.

Methods: A retrospective cohort study was conducted. Individuals with suspected DILI were identified from the electronic medical database using the ICD-10 code of toxic liver diseases (K71) and additional codes (T36–T65) between 2005 and 2015. The Roussel Uclaf Causality Assessment Method was used to quantify the strength of association between liver injury and medication implicated as causing the injury. The pattern of DILI was defined by biochemical criteria using the R ratio.

Results: The causality was assessed in 3,279 patients, and 764 were considered to have highly probable, probable, or possible DILI. The mean age of patients with DILI was 53±17 years; 52% were female and 62.4% required hospitalization. The annual incidence rate of DILI was 30.5 per 1 million patients with increasing from 11.4 to 44.8 per 1 million patients from 2005 to 2008, followed by decreasing to 16.0 per 1 million patients in 2015 (p for trend=0.059). A total of 284 patients (37.2%) had a hepatocellular type of DILI, while 269 patients (35.2%) had a cholestatic type and 211 patients (27.6%) had a mixed type of injury. Patients with a cholestatic/mixed type of injury were older than those with a hepatocellular type (55±18 vs 50±16 years, p=0.001). DILI was caused by single prescription drug in 68.9% of cases, followed by herbs (21.1%) and multiple agents (10%). The most commonly implicated drug was anti-tuberculous drugs (34.4%), followed by antibiotics (19.9%), immunosuppressive agents (11.1%), lipid-lowering agents (10.6%), anticonvulsants (7.1%), and antineoplastic agents (5%). In-hospital mortality was 14.5% and 8 (11.5%) of 69 cases died of acute liver failure. The mortality was not different between patients hospitalized with hepatocellular injury and those with cholestatic/mixed pattern (11.7% vs 15.8%, p=0.22). Factors associated with in-hospital mortality were age ≥60 years (OR 5.95, 95% CI: 2.11-16.8), prothrombin time at diagnosis of DILI (OR 1.07; 95% CI: 1.03-1.12), and baseline hemoglobin level (OR 0.72; 95% CI: 0.57-0.89).

Conclusion: The incidence of DILI cases in a tertiary academic center tends to decrease over the last decade. Antituberculous drugs and herbs are the leading causes of DILI. Patients’ age and initial severity of liver injury are significant determinants of the likelihood of death.

Keywords: Drug-induced liver injury, Incidence, Hepatocellular injury, Cholestatic pattern, Mixed pattern