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Clinicoetiological Profile of Patients Presenting With Drug Induced Liver Injury

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Abstract

Introduction: Drug-induced liver injury (DILI) is common worldwide and has a potentially fatal outcome. We present here the clinical characteristics and outcome of patients with drug induced liver injury from our hospital.

Materials and methods: we retrospectively looked at 25 cases of DILI who presented to our hospital in whom there was a causal or highly probable relationship between drug use and liver disease. Data was collected from MRD section of hospital.

Results: The mean age of patients was 36 years; sexual distribution was 14 females and 11 males. The major cause of hepatotoxicity was drugs (88%), with herbal medicine accounting for 12%. The leading causative agents were Anti tubercular drugs (44%), followed by acetaminophen (20%). The pattern of hepatotoxicity was hepatocellular in 17 patients (68%), mixed in 4 (16%), and cholestatic in 4 patients (16%).Acute liver failure developed in 5 patients (two patients related to ATT, two related to acetaminophen and one patient due to Herbs).

Conclusion: ATT and acetaminophen were the most common etiologic agents for drug-induced liver injury.

Keywords: Drug, Hepatocellular, Acute Liver Failure.

Introduction

Almost all drugs or compounds, including herbal medicines, have potential hepatotoxicity. DILI has an estimated annual incidence between 10 and 15 per 10,000 to 100,000 persons exposed to prescription medications. DILI accounts for approximately 10 percent of all cases of acute hepatitis, and it is the most common cause of acute liver failure in the United States. In general, adults are at higher risk for DILI than children. Women may be more susceptible to DILI than men.

Materials And Methods

We retrospectively studied all patients diagnosed with DILI in the Department of medicine of Government Medical College from September 2017 to June 2019. The data were collected from in patient records of SMHS Hospital Srinagar. A clinical investigation was completed for all patients, including a detailed history and physical examination, biochemical and serological tests, and radiologic imaging. The inclusion criteria were as follows: 1) age above 15 years, 2) alanine amino- transferase, as partate amino transferase, alkaline phosphatase, or conjugated bilirubin greater than twice the upper normal limit, 3) history of drug or herbal medicine use within 6 weeks, and 4) elimination of any other causes of liver injury. The exclusion criteria were as follows: 1) history of any pre-existing liver disease, 2) alcohol consumption or receipt of blood products over the last 6 months, 3) suspicious or proven viral, metabolic, or any other etiology,4) any radiological findings indicating other causes of liver injury, including significant

hepatosteatosis, and 5) severe cardiopulmonary or renal disease.Biochemical tests, including serum alanine aminotransferase (ALT), aspartate aminotransferase, gamma-glutamyl transpeptidase, alkaline phosphatase (ALP), bilirubin, fasting glucose, cholesterol, triglyceride levels, complete blood cell counts, and pro- thrombin time, were recorded for all patients. Serological markers were studied, including for viral hepatitis: anti-hepatitis A virus IgM and IgG, HBsAg, anti-HBs, HBeAg, anti-HBe, anti-HBc IgM and IgG, anti-hepatitis C virus; for autoimmune hepatitis, including anti-nuclear antibodies and for metabolic liver disease, including serum iron, total iron binding capacity, ceruloplasmin.

Hepatobiliary imaging study was performed via abdominal Ultrasonography. Portal Doppler Ultrasonography for patients with suspected vascular liver disease and computed tomography and/or magnetic resonance imaging for suspicious space-occupying liver lesions were also performed. In patients with cholestatic liver disease, biliary tract abnormalities were ruled out. The diagnosis of DILI was established on the basis of a patient's history, clinical condition, biochemical and serological markers, and imaging studies. Standard definitions and criteria for assessing the causality of adverse drug reactions were characterized and adopted in accordance with the International Consensus Meeting. The pattern of DILI was defined according to the ratio of ALT to ALP (as a multiple of their upper normal limits): >5 hepatocellular, 2-5 mixed, and <2 cholestatic pattern.

Results

In total, 25 patients with drug induced liver injury (mean age 36 years; 14 females, 11 males) were assigned.

The major cause of hepatotoxicity was drugs (88%), with herbal medicine accounting for 12%. The leading causative agents were ATT (44%), followed by acetaminophen. Amoxicillin-clavulanate was the most common antibiotic and responsible in 3 cases (12%).Herbs used mainly for jaundice was the most common cause of HILI and responsible in 12% of cases. The demographic, etiologically featured, and laboratory data are summarized in Table.

The pattern of hepatotoxicity was hepatocellular in 17 patients (68%), mixed in 4 (16%), and cholestatic in 4 patients (16%).A hepatocellular and mixed pattern was seen in 2 of 3 patients of the HILI group without the cholestatic pattern.

Acute liver failure with encephalopathy developed in 5 patients (in two patients, this was related to ATT,two patients related to acetaminophen,one patient to herb. Two of five patients survived by supportive treatment.three patients died awaiting liver transplantation. Except for these three patients, all patients fully recovered without chronicity in the follow-up after cessation of the suspected drug.

Disease group	n	%
ATT	11	44
Acetaminophen	5	20
Herb	3	12
Antibiotic	3	12
phenytoin	2	8
Statin	1	4

Injury pattern	n	%
hepatocellular	17	68
Cholestatic	4	16
mixed	4	16

Discussion

Over 1000 medications and herbal products have been implicated in the development of DILI, and the list continues to grow.The most common drug implicated in acute DILI in the United States is acetaminophen, followed by antibiotics. Worldwide, amoxicillin and

clavulanate is one of the most commonly reported causes of DILI.

DILI can be classified in several ways, including by its

1. Clinical presentation:
   - Hepatocellular (cytotoxic) injury
   - Cholestatic injury
   - Mixed injury
2. Mechanism of hepatotoxicity:
   - Predictable
   - Idiosyncratic
3. Histologic findings, such as:
   - Hepatitis
   - Cholestasis
   - Steatosis.

Acute presentations of DILI include mild, asymptomatic liver test abnormalities, cholestasis with pruritus, an acute illness with jaundice that resembles viral hepatitis, and acute liver failure.

A number of scales have been developed that attempt to codify causality of drug toxicity into objective criteria. Examples include the CIOMS Roussel-Uclaf Causality Assessment Method (RUCAM) scale and the Maria & Victorino (M & V) clinical scale. The Drug-Induced Liver Injury Network (DILIN) developed the DILIN Causality Scoring System to adjudicate the causality of drug-induced injury for patients enrolled into its prospective clinical trial.

The primary treatment for DILI is withdrawal of the offending drug and monitoring to ensure the liver tests normalize.Recovery will occur in the majority of patients with DILI once the offending medication is stopped.

Conclusion

Many patients with DILI are asymptomatic and are only detected because of laboratory testing. Patients with acute DILI who are symptomatic may report malaise, low-grade fever, anorexia, nausea, vomiting, right upper quadrant pain, jaundice, acholic stools, or dark urine.A comprehensive approach is needed for diagnosis and management of drug induced liver injury.

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