LETTER TO EDITOR

DRUG INDUCED SERIOUS HEPATIC ADVERSE REACTIONS IN A TERTIARY CARE CENTRE: A FIVE-YEAR RETROSPECTIVE ANALYSIS

Sir,
A serious adverse drug reaction (ADR) is defined as one that requires hospitalization, is permanently disabling, or results in death. This study was performed to determine the characteristics of serious hepatic ADRs in the Department of Gastroenterology in a tertiary care center and to establish a causal relation between drug and disorder based on World Health Organization (WHO) causality definitions.

A retrospective review of case records of hospitalized patients with the diagnosis of hepatic ADRs (January 1998 to December 2002) in the Department of Gastroenterology, St. John’s medical college, Bangalore was done after obtaining Institutional ethical review board clearance. The hepatic disorders were considered as drug induced when:

1. No alternative explanations for the disorder were available.
2. There was a temporal relation with the drug ingestion and liver disease (5-90 days).
3. Improvement in the condition of the patient after dechallenge.

Liver injury was designated hepatocellular, when alanine aminotransferase (ALT) was greater than two times the upper limit of normal (ULN), or the ALT/ alkaline phosphatase (AP) was ≥ 5; cholestatic when the AP is greater than two times ULN or the AP/ ALT ratio was £ 2: and mixed when the ALT/ AP ratio was two to five and the individual values were greater than two times ULN. The relevant data were collected which included age, sex, clinical presentation, viral markers (HAV-IgM, HBs Ag, HBC-IgM, anti HCV), Liver Function Tests (LFTs), complete diagnosis, the details of the drugs used, reaction time (time taken for the ADR to occur after the last exposure to the drug (RT)) and the outcome. The data was subjected to descriptive analysis.

Out of 6302 case records screened, 25 cases were included in the study and categorized as certain (two), probable (20) and possible (three). Certain and probable cases were analyzed (22). The median for age was 51 years (interquartile range 45-57). Male to female ratio was 1.7. The major drug class implicated was anti-tuberculous drugs (ATD) (17), followed by cisplatin, metformin, low molecular weight heparin, chlorpromazine and leflunomide (one case each). The median for RT 29.5 days (interquartile range 14-40) and that for resolution was 18.5 days (interquartile range 14.3-24.3). Serum viral markers were negative and base line LFTs were normal for the patients considered for analysis. Pattern of acute hepatitis was hepatocellular in 11, cholestatic in seven and mixed in four patients each. The outcome was recovery in 20 patients and mortality in two patients.

The maximum number of patients were 50 years old and had acute hepatitis with majority under hepatocellular category as reported in the study by Sargo et al. However, all the drugs implicated in the present study were different from that identified by Sargo et al. The major drug class implicated in the present study was ATD (77%) similar to a previous Indian study. Hepatotoxicity induced by metformin, cisplatin, LMWH and leflunomide induced death noticed in this study have been rarely documented in literature. Mortality of 0.4% in the Department of Gastroenterology during the study period was due to serious hepatic ADRs.

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most important reason for not using any strategy? (time constraints/ lack of belief in such strategies/ poor response/ financial constraints/ lack of infrastructure/ no access to a trained person/ any other reason (specify)).

In fifteen companies the number of software engineers was between 100 and 500 and five companies had between 500 and 1000 employees. Seventeen out of twenty HRD managers were aware of the health risks. Eleven had got the information from newspapers, five from the employees’ experience, and one from a television program. When asked about the three most likely complaints, fifteen out of seventeen mentioned (i) visual strain, (ii) back pain, and (iii) other musculoskeletal pains. Two mentioned ‘psychological strain’ and ‘weight gain’ as other likely hazards. Two others did not know the likely problems. Ten out of seventeen were using some lifestyle modification strategy, while seven were not. The following strategies were used: indoor and outdoor games, yoga including meditation, health checkups, health advice, recreational facilities, and a ‘rooftop cafeteria’. The use of these strategies was optional. In the case of the seven companies where no strategy was used, five of them gave the reason that they had ‘no access to a trained person to administer the strategy’ and for two of them ‘time constraints’ were the limiting factor.

Hence HRD managers in most software companies are aware of health risks of prolonged computer use and which complaints are most probable. However the management strategies did not seem adequate. In view of the increasing number of software companies across India this topic requires attention.

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TREATMENT

Treatment of iron deficiency anemia should include

1. Treatment of the cause of iron deficiency
2. Correction of anemia with iron supplements

1. Treatment of the cause

It is important to find out the etiological factor of iron deficiency to prevent failure of treatment and recurrence of iron deficiency after stopping treatment. Treatment of worms especially ankylostomiasis or hook worm infection, giardiasis, bleeding from any sites, recurrent infections, is very essential to prevent recurrence. In case of hook worm infection, watch should be also kept for re infection which should be treated periodically. Bleeding from ‘piles’ is another common cause of iron deficiency anemia (IDA) among adults which should be treated by injection or excision. All pregnant women should be started on iron supplements very early in pregnancy and should be continued throughout pregnancy, postpartum period and till she continues to breastfeed her baby.

Patient should be advised to prevent repeated pregnancies at short intervals. Patient should be advised against abuse of ‘pain killers’ especially aspirin as it is a common cause of GI bleed and iron deficiency.

2. Correction of anemia

Iron deficiency can be easily corrected in a majority of patients with iron therapy. This treatment can be given either by oral or parenteral route.

ORAL IRON THERAPY

Iron is usually given in dose of about 200 mg of elemental iron per day in single or divided doses. It is preferably given on empty stomach or between meals to facilitate absorption, but if the patient complains of GI side effects it is better to administer it after meals, although this approach would also reduce the absorption of iron. Doses higher than 200 mg per day are not recommended as it would not be more effective but only give rise to more side effects. Once the patient is started on oral iron therapy, it takes about 6 – 10 weeks for hemoglobin stores to return to normal level. However in IDA, iron stores are exhausted and need to be replenished. Replenishment of iron stores begins only after hemoglobin returns to normal. Hence stopping iron soon after hemoglobin is normal means inadequate therapy and predisposes patient to recurrence. Absorption of iron diminishes after hemoglobin returns to normal and hence replenishing iron...