Drug-induced liver injury

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1 Drug-induced liver injury can be caused by a variety of medications, supplements and herbal products (Appendix 1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.202026/tab-related-content)

Drug-induced liver injury is estimated to have an incidence of 14–19 cases per 100 000 individuals.[1,2] Although asymptomatic liver enzyme elevation is the most common presentation, drug-induced liver injury is the most common cause of acute liver failure in most Western countries, accounting for more than 50% of cases.[1] Drug-induced liver injury can occur in overdose or at therapeutic dosing, either because of direct, intrinsic drug hepatotoxicity or as a result of idiosyncratic (unpredictable) hepatotoxicity.

2 Drug-induced liver injury should be suspected in patients with new elevation of liver enzymes, prompting a review of drug exposures dating back as far as 3 months

Establishing a reliable timeline between exposure and injury onset is critical. Typical latency periods are 1–5 days with direct, and 5–90 days with idiosyncratic hepatotoxicity.[1] Idiosyncratic hepatotoxicity can occur sooner if there has been previous exposure.[2] Patterns of enzyme elevation include hepatocellular, cholestatic or mixed; attributing elevation patterns to specific drugs can be imprecise. LiverTox is a website sponsored by the National Institutes of Health, with descriptions of more than 1000 agents that can cause drug-induced liver injury.[3]

3 Diagnosis requires exclusion of alternate causes

Drug-induced liver injury can be particularly difficult to distinguish from autoimmune hepatitis because antibodies seen in this kind of hepatitis may also be positive in drug-induced liver injury.[2] The Roussel Uclaf Causality Assessment Method (RUCAM) score is a clinical decision tool to help determine the probability of drug-induced liver injury.[2]

4 In most cases, resolution of drug-induced liver injury occurs after drug discontinuation

Liver enzyme levels usually decrease within days to weeks, with less than 10% of patients having chronic disease 1 year later.[2,4] In cases of severe elevation of liver enzyme levels (alanine aminotransferase ≥ 5 × or alkaline phosphatase ≥ 2 × and total bilirubin ≥ 2 × upper limit of normal),[2] clinical signs of liver failure, or if improvement is not seen within the expected time frame, specialist consultation and investigations (e.g., liver biopsy) for alternative causes or complications of drug-induced liver injury should be pursued.[2]

5 Treatment requires identification and discontinuation of the culprit drug

Targeted therapy is appropriate for specific cases (e.g., *N*-acetylcysteine for acetaminophen toxicity[5]), but treatment is primarily to stop the offending drug. Glucocorticoids are not routinely recommended, although they may have a role in patients with features of hypersensitivity reactions and multiorgan involvement, or if autoimmune hepatitis is an ongoing concern.[2] Liver transplantation should be considered in severe cases.

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