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Changing the class of NSAID in cases of hepatotoxicity

SIR, Hepatic side effects with non-steroidal anti-inflammatory drugs (NSAIDs), especially with diclofenac, are rare. Subclinical biochemical abnormalities, however, such as increases in transaminases, serum alkaline phosphatase and glutamyl transferase levels, and acute hepatitis, have been reported.[1–3] When NSAIDs are stopped disturbances generally resolve. The problem then is to determine whether another NSAID can be given and which one to choose.

A man of 44 with ankylosing spondylitis had been taking diclofenac (200 mg/day) for two months. On investigation his sedimentation rate was 100 mm/h, white cell count $9{\cdot}1\times10^9$/l, eosinophils $8{\cdot}1\times10^8$/l, IgE 563 mg/l (normal <350), serum alanine aminotransferase 9 IU/l (normal <30), serum aspartate aminotransferase 16 IU/l (normal <45), serum glutamyl transferase 82 IU/l (normal <50), serum alkaline phosphatase 144 IU/l (normal <90), 5′-nucleotidase 7 IU/l (normal <5), total serum bilirubin 5 μmol/l, prothrombin 75%, amylase 20 IU/l (normal <70). Hepatitis B surface antigen, anti-hepatitis B core antibodies, hepatitis A IgM, cytomegalovirus antibodies, antinuclear and antimitochondrial antibodies were absent. Ultrasonography, tomodensitometry, and cholecystography were normal. Treatment with diclofenac was stopped. Serum liver function tests, IgE concentration, and eosinophils returned to normal in 10 days. Treatment with ketoprofen (150 mg/day) was started. Three months later biochemical liver tests were normal. Diclofenac was the most likely cause of the hepatic abnormalities according to imputability criteria[4] as the patient had no history of hepatic disease and was not alcoholic, there was no sign of a viral hepatitis or of biliary tract obstruction, diclofenac was the only drug given, disturbances of serum liver function tests normalised after diclofenac was withdrawn. High levels of eosinophils and IgE suggest an immunoallergic mechanism.

Similar cases of patients developing abnormalities of serum liver function tests without clinical symptoms have also been reported,[5] and it is advisable to stop the drug. If NSAIDs are still required the same drug should be avoided as illustrated by a case of relapsing hepatitis in a patient rechallenged with diclofenac.[3] NSAIDs of the same chemical class should also not be given, as demonstrated by a case of cross hepatoxicity between two propionic acid derivatives: naproxen and fenoprofen.[6] We suggest an NSAID of another chemical class be used. Further studies are necessary to confirm our hypothesis that changing to an NSAID of a different chemical class resolves the disturbances of hepatic toxicity and does not produce new features of liver damage.

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