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Serious liver injury induced by Nimesulide: an international collaborative study

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Abstract

Nimesulide is a non-steroidal anti-inflammatory drug still marketed in many countries. We aim to analyze the clinical phenotype, outcome, and histological features of nimesulide-induced liver injury (nimesulide-DILI). We analyzed 57 cases recruited from the Spanish and Latin American DILI registries. Causality was assessed by the RUCAM scale. Mean age of the whole case series was 59 years (86% women) with a median time to onset of 40 days. A total of 46 patients (81%) were jaundiced. Nimesulide-DILI pattern was hepatocellular in 38 (67%), mixed in 12 (21%), and cholestatic in 7 (12%) cases. Transaminases were elevated with a mean of nearly 20-fold the upper limit of normality (ULN), while alkaline phosphatase showed a twofold mean elevation above ULN. Total bilirubin showed a mean elevation of 13-fold the ULN. Liver histology was obtained in 14 cases (25%), most of them with a hepatocellular pattern. Median time to recovery was 60 days. Overall, 12 patients (21%) developed acute liver failure (ALF), five (8.8%) died, three underwent liver transplantation (5.3%), and the remaining four resolved. Latency was ≤ 15 days in 12 patients (21%) and one patient developed ALF within 7 days from treatment initiation. Increased total bilirubin and aspartate transaminase levels were independently associated with the development of ALF. In summary, nimesulide-DILI affects mainly women and presents typically with a hepatocellular pattern. It is associated with ALF and death in a high proportion of patients. Shorter (≤ 15 days) duration of therapy does not prevent serious nimesulide hepatotoxicity, making its risk/benefit ratio clearly unfavorable.

Keywords: Acute liver failure; Cholestasis; Hepatitis; Hepatotoxicity; NSAID; Nimesulide.