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Autoimmunity in repeated drug-induced liver injury (DILI) episodes

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Objectives: Drug-induced liver injury (DILI) is a complex condition with various clinical and pathological presentations. We have recently demonstrated that a second DILI episode induced by a different drug with regard to the first episode increases the probability of an autoimmune DILI diagnosis (Lucena *et al.*, 2011).

In this study we aimed to analyze the frequency of autoimmune presentations, type of liver injury and drugs involved in a cohort of Spanish and Latin American patients, who have suffered two DILI episodes caused by the same or different drugs.

Material and methods: The cases included in the study were retrieved from those submitted to the Spanish and Latin American DILI Registry as having experienced reexposure to the same drug or multiple DILI episodes due to different causal agents (n=45). The cohort was analyzed for demographic, clinical and biochemical data as well as for causative pharmacological groups.

Results: Of the 811 cases in the DILI registry 679 contained autoimmunity data, of which only 17% displayed positive autoantibody titres. However, 40% of the 45 patients with multiple DILI episodes due to the same or different causal agents were found to be autoimmune positive in the second episode. In the 31 patients with reexposition to the causal agent 29% (9 cases) presented autoantibodies, 67% anti-nuclear antibodies (ANA) and 33% anti-smooth muscle antibodies (ASMA).

In comparison, in 14 patients with two DILI episodes due to different causal agents 60% (9 patients) were found to have positive autoantibodies, mainly ANA, in the second episode. Hepatocellular damage was the most prevalent type of injury in both groups and remained in both episodes. The pharmaceutical groups associated with positive autoantibodies were mainly cardiovascular system drugs (especially statins) and antibiotics.

Conclusions: The probability of presenting positive antibody titres increases in second DILI episodes, independent of the causal agent being the same or different to that in the first episode. Statins is the pharmacological group associated with the highest risk of developing positive autoantibodies during a second DILI episode. These drugs may produce a breakdown of immune tolerance that is able to trigger liver autoreactivity.

Referencias Bibliográficas: Lucena MI *et al.* Recurrent drug-induced liver injury (DILI) with different drugs in the Spanish registry: The dilemma of the relationship to autoimmune hepatitis. *J Hepatol* 2011;55:820-827.

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