ADVERSE DRUG REACTIONS, INCLUDING SJS, TEN

IMMUNOLOGICALCONFIRMATION OF DAPSONE HYPERSENSITIVITY SYNDROME BY IN VIVO PATCH TESTING AND IN VITRO ENZYME-LINKED IMMUNOSPOT AND LYMPHOCYTE TRANSFORMATION TESTS

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Background: Dapsone hypersensitivity syndrome (DHS), a life-threatening condition, is the most serious adverse reaction associated with dapsone administration, whose diagnosis is unspecific. The utility of in vivo patch testing and in vitro enzyme-linked immunospot (ELISpot) and lymphocyte transformation test (LTT) in DHS remains ill-defined.

Objective: The aim of the study was to prove whether in vivo and in vitro tests are promising for the diagnosis of DHS.

Materials and Methods: 16 patients with DHS and 6 healthy controls were recruited. In vivo patch testing was performed with dapsone at a range of concentrations and read at 48 hours and 72 hours. Kinetics of multiple cytokines in supernatant of peripheral blood mononuclear cells (PBMCs) stimulated by dapsone or dapsone hydroxylamine were measured using electrochemiluminescense (ECL) on a platform from MesoScale Discovery (MSD). The release of drug specific cytokines (IFN-γ and IL-5) was measured using a novel modified ELISpot. The proliferation of T cells to drugs in vitro was measured using LTT.

Result: Cytokine profiles analyses showed that IFN-γ, IL-5 and IL-13 production stimulated by drugs arise at 4 days and peak at 8 days in patients, which was absent in control subjects. In 16 patients with DHS, 4/11 (36.4%), 12/16 (75%) and 10/16 (62.5%) patients were positive on patch testing, IFN-γ/IL-5 ELISpot, and LTT, respectively. When combination of in vivo and in vitro tests, the sensitivity increased to 93.8% (15/16) with the specifity of 100%.

Conclusion: We demonstrate cytokine profiles serve as a promising tool for exploring the biomarkers of DHS, and combination of in vivo and in vitro tests could increase the sensitivity in diagnosing DHS.