

Letter To The Editor

Corticosteroid cross-reactivity

Dear Sir

In the study on cross-reactivity patterns to budesonide by Ferguson et al (1), it is stated that patch tests are less reliable than intradermal tests when testing for corticosteroid allergy and investigating cross-reactivity patterns among corticosteroids. While this may be true, before making such a statement, several points should be considered. When discussing cross-reactivity, there are three particular points that need to be addressed: (a) exposure, (b) dose and (c) purity.

Concerning exposure, no contact with the potential cross-reacting substance should ever have taken place. In humans, it is impossible to perform such studies without some uncertainty, as we never know for sure the exposure patterns. Patients everywhere borrow each other's medications and drugs, so a search through hospital and general practice records may not paint a completely true picture. There have even been cases of illegal addition of corticosteroids to herbal remedies in both Sweden and Britain (2–4). Studies on cross-reactivity are better performed on naïve animals. The local lymph node assay, however, does not work in studies on cross-reactivity. Guinea pigs have not been possible to sensitize using corticosteroids, except for tixocortol pivalate (5, 6). Therefore, until such studies are performed, in humans, it is probably better for us to talk about simultaneous sensitivity and possible cross allergy between these substances.

Concerning dosage, for one and the same method of testing (epicutaneous or intradermal), one should use equimolar concentrations and serial dilutions of the respective substances, provided their penetration is similar, such that the same amount of molecules reaches the viable parts of the skin, where the immunologic reaction takes place. With corticosteroids, however, the anti-inflammatory effect must also be taken into consideration (7, 8). This may not be the same even if the corticosteroids are tested at one and the same equimolar concentration. The anti-inflammatory effect may suppress a positive patch test reaction at an early reading in a patient with a moderate corticosteroid allergy. Thus, we should test with a range of equimolar concentrations

of the respective corticosteroid in each of the test systems and perform test readings at optimal reading times for that particular method, including late readings in the patch test method (9, 10). It has been shown for budesonide, tixocortol pivalate and hydrocortisone-17-butyrate that negative patch test readings may be seen at early readings despite patients being allergic to them. Up to 53% of such allergy may be missed in consecutively patch-tested dermatitis patients (11).

Furthermore, when discussing the dose and to what extent a substance penetrates into the skin, the vehicle used can be of crucial importance. Besides being important for penetration, the vehicle itself can influence the patch test, provoking a false-positive reaction. When testing for contact allergy, corticosteroids in vehicles such as ethanol may give false-positive results, seen both in patch testing and in intradermal testing. Therefore, it is important that the vehicle alone is tested as such as a control (12–14). In the above-mentioned paper, no clear information was given as to the vehicles used for the different corticosteroids for intradermal testing or whether ethanol was tested epicutaneously and intradermal as such, in the case that saline was not the vehicle for all the intradermal test preparations.

Finally, regarding purity, one prerequisite to be fulfilled when speaking of cross-reactivity, provided that a patient has reacted positively to the investigated putatively cross-reacting substances, is that the investigated substances should be of high purity (15, 16), so that they do not contain common contaminants and that the substances do not contaminate each other.

Furthermore, even if the substances are of high purity, they must be chemically separable (16).

Nevertheless, the subject remains interesting: other cross allergies may exist but more investigations are needed.

Yours sincerely,

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