DIISOCYANATES PANEL

Scientific Information Statement (with references)

Patch Testing For MDI

Dermatitis may occur as a result of exposure to chemicals in the workplace. Approximately 30 percent of cases of chemical dermatitis are classified as allergic contact dermatitis (ACD). Irritant contact dermatitis (ICD), due to the irritant effect of chemicals, is much more common. A few papers have reported relatively few cases of ACD after exposure to products containing methylene diphenyl diisocyanate (MDI). Patch testing often is used to establish a relationship between ACD and a specific causative agent, and to differentiate between ACD and ICD, which often is not possible on clinical or even histological grounds. There are limitations on the use of patch testing for compounds such as MDI.

Background

There currently are three widely used, standardized patch tests: 1) Finn Chamber, 2) True Test, and 3) Epiquick. There is approximately 67 percent concordance of results among these methods. In these tests, the suspected sensitizing agent is dissolved in a solvent and diluted to a concentration that will not cause irritation. A patch containing the diluted agent is applied to the skin and read at 48, 72, and 96 hours. The patch test is interpreted based on the observation of redness, itching, and hardening of the skin at the site of the patch. Given the importance of patch testing in diagnosing ACD, organizations such as the International Contact Dermatitis Group have recommended the use of a standard methodology for the test and its interpretation. However, standardized test concentrations have been published only for the most common of the approximately 100 environmental substances that are frequently associated with ACD. This is in contrast to the 2,200 chemicals (out of 2-3 million chemicals) that have been identified as sensitizers. Diisocyanates, including MDI, although associated with dermal sensitization, are not among the commonly identified substances for which standardized test concentrations have been developed. The largest group of patients reported were 360 persons tested for allergy to 50 plastic and glue allergens in an occupational clinic in Finland between 1991-96. Only three of the group (0.8%) reacted to MDI, ranking it as a weak sensitizer as compared to more common allergens.

With respect to the few reports of ACD from products containing MDI, the majority of individuals also reacted to diaminodiphenylmethane (MDA), which is the corresponding aromatic amine. MDA is known to be a skin sensitizer. The authors of several of the reports of ACD from MDI hypothesize that the primary sensitization in these cases might have been to MDA formed from hydrolysis of MDI, or that the response might have been a cross-reaction due to structural similarities. Biochemical in vivo data from skin exposure with MDI suggests that the formation of MDA from MDI on exposed skin practically does not occur; therefore, cross-reactivity to the patch testing antigens appears to be the more plausible explanation.

* Material Safety Data Sheets, available from MDI suppliers, provide additional health and safety information regarding this chemical.
Accuracy and Validity of Patch Testing

The accuracy and validity of the patch test is determined by its ability to truly diagnose those individuals with ACD, which defines the sensitivity of the test, and to eliminate those without it, which is the specificity of the test. A number of factors affect the accuracy of patch testing, including pre-selection of patients by a physician, selection of allergen, appliance vehicle, and use of proper technique.\(^8\) Even when the test is performed using the methodology recommended by the International Contact Dermatitis Group and standard series of allergens, with high pre-test probability that the patient has ACD, false positive and false negative results may be encountered.\(^7\) There is greater uncertainty in interpreting patch test results when less common (non-standard) allergens are used, particularly if the test substance also is an irritant.\(^2\) Based on animal studies, MDI is reported to be a weak to moderate irritant.\(^11\)

The concentration that is used in the patch test procedure is vitally important for the following reasons:

- The concentration affects the sensitivity and specificity of the test. At a given concentration, there might be 5 percent of individuals who will show a response but do not have ACD (false positives), and 5 percent of individuals with ACD who will not respond (false negatives). This is considered to be acceptable test performance.\(^7\)

- If an irritating concentration of the chemical is used in the testing, there will be an overlap of the irritant and the allergic responses. This overlap results in a much higher percentage of false positives, unless the concentration is set very low, which increases the risk of false negatives.\(^7\)

- Standard series of allergens have been studied in diseased and reference populations. This is not often the case with less-commonly-used substances. To establish the validity of the test concentrations for such chemicals, "[i]t is common practice to test 20 [control] subjects," taking steps to ensure that they will not be injured by the test.\(^7\)

- There may be a risk of sensitizing someone through patch testing, especially if not using standard test concentrations.\(^7,9\) Accordingly: "Such patch tests must not be applied indiscriminately since the induction of ACD may result in chronic disability for the test subject."\(^7\)

The vehicle for applying the test substance to the skin also is important. One source recommends that only freshly prepared solutions in water-free acetone be used for patch testing with diisocyanates in order to avoid hydrolysis to the corresponding aromatic amine.\(^5\) The same source recommends that when testing diisocyanates, patch tests for the corresponding amines also be conducted.

Diisocyanates are among the substances for which no generally accepted, standardized patch test method has been adopted. Various concentrations have been recommended and used. For MDI, concentrations have ranged among 0.01%\(^12\), 1%\(^13\) and 1.5-2%.\(^3,9\) Testing may have been confounded by cross-reactions with MDA resulting in some confusion as to the origin of the allergic reaction.
Summary

Patch testing can be used effectively as a diagnostic test if patients are properly selected and tested against standard series of allergens. There are real limitations in the validity of the test results if using substances without established standard test concentrations or without hands-on experience with the test methodology. Care in performing the test is important to reduce spurious irritant responses. In the case of an irritant chemical, it is not always possible to differentiate between irritant and allergic contact dermatitis through patch testing. In diagnosing ACD, patch test results should always be correlated with the patient’s symptoms and a dermatologist’s examination. For MDI, care may be necessary to avoid confounding of the test results by cross-reactivity with the MDA antigen during patch testing.

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References


