

A comparison of multiheaded devices for allergy skin testing

To the Editor:

Previous studies comparing devices for percutaneous (ie, prick and puncture) skin testing have revealed significant differences in the size of wheal reactions to both the positive (allergen extract or histamine) and negative (saline) challenge sites.¹⁻³ The tendency has been for devices that produce larger reactions with histamine to also be more likely to produce reactions at the negative control sites. The size of the reaction at both positive and negative control sites appears to reflect the degree of trauma imparted to the skin by the device, an interpretation that was reinforced by the fact that those devices producing larger wheals also caused greater patient discomfort.² To some extent, the tendency to cause false-negative reactions to histamine corresponds to the tendency to produce smaller wheals. However, an exception is that for any size reaction to histamine, those devices with multiple heads appear to produce more false-negative reactions than single-headed devices.³

This communication presents a comparison of 3 new multiheaded devices marketed for percutaneous skin testing. They were the Greer Track, an 8-headed device (Greer Laboratories, Lenoir, NC); DermaPik II, a 10-headed device (Biomedixs, Spokane, Wash); and the Quick Test, an 8-headed device (Panatrex, Placentia, Calif). These 3 new devices were compared with the Multitest II (Lincoln Diagnostics, Decatur, Ill) and a solid-bore smallpox needle (Hollister-Steir, Spokane, Wash). The methods used were those previously used for similar comparisons of skin testing devices.^{2,3} Twenty-one adult subjects (18-70 years of age) underwent 2 sessions of testing on both the back and arms. Subjects withheld antihistamines for 1 week, antidepressants for 2 weeks, and H₂ and leukotriene antagonists for 48 hours. The technician applying the tests was unblinded to device but was blinded as to whether the device was loaded with histamine or saline (10 mg/mL histamine dihydrochloride in 50% glycerin or 50% glycerol-saline; Hollister-Steir). This was accomplished by having a second technician load the device or place the drops on the skin and also record the reactions at the test site. The purpose of blinding was to prevent unconscious variation in the pressure with which the device was applied. Before testing study subjects, the technician performing the tests received instruction from a representative of each of the companies marketing the device and tested 5 preliminary subjects to develop a reproducible technique.

Test sites were randomly rotated to ensure equal distribution for each device in different areas of the back and forearm. On completion of testing, the subject was asked to rate the discomfort with each device on a scale of

0 (none) to 10 (most uncomfortable). The results were recorded by tracing with a ballpoint pen and transferring the impression with transparent tape to the clinical record. Histamine test results were recorded after 8 minutes, and saline results were recorded after 15 minutes. The longest and transverse diameters were later measured. Reactions at histamine sites were considered positive if the wheal was 3 mm or larger and the flare was 10 mm or larger. If both were less than this size, the test result was considered false-negative. If only the wheal or only the flare failed to reach the criteria for a positive result and another of the same set of tests resulted in a wheal of 5 mm or greater and a flare of 10 mm or greater, the reaction was termed pseudo-false-negative. To assess the potential for producing false-positive reactions at the saline sites, all reactions were measured, and the 95th and 99th quantiles were calculated. Thus 95% of all reactions to saline would be less than the 95th quantile figure, and 99% would be smaller than the 99th quantile figure. In addition to calculation of quantiles at saline sites, the mean and SD of the wheal at histamine sites was calculated. The results for the comparison are presented in Table I.

The only significant differences were the size of the histamine wheals, which were significantly larger with the smallpox needle on the back ($P < .05$) and significantly smaller with the Greer Track on the arm ($P < .05$). The overall ANOVA for histamine wheal size on the back and on the arm was ($P < .0001$). On the arm, the reactions to saline were significantly larger with DermaPik II and Quick Test than with the other 3 devices ($P < .0001$, ANOVA). There were not significant differences in the reaction to saline on the back.

The rating of the devices for discomfort did not differ greatly (Table I).

The 2 devices that produced the smallest reactions with histamine were associated with the highest number of false-negative and pseudo-false-negative reactions. The number of the false-negative and pseudo-false-negative reactions that occurred with clusters located at the end of the devices and in the middle of the devices was similar. With the Greer Track device, the false-negative reactions were similar whether the device was autoloading (ie, dipped into the vials) or loaded by means of direct application to the heads.

It is concluded from this study that there is a range of reliability in the devices being offered for allergy skin testing. Unlike some devices previously tested,³ all of the devices tested in this study produced negative reactions to saline with a high rate of consistency. Two of the devices, however, had sufficiently high rates of failure to produce positive reactions with histamine, suggesting the need for performing tests with these devices in duplicate or, alternatively, performing intradermal testing to confirm negative reactions to important allergens.

TABLE I. Reactions to testing with histamine and saline

Device	No. of tests, histamine	Mean wheal size, histamine (mm)	SD, histamine (mm)	Pseudo-false-negative reactions (%) [*]	False-negative reactions (%) [†]	Wheal size specificity, saline, 0.95 quantile (mm)	Wheal size specificity, saline, 0.99 quantile (mm)	Specificity of 3 mm wheal to saline (%)	Discomfort (0 = none to 10 = severe) mean
Smallpox needle	Arm, 84	6.15	1.44	2.4	0	0	0	100	—
Multitest II	Arm, 80	6.2	1.4	1.1	1.1	0	0	100	—
DermaPik II	Arm, 100	6.33	1.5	2.0	0	0	4.5	0.98	—
Quick Test	Arm, 72	6.09	1.54	4.2	1.3	0	4.5	0.99	—
Greer Track	Arm, 96	5.01 [‡]	1.68	6.2	5.2	0	0	100	—
Smallpox needle	Back, 158	7.06 [§]	1.63	0.6	0.6	0	3.5	0.99	3.8
Multitest II	Back, 168	6.34	1.49	0	0.6	0	3.5	0.97	4.4
DermaPik II	Back, 200	6.42	1.78	0.5	1.5	0	0	100	4.6
Quick Test	Back, 176	5.44	2.15	2.3	5.1	0	4	0.99	5.0
Greer Track	Back, 352	5.12	1.8	4.0	6.3	0	3.5	0.98	4.4

^{*}Either the wheal with histamine was less than 3 mm or the flare with histamine was less than 10 mm.

[†]Both the wheal with histamine was less than 3 mm and the flare with histamine was less than 10 mm.

[‡]Significantly smaller than the reactions with the other devices ($P < .05$).

[§]Significantly larger than the reactions with the other devices ($P < .05$).

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Quantitative assessment of the adherence to sublingual immunotherapy

To the Editor:

For historical reasons, immunotherapy has been administered subcutaneously for many decades. After serious adverse events caused by subcutaneous immunotherapy (SCIT) were reported,¹ safer administration routes were studied, and sublingual immunotherapy (SLIT) immediately appeared as a promising option. Currently, SLIT is considered a viable alternative to SCIT² on the basis of its clinical efficacy and good safety profile (see review³). SLIT is self-administered at home; therefore, one of the most important concerns is the adherence (“the degree to which the patient’s behavior coincides with the medical prescription”).⁴ To date, no quantitative study is available on this topic. With SLIT in tablets, the adherence could be evaluated by randomly asking patients to count the remaining tablets at a given moment. We used that method to assess the adherence to SLIT in real life.

This multicenter observational study involved outpatients receiving SLIT for respiratory allergy. Patients were diagnosed to have allergic rhinitis and/or asthma on the basis of the typical clinical history of symptoms for at least 2 years, positivity of skin prick tests, and spirometry with methacholine challenge, when indicated. Asthma and rhinitis were graded according to GINA and ARIA guidelines, respectively.² SLIT for a single relevant allergen was prescribed to patients with comorbid rhinitis and asthma, persistent rhinitis and positive methacholine test, or severe rhinitis during the allergen exposure. SLIT was prepared as soluble tablets to be taken in the morning, kept under the tongue until dissolution (1-2 minutes), and then swallowed. The vaccine was a monomeric allergoid obtained by chemical modification.⁵ Patients allergic to dust mite received a continuous treatment, whereas for pollens, a preseasonal schedule was used. In both cases, SLIT involved a build-up and a maintenance phase. Detailed printed instructions and additional oral explanation on how taking and managing SLIT were given. All patients received a standard drug therapy for symptoms (oral/nasal antihistamines, inhaled salbutamol, inhaled/nasal steroids) and were seen for follow-up at regular intervals.

Patients were contacted by telephone, without planning an exact date. At the telephone interview, they were asked to count the tablets remaining in the blister. A computerized program, based on the starting date of SLIT and the administration schedule, calculated the expected consumed tablets and the expected remaining tablets. The adherence was measured after 1 year for mite SLIT and at the beginning of the pollen season for pollen SLIT. It was calculated in percentage as expected consumed tablets – remaining tablets/expected consumed tablets $\times$ 100. Patients recorded in a diary the occurrence of side effects after each dose. Local (oral itching/swelling, edema of lips/tongue, nausea or vomiting) and systemic (rhinitis, conjunctivitis, asthma, urticaria/angioedema) side effects