
Comparison of the Multi-Test II and Skintestor Omni allergy skin test devices

Mark S. Dykewicz, MD; J. Keith Lemmon, MD; and Deborah L. Keaney, RN

Background: Different devices for percutaneous allergy skin testing have demonstrated statistically and clinically significant differences in performance characteristics.

Objective: To compare 2 Food and Drug Administration–approved multihead allergy skin testing devices: Multi-Test II (Lincoln Diagnostics) and Skintestor Omni (Greer Laboratories).

Methods: Skin tests with glycerinated histamine (6-mg/mL base) and glycerinated saline were applied to 31 adults using Multi-Test II on the volar surface of one forearm and Skintestor Omni on the opposite forearm.

Results: Data were accumulated from 155 histamine sites and 93 negative control sites for each device. Using cutoff wheal sizes of 5 vs 3 mm inclusive to define a positive result, Multi-Test II sensitivity remained at 100%, but specificity increased from 74% to 97%, whereas Skintestor Omni sensitivity decreased from 94% to 87%, and specificity increased from 58% to 88%. For Multi-Test II vs Skintestor Omni, histamine mean (SD) wheal sizes were 9.23 (1.37) vs 7.74 (2.83) mm ($P < .001$), mean coefficients of variance were 14.8% vs 36.6%, and pooled estimates of variance were 0.642 vs 6.974. Multi-Test II produced similar histamine wheal sizes regardless of test head position used, whereas Skintestor Omni produced statistically significantly smaller wheals at certain test head positions.

Conclusions: Multi-Test II had higher sensitivity and specificity than Skintestor Omni and produced reproducible wheal sizes from all test head positions. Because some Skintestor Omni test head positions produced significantly smaller histamine wheal sizes, skin testing using this device might result in underdiagnosis of allergy.

Ann Allergy Asthma Immunol. 2007;98:559–562.

INTRODUCTION

The use of skin tests for the diagnosis of IgE-mediated allergic disease was introduced by Charles Blackley during his study of hay fever in the 1860s.¹ Nearly 60 years later, in 1924, Lewis and Grant² described the prick test in their studies investigating vascular reactions of the skin. Despite the development of in vitro testing for specific IgE, percutaneous skin testing remains the standard clinical method for the diagnosis of IgE-mediated allergic disease, and its use in this regard is well-established and recommended.³

Immediate hypersensitivity skin testing has many attractive characteristics, including technical simplicity, low cost, good patient acceptance, and high diagnostic sensitivity. Since the 1970s, percutaneous skin testing devices have undergone constant modification and improvement. The most notable

change has been a trend toward using multihead devices. These devices, which allow the simultaneous application of multiple allergen extracts to the skin, are not only more time efficient but also have been shown to be more accepted by children compared with individual needle prick testing methods.^{4,5}

Because immediate hypersensitivity skin test results help guide therapeutics, it is important that a skin test device reliably minimize false-negative and false-positive results. Previous studies^{6–9} comparing percutaneous skin test devices have demonstrated statistically and clinically significant differences in characteristics such as the size of reactions to histamine or allergen extract and the likelihood of reactions at negative control sites. With the constant evolution of skin testing devices and the increased popularity of multihead devices, comparison studies examining the performance characteristics of the products available in the marketplace provide useful and important information for the physician. The purpose of this study was to compare 2 Food and Drug Administration (FDA)–approved multihead allergy skin testing devices: Multi-Test II (Lincoln Diagnostics, Decatur, IL) and Skintestor Omni (Greer Laboratories, Lenoir, NC).

METHODS

Study Design

This study was conducted with the approval of the Saint Louis University institutional review board, and informed consent was obtained from all research participants. Skin tests with glycerinated histamine (6-mg/mL base) and glyc-

Section of Allergy and Clinical Immunology, Division of Immunobiology, Department of Internal Medicine, Saint Louis University School of Medicine, St Louis, Missouri.

This study was sponsored by Lincoln Diagnostics, which advised the investigators in the design of the study. The conduct of the study, the data analysis, and the writing of the manuscript were performed solely by the investigators without interference by the sponsor. The sponsor had the opportunity to review the data analysis and to provide comments about the manuscript that were considered by the authors before they submitted the manuscript for publication. No substantive changes in the data analysis or the stated conclusions of the author-investigators occurred because of sponsor review or comments.

Received for publication August 2, 2006.

Received in revised form December 13, 2006.

Accepted for publication February 8, 2007.

(Pointed toward the head)

1	5	1	6
2	6	2	7
3	7	3	8
4	8	4	9
		5	10

MULTI-TEST II



SKINTESTOR OMNI



Figure 1. Test head numbering. As indicated in the “Methods” section, the numbering scheme used for Multi-Test II in this study is the mirror image of that recommended in the product insert.

erinated saline were applied to 31 adults on the volar surface of one forearm using Multi-Test II and on the opposite forearm using Skintestor Omni. Participants alternated between receiving Multi-Test II on the right forearm and Skintestor Omni on the left forearm and Multi-Test II on the left and Skintestor Omni on the right. One person administered the skin tests (D.L.K.), and a second (M.S.D.) read and recorded all the results. Wheal sizes were calculated from the average of the longest diameter and its midpoint orthogonal diameter using the central portion of the wheal. Wheals were measured for both devices at 20 minutes, consistent with the 15- to 20-minute interval recommended in the product insert for Multi-Test II when skin tests are performed with glycerinated extracts. Skintestor Omni does not have a product insert that provides recommendations about when skin tests should be read. Before each session, medications were withheld for the following periods: oral antihistamines, 7 days; intranasal antihistamines (azelastine), 2 weeks; phenothiazines, 7 days; all antidepressants, 2 weeks (albeit skin test inhibition by antidepressants is primarily a function of tricy-

clic antidepressants); and histamine₂ receptor antagonists, 24 hours.

To permit easier comparison between the 2 devices, we assigned numbers to test heads in an analogous scheme for both devices, although this resulted in Multi-Test II test heads being numbered in a mirror image of that indicated in the product insert (Fig 1). Of the 8 skin test heads of the Multi-Test II device, histamine was applied with heads 1 through 5, and the negative control was applied with heads 6 through 8. This yielded 5 histamine skin test sites and 3 glycerinated saline skin tests sites per participant. Of the 10 test heads of the Skintestor Omni device, histamine was applied with heads 1 through 5, and negative control was applied with heads 6 through 8; no test solutions were applied with heads 9 and 10. This yielded the same number of histamine and glycerinated saline sites as for Multi-Test II.

Statistical Analysis

Mean wheal sizes of the 2 devices were compared using *t* tests and analysis of variance. Statistical significance was determined using $\alpha = .05$ for all tests. For each device the variance between participants was removed to examine the pooled estimates of variance. To determine precision, intradevice variability was described by using the coefficients of variation of the mean diameters of wheal sizes of individual heads. The Tukey Honest Significant Difference test and the Games-Howell test were used to examine the differences in mean wheal size for each histamine position on the arm for each device separately. Additional presentation of medians with interquartile ranges for each device was produced in the form of box plots. Separate sensitivity and specificity analyses were performed using a wheal of at least 3 mm or at least 5 mm to indicate a positive result and a wheal of less than 3 mm or less than 5 mm to indicate a negative result. Specificity was calculated by dividing true-negative results by the sum of true-negative and false-positive results.

RESULTS

Collectively, the trial accumulated data from 155 histamine sites and 93 negative control sites for each device. Using cutoff wheal sizes of 5 vs 3 mm inclusive to define a positive result, Multi-Test II sensitivity remained at 100% (95% confidence interval [CI], 97%–100%) for both cutoff sizes, but specificity increased from 74% (95% CI, 64%–83%) to 97% (95% CI, 90%–99%), whereas Skintestor Omni sensitivity decreased from 94% (95% CI, 88%–97%) to 87% (95% CI, 81%–92%), and specificity increased from 58% (95% CI, 47%–68%) to 88% (95% CI, 79%–94%).

Table 1. Histamine Wheal Sizes for Both Allergy Skin Test Devices

Device	Patients, No.	Wheal diameter, mean (95% CI), mm	SD	CV, mean, %	Pooled estimate of variance
Multi-Test II	155	9.23 (9.0–9.4)	1.37	14.8	0.642
Skintestor Omni	155	7.74 (7.3–8.2)	2.83	36.6	6.974

Abbreviations: CI, confidence interval; CV, coefficient of variation.

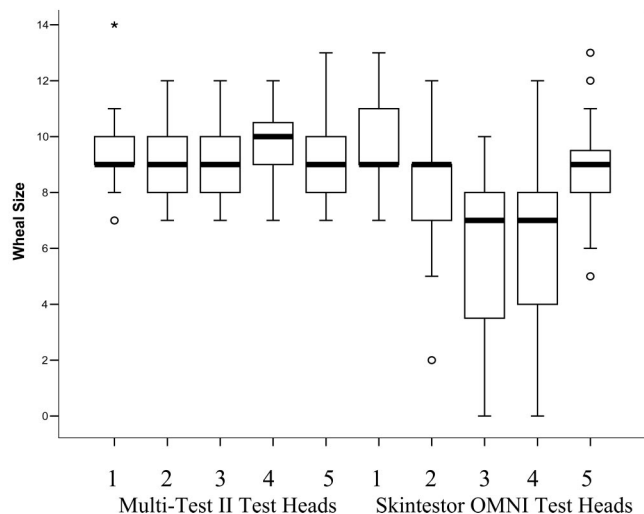


Figure 2. Box plot of histamine mean wheal diameters (in millimeters) by device and test head. Heavy line indicates median; box, interquartile range (25th-75th percentile) of the data; and the whiskers run from the 25th and 75th percentile to the furthest observation or 1.5 times the length of the box, whichever is shorter. Outliers (circles) lay within 1.5 to 3 box lengths from the edge of the box, and extreme cases (asterisks) lay more than 3 box lengths from the edge of the box.

Compared with Skintestor Omni, Multi-Test II histamine mean wheal sizes were larger and more reproducible (Table 1). The results of analysis of variance indicate that the wheal sizes of Multi-Test II and Skintestor Omni do not have equal variances (Levene statistic = 43.6; $P < .001$). Also, the mean wheal size of the 2 devices is significantly different ($P < .001$). These results can also be seen in the box plots in Figure 2. According to the Tukey Honest Significant Difference test, Multi-Test II produced similar histamine wheal sizes regardless of the test head position used, whereas Skintestor Omni produced statistically smaller histamine wheals at certain test head positions. Specifically, Skintestor Omni gave lower results at positions 3 and 4 than the other 3 histamine positions, whereas the results at locations 1, 2, and 5 are statistically similar according to the Games-Howell test (Fig 2 and Table 2).

DISCUSSION

We performed a prospective, head-to-head trial comparing 2 FDA-approved multihead allergy skin testing devices: Multi-Test II and Skintestor Omni. We found statistically signifi-

cant differences among various performance measures between the 2 devices. Compared with Skintestor Omni, Multi-Test II mean histamine wheal sizes were larger. Previous studies^{6,7} have reported that testing devices producing smaller wheals with histamine are more likely to yield false-negative reactions, whereas devices producing the largest wheals are most likely to produce wheals at negative control sites. This might lead one to reasonably suspect that Multi-Test II is more traumatic to the skin than Skintestor Omni. Of note, however, as reported based on our skin testing using histamine and negative glycerinated saline control, Multi-Test II had higher skin test sensitivity and specificity compared with Skintestor Omni.

In addition, the mean coefficient of variance for histamine reactions was smaller for Multi-Test II than for Skintestor Omni. Reasons for this lower precision of Skintestor Omni are speculative. Compared with Multi-Test II, Skintestor Omni is a larger device with 10 test heads (instead of 8) distributed along the length of a rigid framework handle that measures nearly 1.2 cm longer than the Multi-Test II. One could speculate that as both skin test devices are applied to the forearm skin using a "rocking" motion, the longer handle of Skintestor Omni causes more variable contact and pressure between test heads and the irregular contour of the forearm skin. Therefore, it may be that increasing the size of multi-head skin test devices beyond that of Multi-Test II (eg, to accommodate ≥ 10 skin test heads as with Skintestor Omni) will compromise device performance. For the Skintestor Omni device, the smallest mean histamine wheal diameters and the largest standard errors of the mean were noted for test heads positioned toward the center of the device. Data from these center test heads strongly contributed to the inferior performance of the Skintestor Omni in terms of sensitivity and intradevice variability. For studies of multihead skin test devices such as Skintestor Omni that have variable performance at different test head positions, it is, therefore, important to evaluate not only sensitivity and intradevice variability (statistical parameters that might be affected by the choice of which test head positions are used to apply histamine) but also skin test responses at each test head position, as done in the present study. Another possible factor in the inferior performance of Skintestor Omni is that the sharp tines on the Skintestor Omni test heads are shorter than those of Multi-Test II test heads (apparent on examination at $\times 100$ magnification), which might result in less reliable epicutaneous puncture by Skintestor Omni if there is variability of contact

Table 2. Histamine Wheal Diameter by Device and Test Head Position*

Device	Test head position				
	1	2	3	4	5
Multitest II	9.35 (0.23)	9.03 (0.26)	8.90 (0.22)	9.55 (0.23)	9.29 (0.29)
Skintestor Omni	9.65 (0.26)	8.39 (0.39)	5.61 (0.60)†	6.39 (0.52)†	8.65 (0.34)

* Data are given as mean (SEM) millimeters.

† Statistically significantly different mean values compared with positions 1, 2, and 5 using the Games-Howell test ($P < .05$).

pressure. Whether Skintestor Omni would have a similar degree of variation in test head responses when applied to the skin of the back, with its different anatomical contour, requires study.

In this study, we read skin tests at 20 minutes, consistent with the 15- to 20-minute interval recommended in the product insert for Multi-Test II when skin tests are performed with glycerinated extracts. Wheals from histamine may peak earlier than 20 minutes,¹⁰ particularly with aqueous histamine extracts, which may peak as early as 10 minutes after application.¹¹ However, in current clinical practice the wheals from glycerinated histamine and allergen extracts are often read simultaneously for comparison, and a 20-minute reading interval reflects a time when histamine wheals are commonly measured.

In conclusion, we completed a prospective, head-to-head trial comparing 2 FDA-approved multihead allergy skin testing devices: Multi-Test II and Skintestor Omni. Of the 2 devices, Multi-Test II performed better, with a larger mean histamine wheal size, higher sensitivity and specificity, and less intradevice variability. In clinical testing with allergen extracts, application of skin tests with Skintestor Omni might lead to underdiagnosis of allergy when tested extracts are applied with test heads prone to produce smaller wheal sizes. Because this study only looked at responses to histamine and glycerinated saline, results may not be directly applicable to testing with allergens. Further study is required to compare these 2 devices for this purpose.

ACKNOWLEDGMENTS

We thank Paula Buchanan of the Saint Louis University Center for Outcomes Research for performance of statistical analysis.

REFERENCES

1. Taylor G, Walker J. Charles Harrison Blackley, 1820–1900. *Clin Allergy*. 1973;3:103.
2. Lewis T, Grant RT. Vascular reactions of the skin to injury, part II: the liberation of a histamine-like substance in injured skin;

the underlying cause of factitious urticaria and of wheals produced by burning; and observations upon the nervous control of certain skin reactions. *Heart*. 1924;11:209.

3. Li JT, Lockey RF, Bernstein IL, Portnoy JM, Nicklas RA. Allergen immunotherapy: a practice parameter. *Ann Allergy Asthma Immunol*. 2003;90(suppl):1–40.
4. Rizzo MC, Naspitz CK, Sole D. Comparative performance for immediate hypersensitivity skin testing using two skin prick test devices. *J Allergy Clin Immunol*. 1995;5:354–356.
5. Huber B, Berdel D. A comparison of the Multi-Test with the prick test and Multi-Test 2. *Clin Allergy*. 1983;13:467–472.
6. Adinoff AD, Rosloniec DM, McCall LI, Nelson HS. A comparison of six epicutaneous devices in the performance of immediate hypersensitivity skin testing. *J Allergy Clin Immunol*. 1989;84:168–174.
7. Nelson HS, Rosloniec DM, McCall LI, Ikle D. Comparative performance of five commercial prick skin test devices. *J Allergy Clin Immunol*. 1993;92:750–756.
8. Nelson HS, Lahr J, Buchmeier A, McCormick D. Evaluation of devices for skin prick testing. *J Allergy Clin Immunol*. 1998;101:153–156.
9. Carr WW, Martin B, Howard RS, Cox L, Borish L; Immunotherapy Committee of the AAAAI. Comparison of test devices for skin prick testing. *J Allergy Clin Immunol*. 2005;116:341–346.
10. Bernstein IL, Storms WW; Joint Task Force on Practice Parameters for the Diagnosis and Treatment of Asthma; The American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology. Practice parameters for allergy diagnostic testing. *Ann Allergy Asthma Immunol*. 1995;75:543–625.
11. Aas K. Some variables in skin prick testing. *Allergy*. 1980;67:64–67.

No reprints available.

Correspondence to:

Mark S. Dykewicz, MD

Section of Allergy and Clinical Immunology

Saint Louis University School of Medicine

1402 S Grand Blvd, R209

St Louis, MO 63104

E-mail: dykewicz@slu.edu