

# Comparison Of The Sensitivity, Precision And Reproducibility Of The Multi-test Device And Blood Lancet

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## Abstract

### Background:

In studies using allergen extracts, patients with 1+ reactions had been usually excluded. However, the borderline allergen reactions may give false positive or false negative results, in respect to chosen cutoff point.

**Objective:** This study aimed to compare the skin prick test device Multi-Test applicator with blood lancet, in respect to their sensitivity, precision and reproducibility.

**Methods:** The first group consist of 14 healthy subjects. The second group consist of 14 patients with allergic rhinitis, recruited from the Out-patient Allergy Clinic. The patients had known sensitivity to at least one allergen. Skin prick tests were performed with the single blood lancet and the Multi-Test device. The solutions used for testing were histamine, negative control for both group, and allergens (Dermatophagoides pteronyssinus, Dermatophagoides pharinae, grass, tree, weed, epidermal) for the second group.

**Results:** For all three tested solutions, mean wheal sizes were larger for the Multi-Test device than for the lancet, in healthy group ( $p < 0.0001$ ) and in allergic rhinitis group ( $P < 0.001$ ). The coefficients of variations for Multi-Test device were always lower than lancet. (Multi Test vs. lancet; for negative control: 49.81 vs 76.74, for histamine: 23.36 vs 36.76, for allergens: 79.60 vs. 100.56). If 3 mm was chosen as a cutoff point 22.9 % of the reactions were false positive for Multi-Test device.

**Conclusions:** According to results of our study cutoff point of 4.5 mm for Multi-Test device was comparable with cutoff point of 3 mm for lancet, with no false positive reactions for both devices.

## INTRODUCTION

In studies using allergen extracts, patients with 1+ reactions had been usually excluded. (1,2). However, the borderline allergen reactions may give false positive or false negative results, in respect to the chosen cutoff point.

This study aimed to compare the skin prick test device Multi-Test applicator with single blood lancets, widely used in Turkey, in respect to their precision (sensitivity and specificity) and reproducibility.

## METHODS

### SKIN PRICK DEVICES AND ALLERGEN EXTRACTS

Skin prick tests were performed with the single blood lancet and the Multi-Test device (Lincoln Diagnostics ). The blood lancet is a disposable individual needle, pricking epidermis at one point. The Multi-Test applicator is a disposable plastic device, pricking epidermis, by nine needle, at nine

point. The Multi-Test applicator has the ability of simultaneous prick puncture administration of eight different test solutions, by eight test heads. The solutions used for testing were histamine phosphate (1 mg/ml Histamine base) in 50% glyserosaline, Dermatophagoides pteronyssinus (D. pter.), Dermatophagoides Pharinae (D. phar.), grass mix, tree mix, weed mix, epidermal mix. The negative control was 50% glyserosaline. The solutions used for lancet and for Multi-Test were identical, all provided by the Center lab.

## STUDY POPULATION

The first group consisted of 14 healthy subjects with no known allergic disease.

The second group consisted of 14 patients with allergic rhinitis, recruited from the out-patient Allergy Clinic of Otolaryngology Department of Pamukkale University, in Denizli, Türkiye. The patients had known sensitivity to at least one of the allergens (D. pter., D. phar., grass, tree, weed

and epidermal), previously diagnosed with the use of Multi-Test applicator and allergen extracts (Center Lab, N.Y).

Exclusion criteria were the use of astemizol in the last 4 weeks, other antihistamines or oral steroids within 1 week, antidepressants within 2 week and histamine H-2 antagonists 24 hours before testing, as well as eczematous skin lesions at the site of testing. Each test subject gave written consent.

**STUDY DESIGN**

Skin prick tests were applied before noon (10 00-12 00) on the volar surface of both forearms, 3 cm distal from elbow crease. The Multi-Test device and lancet were randomly applied to the right and left arms. Finally, the application of the skin prick test devices to the left or right arm was equal. The distances between application sites of extracts for Multi-Test device were 2.5 cm in the transversal and 1.5 cm in the longitudinal axis. These distances were approximately 3 cm for lancet device. A single trained physician applied the skin prick tests. A second blinded experienced physician recorded the results.

In the first group, totally, eight tests were performed on each subjects, (four glyserosaline and four histamine) for each testing device.

In the second group, test solutions were applied on each arm of patients in the following order (proximal to distal)

The tests were read after 10 min for histamine and 15 min for others. All wheal sizes were measured as the mean of the longest diameter (a) (excluding pseudopodia) and midpoint perpendicular diameter (b); i.e., (a+b)/2. The wheal was first circled with a thin, felt-tip pen, then measured directly on the site by a transparent, flexible ruler.

**STATISTICAL ANALYSIS**

In a first step, the mean, the standard deviation (SD), and, as a measure of reproducibility, the coefficient of variation (CV = standard deviation/meanx100) of wheal reactions to negative control, histamine, and the allergen extracts were computed for each skin prick testing method. The wheal sizes resulting from the two prick methods were compared for each of the test solutions with the non-parametric Wilcoxon rank-sum test.

**RESULTS**

Thirteen women and 15 men participated in the study. Their mean age was 35,96 years, with a range of 19-60 years.

The results of comparative testing in the healthy group are

presented in tables 1 and 2. The Multi-Test device produced substantially larger reactions than that produced by lancet, for the size of the mean wheal with histamine (p<0.0001), and glycerosaline (p<0.0001).

**Figure 1**

Table 1: Comparison of devices for positive control in the healthy group.

Devices	Number of tests	Mean histamine wheal	SD	CV	False negative (%) (cutoff point 3mm)	Specificity Of 0.99	Specifity of 3 mm wheal
Lancet	48	4.27	0.74	17.23	0	2.5 mm	1.00
Multi-Test	48	5.48	0.71	12.90	0	4.5 mm	77.1

**Figure 2**

Table 2: Comparison of devices for the negative control in the healthy group.

Devices	Number Of tests	Mean saline wheal	SD	CV	False positive (%) (cutoff point 3mm)
Lancet	48	0.77	0.47	61.21	0
Multi-Test	48	2.34	1.46	62.41	60.4

Table 3 shows the number of performed skin prick tests, and the mean, the standard deviation, and the coefficient of variation of the histamine, negative control and allergen extracts for both skin prick test devices in the allergic rhinitis group.

**Figure 3**

Table 3: Comparison of devices for the negative control, histamine and allergens in the allergic rhinitis group.

Test substance	Wheal size	Multi-Test	Lancet
Negative kontrol	N	14	14
	Mean (mm)	2.71	0.86
	SD (mm)	1.35	0.66
Histamine	Mean (mm)	6.25	4.79
	SD (mm)	1.46	1.75
	CV (%)	23.36	36.76
Allergens	N	84	84
	Mean (mm)	4.61	3.51
	SD (mm)	3.67	3.53
	CV (%)	79.60	100.56

In the allergic rhinitis group, the skin pricks applied by the Multi-Test device resulted in significantly larger mean wheal sizes for all of the test solutions; negative control ( $P < 0.001$ ), histamine ( $P < 0.001$ ) and allergen extracts ( $P < 0.001$ ). The coefficient of variation not only varied between devices, but was also dependent on the corresponding test solutions used. For both test devices, the coefficients of variation were lowest for histamine and highest for allergens, with negative control ranging in the middle.

Only, the coefficient of variation for histamine, in healthy group, for both devices, met the criteria recommended in the literature (3); i.e.,  $CV < 20\%$ . The coefficients of variations for Multi-Test device were always lower than lancet, except for negative control in the healthy group.

According to the chosen cutoff point of 3 mm for positive reactions, 48 positive skin prick tests reactivity were obtained in 14 patients, for the Multi-Test device, and 37 for the lancet. If the cutoff point was chosen as 4 mm for Multi-Test device, the number of skin prick test reactivity was 37. When the characteristics of clinical symptoms were taken into account the number of 37 seems to be more logical, i.e. a patient with perennial allergic rhinitis had 12 mm and 14 mm skin reactivity for D. Pter. and D. Phar. respectively. The same patient had 2 mm skin reactivity for negative control and 3 mm for grass which was not concordant with the clinical outcome. In conclusion, if 3 mm was chosen as a cutoff point, 22.9 % of the reactions were false positive for Multi-Test device.

When asked which of the two devices they preferred, patients and control group preferred the Multi-Test, since it was less uncomfortable and easier and quicker to apply.

**DISCUSSION**

As has been true in previous comparisons (4,5,6), this study revealed highly significant differences in the size of test reactions obtained with two different devices and techniques studied. Another result of these previous studies is that, devices producing the smaller wheals with histamine were more apt to give false-negative reactions, whereas those producing the larger wheals with histamine were more apt to produce false positive reactions and whealing at the negative control sites. On the other hand, the larger wheal sizes positively affects the reproducibility (2). Several studies (2,6,7,8) have investigated the reproducibility of the Multi-Test device, either as a comparison with other skin prick test devices (4-8) or as an evaluation of the Multi-Test by itself (2). Most of these studies concluded that the Multi-Test is a highly reproducible device (2,6-8). Our study resulted in smaller coefficients of variation for Multi-Test than lancet. As it is reported (1), the coefficients of variation for allergens were higher than those for histamine, since the natural variability of sensitization to allergens in the study adds up to variability of the testing device.

Most of the previous studies on the performance of skin prick tests analyzed only the reproducibility of wheal sizes. Of equal importance, however, is the correlation of results defined as positive or negative, with clinical diagnosis of patient. It is recommended that, a positive definition based on a cutoff point of 1 mm might be preferred when comparing prevalence of atopy among centers (1,9). However, it is important to note that if a detection of clinically relevant atopy with respect to the relation between allergen sensitivities and respiratory illness is of major interest, a larger cutoff point should be chosen (1). Peat and Woolcock (10), who tested 13 common allergens, reported that children with one or more positive skin wheals of greater than or equal to 3 mm had significantly more recent clinical symptoms than children with smaller wheals. On the other hand, it was proposed that for each device a different size of wheal must be produced at the allergen site to have confidence that it exceeds the control site. The wheal size necessary for 99% specificity had been proposed as follows (6): Hollister-Stier lancet, 2 mm; ALK lancet, 3.0 mm; bifurcated needle prick, 4.0 mm; bifurcated needle puncture, 4.5 mm; Multi-Test device, 5.0 mm; and DermaPIK device, 5.5 mm.

According to the results of our study, a cutoff point of 4.5 mm for Multi-Test applicator was comparable with a cutoff point of 3 mm for the lancet. Although, the Multi-Test package insert states that wheals up to 5 mm in diameter can occur at negative control sites in some patients, and it stresses reading all results against the negative control, the negative control was not always an acceptable reference in our study.

In studies using allergen extracts, patients with 1+ reactions had been usually excluded. (1,2). However, the borderline allergen reactions may give false positive or false negative results, in respect to chosen cutoff point. Therefore, the main aim of this study was to compare the skin prick test device Multi-Test applicator with nine prick points which enables introduction of more test solutions by nine pricks into epidermis with the recommended method of lancets with single skin prick point, in respect to their precision. According to the chosen cutoff point of 3 mm for positive reactions, 22.9 % of the reactions were false positive for Multi-Test device. If the cutoff point was chosen as 4.5 mm for Multi-Test device, there was no false positive reaction.

## **CONCLUSION**

The Multi-Test device, highly reproducible, comfortable for patient, easier and quicker to apply, is a suitable device in office procedures, and the cutoff point of 4.5 mm should be chosen in order to avoid false positive reactions.

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