Multi-Center Study on the Performance Characteristics of Two Skin Test Devices – ComforTen® and Multi-Test®

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PURPOSE

To compare a new 10-leg, single-tip multi-test device (ComforTen) with an 8-leg, cluster-tip multi-test device (Multi-Test II), which has a known performance pattern, in a head to head manner. The performance of, and patient preference for, the two FDA allowed skin test devices were evaluated in a single blinded fashion at two allergy clinics. The outcomes may assist clinicians in making an informed decision when selecting a skin test device.

BACKGROUND

The results of allergen skin testing are clinically important because they guide the allergy specialist in devising an avoidance plan and in writing immunotherapy prescriptions. The goal for the allergy specialist is to apply allergen skin testing using a device that minimizes both false negative and false positive findings, and that results in minimal patient discomfort.

Multi-test devices offer the advantage of application of several antigens simultaneously. Many of those devices on the market have been evaluated against each other to compare performance. Studies have revealed significant differences in the size of wheal and flare reactions; for both positive (allergen extract or histamine) and negative (glycerol-saline) sites[1-4]. Differences appear to result from the degree of skin trauma imparted to the skin, an interpretation that was reinforced by the observation that those producing larger wheals also caused more patient discomfort[4].

STUDY DESIGN

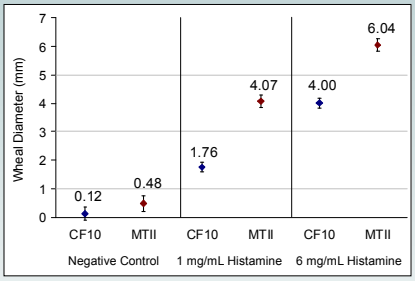
- Single blinded study executed per IRB-approved protocols at two clinical sites.
  Allergy & Asthma Clinic (AAC, Fort Lauderdale, Florida; Linda Cox, MD)
  National Jewish Health (NJH, Denver, CO; Rohit Katial, MD)
- Inclusion Criteria: 18-70 years of age, male or female, atopic or non-atopic
- Exclusion Criteria: dermatographism, severe atopic dermititis, inability to withhold medications that may influence the test (antihistamine, H2 blockers, tricyclic antidepressants, prednisone), skin damage/conditions that obscured the readings (NJH only), and pregnancy (NJH only).
- Patient Participation: N=24 (AAC), N=16 (NJH)
- Two multiple test devices were used.
  ComforTen (CF10, HollisterStier Allergy, Spokane, WA)
  Multi-Test II (MTII, Lincoln Diagnostics, Decatur, IL)
- Test Solutions:
  1 mg/mL base (as 2.7 mg/mL Histamine Phosphate, ALK)
  6 mg/mL base (as 10 mg/mL Histamine Dihydrochloride, HollisterStier)
  50% glycerol-saline (HollisterStier) as the negative control.
- Operators trained by each company's representative, according to the respective package inserts, and tested for proficiency.
- Patients were blind skin tested on the back with each device in duplicate.
  – In order to control for variations in response based on anatomic site, each device was used on two horizontal planes on the back with the order of application randomized. Each quadrant of the back was equally represented by both devices.
  – The skin test devices tested with alternating positive and negative controls.
- Measurements were taken 10 minutes after test application.
  – Wheal responses were outlined, transferred using tape to a case report form, and later measured by two independent operators.
  – The presence of flare was noted, as applicable.
- For each device, patients were asked to assess the degree of pain using the Wong Baker FACES pain rating scale (JCAHO compliant).
- Patients were asked their preference for each of two pairs of devices to confirm consistency of response.
- Study data were analyzed using repeated measure ANOVA (SAS, version 9.2)
- Studies were funded by grants from Jubilant HollisterStier LLC.

REFERENCES

1. Carr WW, Martin B, Howard RS, Cox L, Borish L. Comparison of test devices for skin prick testing. J Allergy Clin Immunol 2005; 116: 341-6
2. Nelson HS, Kolehmainen C, Lahr J, Murphy J, Buchmeier A. A comparison of multihead devices for allergy skin testing. J Allergy Clin Immunol 2004; 113: 1218-19
3. Nelson HS, Lahr J, Buchmeier A, McCormick D. Evaluation of devices for skin prick testing. J Allergy Clin Immunol 1998; 101: 153-6
4. Nelson HS, Roslonicc DM, McCall LI, Ikle D. Comparative performance of five commercial prick skin test devices. J Allergy Clin Immunol 1993; 92: 750-6

RESULTS

OUTCOME: Wheal Size



Note: N = 39 patients. 40 patients were enrolled, but one was excluded from analysis due to an incomplete case report form.

- **Smaller wheals using CF10 than those with MTII.**
  Diameter (combined sites and both histamines):
  1.95 mm (CF10) vs. 3.53 mm (MTII), P < 0.001
- **Wheals at NJH were smaller than those at AAC.**
  Diameter (combined devices and both histamines):
  2.33 mm (NJH) vs. 3.16 mm (AAC), P < 0.001
- **Wheal diameters were not significantly different when comparing device-histamine combination, as described by each company's product insert.**
  CF10 with 6 mg/mL histamine
  MTII with 1 mg/mL histamine
  Diameter (combined centers):
  4.00 mm (CF10) vs. 4.07 mm (MTII), P=0.62

OUTCOME: Sensitivity and Specificity

	CF10			MTII		
Number of Test Sites	184	128	312	138	96	234
Cut-Off	AAC	NJH	Overall	AAC	NJH	Overall
SENSITIVITY (Low Control, 1 mg/mL)						
1 mm	39%	69%	51%	86%	84%	85%
3 mm	34%	19%	28%	85%	66%	77%
5 mm	11%	0%	6%	62%	20%	44%
SENSITIVITY (High Control, 6 mg/mL)						
1 mm	88%	99%	93%	93%	99%	95%
3 mm	84%	70%	78%	93%	96%	94%
5 mm	52%	13%	36%	84%	70%	78%
SPECIFICITY (Negative Control)						
Number of Test Sites	92	64	156	92	64	156
1 mm	98%	100%	99%	80%	100%	88%
3 mm	98%	100%	99%	85%	100%	91%
5 mm	99%	100%	99%	92%	100%	96%

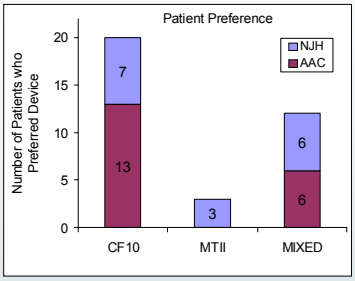
Sensitivity = (True Pos) / (True Pos + False Neg)

Specificity = (True Neg) / (True Neg + False Pos)

Optimal Performance = Sensitivity x Specificity

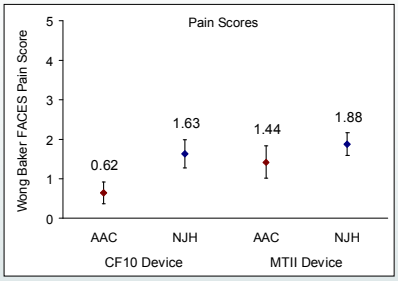
Values highlighted in yellow represent the positive control and cut-off recommended by the device manufacturer.
Values highlighted in green represent the optimal performance, taking into account both sensitivity and specificity.

OUTCOMES: Patient Preference and Pain Scores



Note: N = 35 patients. 40 patients were enrolled. One patient was excluded from analysis due to an incomplete case report form. Patient preference data was not documented for four patients.

- **CF10 Preference: 57% of patients.**
- **MTII Preference: 9% of patients.**
- **Mixed Device Preference: 34% of patients.**



- **At ACC, there were significantly lower pain scores using CF10 than there were using MTII.**
  0.62 (CF10) vs. 1.44 (MTII), p = 0.0015
- **At NJH, there were no significant differences in pain scores using the CF10 and MTII devices.**
  1.63 (CF10) vs. 1.88 (MTII), p = 0.248

CONCLUSIONS

- Under conditions of manufacturer recommended use (CF10 with 6 mg/mL histamine vs. MTII with 1 mg/mL histamine):
  – Two devices produced similar average wheal sizes.
  – Sensitivity and specificity at a 3 mm cut-off are comparable.
- Optimal CF10 outcome used 6 mg/mL histamine control and a 1 mm cut-off.
- Optimal MTII outcomes used 6 mg/mL histamine control and a 3 mm cut-off.
- Differences in operator techniques may account for the observation of some inter-site differences, which highlights the importance of training.
- Patient preference is for the ComforTen device.
- Recommend follow-up studies to confirm these findings with allergen extracts.