

Comparison study between MAST CLA and OPTIGEN

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ABSTRACT

Background: The MAST-CLA system (Hitachi Chemical Diagnostics, Inc., Mountain View, CA) is an *in vitro* diagnostic test for the simultaneous determination of specific IgE to different allergens. Recently, a new generation of MAST-CLA was developed (OPTIGEN; Hitachi Chemical Diagnostics). The purpose of this study was to determine the performance of these two tests for the diagnosis of allergic rhinitis.

Methods: Suspected allergic rhinitis patients were divided into four groups and their medical records were reviewed: group 1 patients were tested with the MAST-CLA and skin-prick tests (251 patients), group 2 patients were tested with the OPTIGEN and skin-prick tests (319 patients), group 3 patients were tested with the MAST-CLA and CAP (104 patients) tests, and group 4 patients were tested with the OPTIGEN and CAP tests (270 patients). The correlation between MAST-CLA and OPTIGEN to skin-prick and CAP tests was determined.

Results: The positivity percentage of MAST-CLA results was higher than with skin-prick and CAP tests, and the results for the OPTIGEN test were comparable with skin-prick test and CAP. This suggests that the MAST-CLA test might have a slightly higher rate of giving false positive results. The OPTIGEN test correlated better with the skin-prick test and CAP.

Conclusion: The OPTIGEN test performed better than the MAST-CLA test for diagnosing allergic rhinitis.

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The number of patients with allergic rhinitis has increased gradually worldwide. In Korea, allergic rhinitis affects ~20% of the population. According to a report from the Korean government, the number of patients who visited clinics or hospitals was 10,884 per 100,000 people in 2001, and increased to 13,508 (24.1%) in 2005. With this dramatic increase, more attention has since been paid to the disease. Specific allergen diagnosis is important before treating allergic rhinitis. To determine the diagnosis, several tests are available, including the skin-prick test and allergen-specific IgE, *in vitro*, diagnostic tests.

The skin-prick test is generally accepted as the decisive test because it is highly sensitive and reproducible. The response to the test correlates with serum total IgE, specific IgE, and the results of provocation tests.^{1–3} However, the test can not be performed on patients with dermatographism, severe eczema, or urticaria. It also can not be performed on patients taking some medications such as antihistamines, antacids, and antipsychotics. Finally, the patients age and the test site may affect the outcome.⁴

There are tests in the Korean market that can specifically detect IgE in serum, *viz.*, radioallergosorbent test, CAP system, and the MAST-CLA system (Hitachi Chemical Diagnostics, Inc., Mountain View, CA). The radioallergosorbent test was the first in the market.⁵ However, this test has disadvantages. To begin, it uses radioisotopes, can detect only one allergen at a time, and requires expensive equipment. For this reason, it is seldom used. The CAP system uses cellulose in the solid phase, which contains specific allergens.⁶ The patient's specific IgE in the serum attaches to the allergen in the solid phase and is detected with a chemiluminescence reaction. This system is very accurate and provides quantitative results on the amount of specific IgE.^{7,8} However, only six allergens per person are covered by the medical insurance system in Korea, because of the high cost of the test.

The MAST-CLA system is another *in vitro* test that measures allergen-specific IgE in serum, using a plastic test chamber with thread as the solid phase.⁹ It has a very simple protocol that allows for the

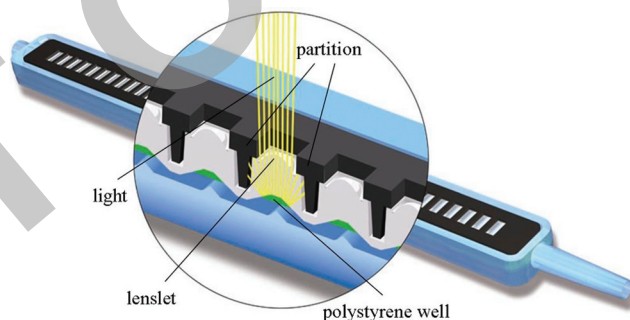


Figure 1. Schematic illustration of OPTIGEN. It is composed of >33 wells that are separated by partitions. Each well is made from polystyrene, which different allergens are attached to and covered by the lenslet. Once the patient's serum is injected into this device, specific IgE in the serum binds to specific allergens on the well. Next, reagents are added and the binding emits light through the lenslet. (This illustration is kindly provided by Hitachi Chemical Diagnostics, Inc., Mountain View, CA).

simultaneous measurement of up to 35 allergens. To further prove its effectiveness, the MAST-CLA Korean inhalant panel has been using it as a diagnostic test for allergic rhinitis since 1996.¹⁰ On the other hand, a disadvantage for this method is the observed higher positivity and lower sensitivity rates compared with that of the skin-prick test.^{11,12}

Recently, a new generation of MAST-CLA (OPTIGEN; Hitachi Chemical Diagnostics) has been introduced. The OPTIGEN device consists of small wells that contain different allergens, a partition that separates the wells, and a lenslet that collimates the light (Fig. 1). The biggest difference is that OPTIGEN uses a polystyrene as well as a solid phase instead of thread. We believe, for these reasons, that OPTIGEN provides more accurate results compared with the MAST-CLA test. The purpose of this study was to compare the diagnostic effectiveness for allergic rhinitis of the OPTIGEN and the previous MAST-CLA systems, relative to the skin-prick test and CAP systems.

METHODS

Patients and Study Design

We reviewed the medical records of all the chronic rhinitis patients who took two different diagnostic tests simultaneously. The tests were

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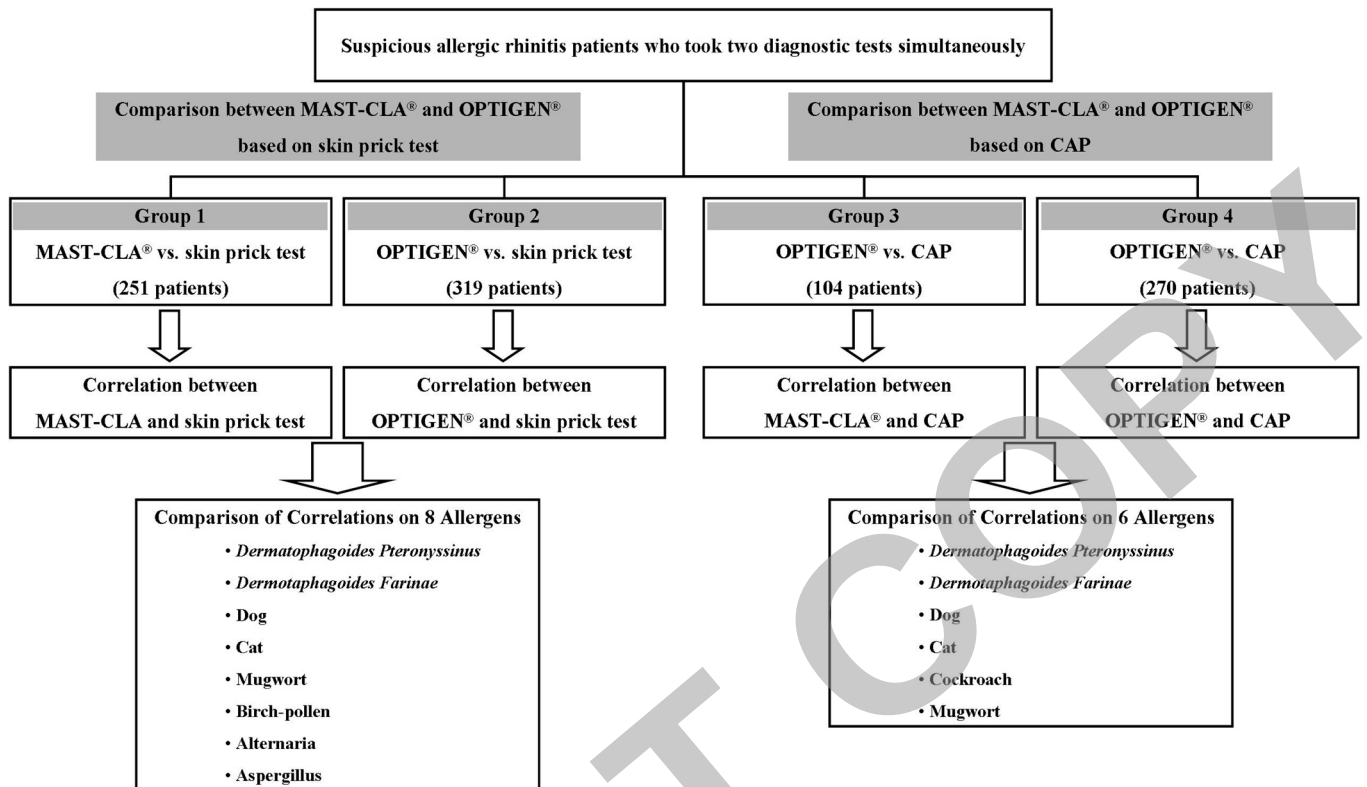


Figure 2. Overall design of study.

performed at the Department of Otorhinolaryngology in the Head and Neck Department of Kon-Kun University Hospital from June 2005 to December 2008. The patients who had symptoms of rhinitis such as nasal obstruction, rhinorrhea, itching, or postnasal drip for >3 months were included in the study. The only exclusions were the patients who had taken any kind of medication during the previous month. The diagnostics tests were randomly chosen among the skin-prick, MAST-CLA, OPTIGEN, and CAP tests. Our laboratory used the MAST-CLA test until October 2006 and switched to the OPTIGEN test in November 2006. The methods and reagents for the skin-prick test and CAP have not changed. We sorted the patients into the following four different groups: group 1, patients tested with the MAST-CLA and the skin-prick tests simultaneously (251 patients); group 2, the OPTIGEN and the skin-prick tests (319 patients); group 3, the MAST-CLA and CAP tests (104 patients); and group 4, the OPTIGEN and CAP tests (270 patients). For groups 1 and 2, the correlation between the two test results were calculated for eight allergens (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, dog, cat, mugwort, birch-pollen, *Alternaria*, and *Aspergillus*). For groups 3 and 4, the correlation was calculated for six allergens (*D. pteronyssinus*, *D. farinae*, dog, cat, cockroach, and mugwort; Fig. 2). This study was exempted from the Internal Review Board of Konkuk University Hospital.

Skin-Prick Test

Skin-prick tests on the forearm were performed using the eight most common allergens among Koreans, viz., *D. pteronyssinus*, *D. farinae*, dog, cat, mugwort, birch pollen, *Alternaria*, and *Aspergillus* (Bencard Co., Brentford, England). Wheal size was measured 15 minutes after pricking and compared with that produced by a histamine control. When the wheal was twofold larger in diameter than the histamine control, or showed a pseudopod, the result was classified as +4 (>200%). If the wheal was the same size as the histamine control, up to twofold larger, or >3 mm, it was classified as +3 (100–200%). If it was more than one-half the size of the control, it was

Table 1 Age distribution of groups 1 and 2

Age (yr)	No. (%) of Patients	
	Group 1, MAST-CLA vs Skin-Prick Test	Group 2, OPTIGEN vs Skin-Prick Test
<10	10 (4.0)	17 (5.3)
10 ≤ <20	55 (21.9)	74 (23.2)
20 ≤ <30	68 (27.1)	83 (26.0)
30 ≤ <40	45 (17.9)	52 (16.3)
40 ≤ <50	38 (15.1)	44 (13.8)
50 ≤ <60	20 (8.0)	37 (11.6)
60 ≤	15 (6.0)	22 (6.9)
Total	251 (100)	319 (100)

scored as +2; if it was more than a one-quarter the size of the control it was scored as +1 and if it was less than one-quarter of the size of the control it was scored as 0.

MAST-CLA System

The Korea IgE Inhalant Panel MAST-CLA test (Hitachi Chemical Diagnostics, Inc.) was used. All of the procedures were performed according to the manufacturer's instructions, and the results were read with a luminometer (CLA-1; Hitachi Chemical Diagnostics, Inc.) and graded into classes 0, 1, 2, 3, and 4.

OPTIGEN System

The same panel composition used for MAST-CLA was used for the OPTIGEN test. All of the procedures were performed as per the manufacturer's instructions; the OPTIGEN pette was read by

Table 2 Comparison between the MAST-CLA and OPTIGEN tests to the skin-prick test

Allergen	Group 1, MAST-CLA vs Skin-Prick Test (251 patients)			Group 2, OPTIGEN vs Skin-Prick Test (319 patients)			Comparison of Correlation
	No. (%) of Positivity		Correlation Coefficient	No. (%) of Positivity		Correlation Coefficient	
	MAST-CLA	Skin-Prick Test		OPTIGEN	Skin-Prick Test		
<i>Dermatophagoides farinae</i>	170 (67.7)	128 (51.0)	0.699	136 (42.6)	144 (45.1)	0.787	$p<0.05$
<i>Dermatophagoides pteronyssinus</i>	177 (70.5)	121 (48.2)	0.695	142 (44.5)	138 (43.3)	0.797	$p<0.01$
Dog	80 (31.9)	28 (11.2)	0.206	30 (9.4)	57 (17.9)	0.371	$p<0.05$
Cat	84 (33.5)	38 (15.1)	0.235	26 (8.2)	53 (16.6)	0.549	$p<0.001$
Mugwort	35 (13.9)	33 (13.1)	0.544	35 (11.0)	39 (12.2)	0.420	$p=0.06$
Birch pollen	60 (23.9)	27 (10.8)	0.423	23 (7.2)	41 (12.9)	0.240	$p<0.05$
<i>Alternaria</i>	45 (17.9)	14 (5.6)	0.083	2 (0.6)	22 (6.9)	0.301	$p<0.01$
<i>Aspergillus</i>	56 (22.3)	7 (2.8)	−0.037	1 (0.3)	12 (3.8)	−0.011	$p=0.76$

the same luminometer as described previously, and the results were graded into classes 0, 1, 2, 3, 4, 5, and 6.

CAP Test

Specific IgE to *D. pteronyssinus*, *D. farinae*, dog, cat, cockroach, and mugwort were determined by the CAP system (ImmunoCAP; Pharmacia Diagnostics, Clayton, NC). The results were graded into classes 0, 1, 2, 3, 4, 5, and 6.

Statistics

The correlations between the two tests in each group, *viz.*, MAST-CLA test versus skin-prick test for group 1, OPTIGEN test versus skin-prick test for group 2, MAST-CLA test versus CAP test for group 3, and OPTIGEN test versus CAP test for group 4, were calculated using Spearman rank correlation provided by SPSS Version 13.0 (SPSS, Inc., Chicago, IL). Comparisons of the correlation coefficient between groups 1 and 2, and between groups 3 and 4 were calculated by comparing the correlation coefficient between the two independent groups provided by dBSTAT version 4.1 (dBSTAT, Seoul, Korea). Positivity of the tests was defined as + 1 or higher for the skin-prick test and class 1 or higher for the MAST-CLA, OPTIGEN, and CAP tests.

RESULTS

Comparison between MAST-CLA and OPTIGEN based on Skin-Prick Test

The age distributions of group 1 (MAST-CLA test versus skin-prick test) and group 2 (OPTIGEN test versus skin-prick test) were similar (Table 1). The positivity percentages of the skin-prick test on eight allergens were also comparable between groups 1 and 2. The positivity percentages of the MAST-CLA test was higher than those of OPTIGEN test on all eight allergens. The correlation between the OPTIGEN and the skin-prick tests was more similar than those between MAST-CLA and the skin-prick tests on six of 8 allergens ($p < 0.05$). Neither the MAST-CLA test nor the OPTIGEN test showed significant correlation with the skin-prick test on *Aspergillus*. For *Alternaria*, OPTIGEN showed correlation with the skin-prick test, but MAST-CLA did not (Table 2).

Comparison between the MAST-CLA and OPTIGEN based on CAP

The age distributions of group 3 (MAST-CLA versus CAP) and group 4 (OPTIGEN versus CAP) were similar (Table 3). The positivity percentages for the skin-prick test for all allergens were also comparable between groups 3 and 4. The positivity percentages of the MAST-CLA test were higher than those of the OPTIGEN test on all allergens. The corre-

Table 3 Age distribution of groups 3 and 4

Age (yr)	No. (%) of Patients	
	Group 3, MAST-CLA vs CAP	Group 4, OPTIGEN vs CAP
<10	33 (31.7)	84 (31.1)
10 ≤ <20	24 (23.1)	50 (18.5)
20 ≤ <30	7 (6.7)	48 (17.8)
30 ≤ <40	11 (10.6)	36 (13.3)
40 ≤ <50	12 (11.5)	20 (7.4)
50 ≤ <60	9 (8.7)	16 (5.9)
60 ≤	8 (7.7)	16 (5.9)
Total	104 (100)	270 (100)

lation between the OPTIGEN and CAP tests was better than between MAST-CLA and CAP tests in five of six allergens (all, $p < 0.001$). The correlation for cockroach was lower for the OPTIGEN test and higher for the MAST-CLA test when compared with CAP (Table 4).

DISCUSSION

In the mid-1960s, Ishizaka *et al.* discovered that IgE was the cause of the allergic hypersensitivity reaction. Since then, several tests for the detection of specific IgE has been introduced.¹³ Among the tests, MAST-RIA system, which used isotopes to detect specific IgE, was described by Miller *et al.* in 1984.⁹ The following year, Brown *et al.* presented a nonisotopic version of the test, MAST-CLA, with a much shorter total assay time. This is a very convenient test requiring only a single blood sample to simultaneously test up to 35 allergens. The test set is composed of a disposable device that contains cellulose threads, each with a different allergen or mix of allergens bound to it.¹⁴ The patient's IgE in serum binds to the specific allergen on the thread, and an enzyme-labeled anti-immunoglobulin antibody binds to IgE. When combined with conjugates, it gives off chemiluminescent signals that are read by the specific reader and provides semi-quantitative results.¹⁴ This system has been used for the diagnosis of allergic rhinitis for >20 years and is known to be very useful.¹⁵ However, false positive results and low sensitivity has been observed in this system. A new generation of this test, the OPTIGEN test, was introduced into the Korean market in 2006.

The basic principal of OPTIGEN is the same as that of MAST-CLA, but the main difference between the two tests is the solid phase when the allergen is attached. Also, OPTIGEN adopted the polystyrene well instead of the thread. According to the manufacturer, the surface of the well is specially treated so that more allergens can be fixed on effectively. In addition, its lenslet makes the detection of the signal

Table 4 Comparison between the MAST-CLA and OPTIGEN tests to CAP

Allergen	Group 3, MAST-CLA vs CAP (104 patients)			Group 4, OPTIGEN vs CAP (270 patients)			Comparison of Correlation
	Number (%) of Positivity		Correlation Coefficient	Number (%) of Positivity		Correlation Coefficient	
	MAST-CLA	CAP		OPTIGEN	CAP		
<i>Dermatophagoides farinae</i>	75 (72.1)	40 (38.5)	0.784	87 (32.2)	97 (35.9)	0.938	<i>p</i> <0.001
<i>Dermatophagoides pteronyssinus</i>	78 (75.0)	45 (43.3)	0.837	95 (35.2)	106 (39.3)	0.939	<i>p</i> <0.001
Dog	59 (56.7)	4 (3.8)	0.170	19 (7.0)	23 (8.5)	0.716	<i>p</i> <0.001
Cat	61 (58.7)	7 (6.7)	0.402	15 (5.6)	13 (4.8)	0.864	<i>p</i> <0.001
Cockroach	37 (35.6)	20 (19.2)	0.421	12 (4.4)	29 (10.7)	0.453	<i>p</i> =0.735
Mugwort	9 (8.7)	7 (6.7)	0.063	21 (7.8)	21 (7.8)	0.757	<i>p</i> <0.001

Table 5 The most effective cutoff values for MAST-CLA and OPTIGEN

Allergen	MAST-CL (area under the ROC curve)	OPTIGEN (area under the ROC curve)
<i>Dermatophagoides farinae</i>	4 (0.791)	4 (0.856)
<i>Dermatophagoides pteronyssinus</i>	4 (0.813)	4 (0.884)
Dog	4 (0.718)	4 (0.900)
Cat	4 (0.800)	3 (0.934)
Mugwort	4 (0.799)	4 (0.872)
Birch pollen	4 (0.925)	3 (0.783)
<i>Alternaria</i>	4 (0.606)	1 (0.974)
<i>Aspergillus</i>	Incalculable*	Incalculable*

*Area under ROC curve is below zero.

ROC = receiver operating characteristics.

more effective. According to this finding, OPTIGEN can detect specific IgE very accurately and its dynamic range of the result are vast. However, we found OPTIGEN was much better correlated with the skin-prick test and CAP compared with MAST-CLA in this study. In other words, OPTIGEN takes precedence over the advantages of MAST-CLA. It maintains a cost-effective screening, is convenient, and reduces the inaccuracy. Overall, OPTIGEN is a very useful diagnostic tool for detecting allergic rhinitis. OPTIGEN was better correlated with CAP than the skin-prick test in this study. It is reasonable because the principals of CAP and OPTIGEN are nearly same, *viz.*, to detect the specific IgE in blood, while the skin-prick test provokes histamine release from the specific IgE-coated mast cell.^{1,6,9}

In this study, positivity of the tests was defined as +1 or higher for the skin-prick test and class 1 or higher for the MAST-CLA, OPTIGEN, and CAP tests. However, this definition did not suggest the clinical positivity. It is widely accepted that +3 and +4 of the skin-prick test are considered as clinically significantly positive,¹ but there are no clear cutoff values for MAST-CLA, OPTIGEN, and CAP tests to diagnose allergic rhinitis. Thus, we included all the positive results of each tests for comparison (Tables 2 and 4). If the skin-prick test is assumed to be the gold standard for the diagnosis of allergic rhinitis, you can calculate the most accurate cutoff values for MAST-CLA and OPTIGEN using the receiver operating characteristic curve. We used this method and summarized the results in Table 5.

There were a few limitations in this study. First, we did not test the MAST-CLA and OPTIGEN systems simultaneously on the same patients; therefore, the exact comparison between the two tests was impossible. In addition, the false positivity and sensitivity were not calculated and compared because the exact cutoff value for MAST-CLA and

OPTIGEN still are not determined. Finally, only a small number of allergens were compared for the convenience of study. If we performed the tests using more allergens, this study could be more informative.

CONCLUSION

The OPTIGEN test performed better than the MAST-CLA test for diagnosing allergic rhinitis.

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