

ImmunoCAP Rapid

Summary from an evaluation under the direction of SKUP Report SKUP/2013/68

Background

The evaluation of ImmunoCAP Rapid was performed on the request in 2007 of the market company in Denmark, Phadia ApS. The evaluation was performed in the Department of Clinical Biochemistry, Odense University Hospital and Hillerød Hospital. Thirteen primary health care centres and one specialised clinic for allergic diseases represented the intended users.

The aim of the evaluation

In primary health care

- Determination of the sensitivity and the specificity of house dust mite (d1), cat epithelia (e1), birch pollen (t3), dog epithelia (e5), mugwort pollen (w6) or timothy grass pollen (g6), and *Alternaria alternata* (m6) with ImmunoCAP Rapid compared to skin prick test and Phadia 250.
- Number of samples/persons included in the evaluation should be at least 100 positive and 100 negative results with skin prick test for at least two of the following antigens: house dust mite (d1), cat epithelia (e1), birch pollen (t3), dog epithelia (e5), mugwort pollen (w6) or timothy grass pollen (g6), and *Alternaria alternata* (m6).
- Count the fraction of positive results for cockroach (i6), olive pollen (t9), wall pellitory (w21) with ImmunoCAP Rapid.
- Determination of the “intra-person agreement in testings” by letting the same person perform repeated tests with the same sample.
- Determination of the “inter-person agreement in readings” by letting two persons perform readings on the same test cassette on 20% of the tests
- Evaluation of user-friendliness of ImmunoCAP Rapid

In the hospital laboratory

- Compilation of facts about the test system
- Repeat approximately 1/5 of the tests from primary health care, but using heparinised venous whole blood with ImmunoCAP Rapid.
- Evaluation of user-friendliness of ImmunoCAP Rapid

The results were compared with: 1. Skin prick test and 2. Phadia 250.

ImmunoCAP Rapid is using the same antigens as Phadia 250. According to internal studies made by the manufacturer ImmunoCAP Rapid has a level of detection of 1-2 kIU/L for all antibodies. In this evaluation 0-1,49 kIU/L with Phadia 250 is considered as negative and concentrations above 1,49 kIU/L are considered as positive when compared to ImmunoCAP Rapid. This is higher than the threshold (0,35 kIU/L) for positive results on Phadia 250. The serum results of Phadia 250 were also compared to the skin prick test using 0,35 kIU/L as the cut-off.

Materials and methods

ImmunoCAP Rapid was evaluated with capillary whole blood samples from 300 patients from 13 primary health care centres and one specialised clinic for allergic diseases. Standard skin prick tests (10 allergens) were performed on all participants with Soluprick, ALK Abello, Denmark. For each patient a serum sample were analysed for six allergens on Phadia 250. About 1/7 of the samples were analysed using heparin whole blood with ImmunoCAP Rapid in hospital.

Quality goals in the evaluation of ImmunoCAP Rapid

	Comparison Skin prick test	Comparison Phadia 250
Sensitivity *	>85%	>95%
Specificity	>85%	>95%
Fraction of technical errors		2% or less
User-friendliness		satisfactory

*the sensitivity is expected to be much lower than 85% for timothy and dog dander

Results

Sensitivity, specificity, percentage of positive skin prick test and positive and negative predictive value of ImmunoCAP Rapid compared to skin prick test (in percent) is given in the table below. The sensitivity and specificity figures are printed in green if the results fulfil the quality goals, yellow if the results are inconclusive or red if the results don't fulfil the quality goals.

Allergen	Name	Percentage of positive skin prick test	Sensitivity	Specificity	PPV	NPV
	Cat epithelium and dander	22,2	71,2	99,6	97,9	92,4
	Common silver birch (pollen)	31,6*	69,1	97,5	92,9	87,2
	Mugwort	17,5	59,6	96,7	79,5	91,9
	Timothy	36,7*	59,6	98,4	95,6	80,8
	Dog dander	26,6	19,0	98,6	83,3	77,1
	House dust mites** <i>Dermatophagoides pteronyssinus</i> <i>Dermatophagoides farinae</i>	31,6	70,2	95,6	88,0	87,4
	Mould** <i>Alternaria alternata</i> <i>Cladosporium hebarum</i>	9,1	59,3	99,3	88,9	96,1

* The inclusions were random until 85 patients with positive skin prick tests for common silver birch and grass (timothy) were enrolled, then patients positive for birch or grass in skin prick test were chosen prior to others. This was agreed in order to finish the evaluation, however; the percent of positive skin prick test for birch and grass did not change. ** These results refer to the sum of skin prick tests positive for either one or both of the two allergens.

Sensitivity, specificity, percentage of positive Phadia 250 test and positive and negative predictive value of ImmunoCAP Rapid compared to Phadia 250 (in percent) is given in the table below. The sensitivity and specificity figures are printed in green if the results fulfil the quality goals, yellow if the results are inconclusive or red if the results don't fulfil the quality goals.

Allergen	Name	Percentage of positive Phadia 250 test	Sensitivity	Specificity	PPV	NPV
	Cat epithelium and dander	10,9	75,0	90,8	50,0	96,7
	Common silver birch (pollen)	22,4*	80,3	92,5	75,7	94,2
	Mugwort	9,2	51,9	90,6	35,9	94,9
	Timothy	22,1*	76,9	92,6	74,6	93,4
	Dog dander	4,4	53,8	96,1	38,9	97,8
	House dust mites** <i>Dermatophagoides pteronyssinus</i> <i>Dermatophagoides farinae</i>	21,4	79,4	89,2	66,7	94,1
	Mould** <i>Alternaria alternata</i> <i>Cladosporium hebarum</i>	5,1	80,0	97,8	66,7	98,9

* The inclusions were random until 85 patients with positive skin prick tests for common silver birch and grass (timothy) were enrolled, then patients positive for birch or grass in skin prick test were chosen prior to others. This was agreed in order to finish the evaluation, however; the percent of positive skin prick test for birch and grass did not change. ** These results refer to the sum of skin prick tests positive for either one or both of the two allergens below.

The fraction of positive results for cockroach (i6), olive pollen (t9), wall pellitory (w21) with ImmunoCAP Rapid was expected to be low. This was also the case: 1,3%, 2,3 and 2,0% of the 298 results were positive. These allergens are therefore not evaluated as the statistical basis is too small.

Intra-person reading agreement: >99,9%

Inter-person reading disagreement: 14 of 1280 test readings were not in accordance with each other ~1,1%

Disagreement, capillary samples / heparin samples: 17 of 780 heparinised whole blood sample results analysed with ImmunoCAP Rapid were not in accordance with the corresponding capillary sample results ~2,2%.

Technical errors: There were technical errors in two test cartridges but both errors just occurred in one of two test windows. The fraction of technical errors was ~0,3% and less than the quality goal <2,0%

The user friendliness was evaluated by more than 10 individuals and they were in general terms pleased with the test. Some concerns were present among the evaluators regarding the interpretation of the test for low concentration of allergens, since the distinction between positive and negative responses was difficult. There was great satisfaction with the fact that the test can be performed even if the patient is on medication for rhinitis symptoms, and that it was possible to perform the test using venous heparinised whole blood after the patient left the clinic.

Overall, ImmunoCAP Rapid showed good user friendliness, and the evaluators expressed that ImmunoCAP Rapid was very easy to operate.

Conclusions

Compared to the skin prick test

The quality goal for sensitivity was >85%. The sensitivity of ImmunoCAP Rapid was expected to be low for timothy (60-70%) and even lower for Dog Dander. The found sensitivities were about 60% and 19%, respectively. All sensitivity results, including confidence intervals are lower than 85% and therefore the quality goal for sensitivity was not fulfilled.

The quality goal for specificity was >85%. This quality goal was reached for all components when compared to skin prick test.

Compared to Phadia 250

The quality goal for sensitivity was >95%. A positive result on ImmunoCAP Rapid should correspond to about 1,50 kIU/L on Phadia 250.

The found sensitivity was lower than the quality goal for all components, lowest for dog, 53,8%, and highest for common silver birch, 80,3%.

The quality goal for specificity was >95%. This quality goal was reached for dog dander and mould. For common silver birch (92,5%) and timothy (92,6%) the confidence interval of the specificity results included the 95% goal. The specificity for cat epithelium and dander (90,8), mugwort (90,6%) house dust mites (89,2%) did not fulfil the goal.

The user-friendliness was satisfying for the manual, time factors and operation facilities. The evaluators found the test easy to use. They think it is an improvement that the patients can be tested during medication for rhinitis, but it was mentioned that the reading of test results can be difficult, as it is sometimes difficult to determine whether a test is positive or negative

Technical errors: There was 0,3% technical errors. The quality goal <2,0% was fulfilled.

The complete report is found at www.skup.nu.