

Accuracy of ImmunoCAP[®] Rapid in the diagnosis of allergic sensitization in children between 1 and 14 years with recurrent wheezing: The IReNE study

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It is estimated that at least one out of three children with recurrent wheezing is atopic. Reliable diagnostic tools are needed in primary care that allow for adequate identification of these children. The purpose of this study was to assess the value of ImmunoCAP[®] Rapid (ICR) *Wheeze-Rhinitis Child* in the identification of atopy with the use of 10 selected allergens in children with recurrent episodes of wheezing. A multicenter population study is based on primary care. It included children managed consecutively at the health center, who had three or more episodes of wheezing, at least one of them in the last 12 months. Each child completed a physical examination, an epidemiological survey, one capillary blood sampling (110 µl) for ICR, and one venous blood sampling for determination of Phadiatop Infant, total IgE and 10 specific IgE measurements. The children were identified as atopic, based on their clinical signs and symptoms and at least one positive specific IgE (0.35 kU_A/l or higher), before knowing the results of ICR, Phadiatop Infant and total IgE. ICR was read by two independent observers. Six classes were evaluated, negative without any color and five positive degrees of pink-red color. Two hundred and fifteen children aged between 1 and 14 years were studied (138 boys); 50.7% were identified as atopic, 39.1% were sensitized only to inhalant allergens, 6.5% to food allergens and 5.1% to both. The predominant allergen was the dust mite (39.3%). For ICR, there were 2134 valid double observations. The Kappa index, comparing the negative results vs. any positive result, was 0.91 (95% CI: 0.88–0.94). The intraclass correlation coefficient was 0.98 (95% CI: 0.98–0.99). In the identification of a child as atopic, the positive post-test probability of ICR depended on the color degrees considered: 88.4% for any positive and 97.6% for the most intense tones. The positive post-test probability of Phadiatop Infant and total IgE was 95.6% and 68.2% respectively. ICR showed good reliability for the most prevalent allergen, the dust mite, with a sensitivity of 90.5% (95% CI: 82.1–95.8) and specificity of 88.5% (95% CI: 81.7–93.4). The analysis of the other allergens was limited by the small number of sensitized children. The analysis of receiver operating characteristic curves revealed an area under the curve of 0.84 (95% CI 0.80–0.88) for the cut-off point of specific IgE of 0.35 kU_A/l and of 0.94 (CI 0.91–0.97) for 2 kU_A/l. A greater intensity of color of the lines of ICR

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was related to higher levels of specific IgE in blood. ICR is a reliable test for the identification of atopy in children, which identifies most children as atopic, and shows a good correlation in allergen-by-allergen identification. This suggests that it should be regarded as a first-rate tool, in the primary care clinic, for the evaluation of children with recurrent wheezing.

Asthma is a highly prevalent disease in children that affects between 5% and 10% of children in Spain (1–2). The associated health costs, together with the physical, psychological, and social impact in children and their families, make this one of the most significant diseases at this age (3–5).

Identification of asthmatic children as atopic or not has important implications, not only from the viewpoint of the therapy and care to be provided, but also in terms of prognosis of the disease for remission or persistence of symptoms in adulthood.

Atopy, as well as the severity of asthma in the pediatric age group, the degree of pulmonary function involvement and the history of asthma in the parents, is identified as one of the main prognostic factors of persistence of asthma in adulthood. There are many cohort studies suggesting that allergy sensitization at low age is an important risk factor for persistence of asthma into adolescence and adulthood (6–9).

In addition to asthma, other conditions as allergic rhinitis-rhinoconjunctivitis and dermatitis/eczema are part of the spectrum of atopic diseases. The ISAAC study has shown the relationship between these conditions and reports that countries with a higher prevalence of asthma are also those with the highest prevalence of rhinitis (1).

Taking this into account, the need for easy, reliable tools which allow for identification of atopy in children with recurrent wheezing is clear. Recently, the Section on Pediatrics of the European Academy of Allergy and Clinical Immunology has published some recommendations on why, who, when and how to carry out allergy tests (10). It concludes with the need for implementing and adapting the document according to the circumstances and health organization of each country.

ImmunoCAP® Rapid *Wheeze-Rhinitis Child* is a new diagnostic test using capillary blood, designed as a point of care test for primary care, giving results within 20 min and identifying individually the presence of specific IgE to 10 prevalent allergens (8 inhalants and 2 foods). The results are read visually: negative without color and positive different degrees of pink–red.

The aim of our study was to evaluate the accuracy of ICR in the identification of atopy and allergen specificities in children with recurrent wheezing. A secondary aim was to evaluate whether or not the test can be used semi-quantitatively.

Methods

Design

A multicenter study of diagnostic tests (diagnostic accuracy), based on primary care, was developed in five primary care centers of Catalonia (Spain). The study was approved by the Scientific Committee of the Foundation Jordi Gol i Gurina, the official clinical trial assessment agency for primary care in Catalonia.

Sample size

A minimum sample of 190 patients was used for a 95% confidence interval, with a precision of 4%, estimated sensitivity and specificity of 95%, and an expected prevalence of allergic sensitization of 60%. Every center included at least 25 children.

Inclusion criteria

The study candidates were children aged between 12 months and 14 yr who regularly visited the primary care center, with a history of recurrent wheezing and with at least one episode in the 12 months prior to inclusion in the study (active disease). Having an episode at moment of inclusion was not necessary.

The ‘episode’ was defined as the clinical condition including generalized respiratory wheezing, regardless of association with cold symptoms and including bronchiolitis. A ‘child with recurrent wheezing’ was considered as a child who had at least three episodes of wheezing in his/her past medical history.

Inclusion procedure

The enrollment period encompassed the months of January, February and March 2006. Children

meeting the inclusion criteria were asked to participate in the study, consecutively as they arrived at the clinic, regardless of the reason for consultation, and up to the number of patients assigned to each center. On acceptance to participate in the study, the parents signed an informed consent.

Clinical assessment

Each child underwent a physical examination and an epidemiological survey, including parents' medical information regarding atopic diseases, the child's exposure to tobacco smoke, presence of pets at home and relevant previous diseases. Capillary blood was taken (110 µl) and used to perform ICR *Wheeze-Rhinitis Child*. Finally, a venous blood sample was performed to determine the total IgE, specific IgE and Phadiatop Infant.

ImmunoCAP[®] rapid

ImmunoCAP[®] Rapid *Wheeze-Rhinitis Child* (Phadia AB, Uppsala, Sweden) is a new, qualitative test designed to measure specific IgE antibodies in the blood of children with symptoms of asthma and rhinitis and for use in primary care (point of care test for primary care). It is a lateral flow test, performed in 20 min, that identifies allergen-by-allergen in the presence of specific IgE in whole blood.

The study device comprise two wells, one for the blood sample and the other for the developing solution, and two rectangular windows with two nitrocellulose membrane strips containing the allergen zone on which allergens have been coated, forming parallel lines (five allergens per window). Each test window has a control area (Fig. 1).

The Wheeze-Rhinitis Child profile thus includes two control areas and 10 allergens (8 inhalants and 2 foods) identifiable on an individualized basis. These are: cat (e1), birch (*Betula verrucosa*) (t3), mugwort (*Artemisia vulgaris*) (w6), timothy (*Phleum pratense*) (g6), egg white (f1), dog (e5), olive pollen (*Olea europaea*) (t9), wall pellitory (*Parietaria judaica*) (w21), house dust mite (*Dermatophagoides pteronyssinus*) (d1) and cow's milk (f2).

Any pink-red degree on a line of an allergen is a positive result and the absence of color on such line indicates a negative test result.

Training in the use of the device. Prior to the study, all readers/investigators participated in a 2 h workshop where they were instructed in the



Fig. 1. General appearance of the ImmunoCAP[™] Rapid device. The image of the device has been reproduced with authorization from Phadia.

theoretical issues of the test and real practices of performance and interpretation of ICR were carried out.

Reading the device in the study. At each site, two readers performed an independent reading, each blind to the reading of the other. The reading included a visual assessment of each line of the ICR device. This assessment was compared with a standardized scale with six possible values of the lines: 1 colorless (negative result); 2 very weak positive (very mild pink-red line, but there is a line); 3 weak positive (mild pink-red line); 4 mild positive (pink-red line less intense than the control); 5 positive (pink-red line of the same intensity as the control); 6 very positive (pink-red line more intense than the control).

The colorimetric scale was decided arbitrarily by the central study team, taking as the starting point the color tone of the control line. For this purpose, prior to the study, readings were made of the color intensity of several control lines, giving a value of 5 to the mean intensity obtained. A value of 6 was generated for color tones greater than the control and three progressive color values (2, 3 and 4) for tones between the negative and the control value.

For each child 10 double readings, allergen-by-allergen, were performed. The results of both readings were recorded. When the readings were concordant, the values obtained were established

as definitive. In the case of a discrepancy, both readers made a joint reading, establishing an agreement value for each allergen, which was used for all further analysis.

Phadiatop infant

Phadiatop Infant (ImmunoCAP® Phadiatop Infant; Phadia AB) is a diagnostic blood test designed to identify IgE sensitization to the most common allergens affecting young children (1–14 yr). This test includes inhalant and food allergens responsible for 98% of the allergic sensitization in this age group, including: hen's egg, cow's milk, peanut, shrimp, dust mite, cat, dog, birch, timothy, ragweed and wall pellitory.

Phadiatop infant is expressed as positive (0.35 kU_A/l or higher) or negative, without discriminating between sensitization to the different allergens.

IgE quantifications

Ten allergen-specific IgE determinations were performed per patient, similar to the panel of the ICR device. A child was considered as allergic-sensitized if at least one result of the specific IgE determinations was ≥ 0.35 kU_A/l. Otherwise, the child was classified as non-sensitized.

Total IgE was also determined and a value was considered as normal (negative result) if it was below the age-specific value of one standard deviation, as given in the directions for use from the manufacturer. A value equal or above the age-specific value of one standard deviation was classified as positive. The IgE measurements were carried out using the ImmunoCAP® System method (Phadia AB).

Classification of subjects

The children were divided into two groups based on the specific IgE result: sensitized; and non-sensitized. This was a classification made without the knowledge of the results of ICR, Phadiatop Infant and total IgE.

Identification of the allergic child with ImmunoCAP® Rapid

Any result between 2 and 6, as determined using the ICR system, identified the participating child as allergic. In contrast, when there were no such results the child was classified as non-allergic.

The allergen-by-allergen agreement was established when a child sensitized to a given allergen had a value of between 2 and 6 on the line of that

allergen in the ICR device or if the child was non-sensitized and the ICR value was 1.

Statistical methods

The ICR between observer agreement was evaluated using the intraclass correlation coefficient for the semi-quantitative scale and the Kappa index for the qualitative scale.

The diagnostic accuracies of ICR, the total IgE and Phadiatop infant were evaluated using, as reference standard, the assessment classifying the children as allergic or not as described above. Sensitivity, specificity, predictive values and likelihood ratios were assessed.

The behavior of the six possible ICR values using different concentrations of specific IgE (0.35, 0.7, 1, 1.5, and 2 kU_A/l), as thresholds for a patient to be classified as negative or positive, was analyzed by ROC curve (15) and the area under the curve (AUC) was evaluated.

All the data was stored in Excel (MS Office 2003 version) and the analysis was carried out using the SPSS statistical package (version 11).

Results

A total of 215 children aged 1–14 yr were included. The main epidemiologic characteristics of these children are shown in Table 1.

With the laboratory specific IgE test, 50.7% of the children were identified as allergic with IgE sensitization to at least one allergen: 39.1% only to inhalant allergens, 6.5% to food allergens and 5.1% to both.

Table 1. Characteristics of the study sample

	n	%
Children in the study	215	100
Male	138	64.2
Female	77	35.8
1–2 yr	53	24.7
3–5 yr	56	26
6–14 yr	106	49.3
Past medical history		
Eczema	103	47.9
Rhinitis	75	34.9
seasonal	40	18.6
persistent	35	16.3
Food hypersensitivity	24	11.1
History in father/mother*		
Inhalant allergen sensitization	48	22.3
Food allergen sensitization	11	5.1
Asthma	54	25.1
Rhinitis	72	33.5
Eczema	37	17.2

*Through survey.

The most prevalent allergen was dust mite (39.3%). The next in percentage of sensitization was olive (9.9%), the same percentage were sensitized to dog and timothy, cat (8.4%), milk (8%), egg white (7%), mugwort (6.6%), *Parietaria* (5.2%), and Birch (3.3%).

Agreement between readers

From the 2150 possible double readings, 10 were invalidated as the corresponding control was not colored. Also, 6 double readings were ruled out because no specific IgE was available. Therefore, 2134 double readings were analyzed.

When two events were considered (negative, value 1, and positive, values 2–6), the Kappa index was 0.91 (95% CI: 0.88–0.94). When using the same semi-quantitative scale the intraclass correlation coefficient was 0.98 (95% CI: 0.98–0.99).

Diagnostic accuracy

Results for the diagnostic accuracy of the ICR (value classes 1 vs. 2–6; 1–2 vs. 3–6 and 1–3 vs. 4–6) using the specific IgE results as reference, are given in Table 2. Also the diagnostic performance of Phadiatop infant and total IgE are given in Table 2. These results were based on 109 positive children and 106 negatives according to the specific IgE results. The distribution in the evaluation of ICR is shown in Fig. 2. In the sample, 52% of the children had at least one positive allergen in ICR, 52.8% of the children had a positive Phadiatop Infant test results and 62.7% of the children had a positive total IgE result.

In ICR, lines with a color intensity close to the control value were commonly found. Thus 76.1% of the atopic children had at least one positive line with values from 4 to 6 and 87.1% at least one line with values from 3 to 6. The positive predictive value obtained when these values were considered ranged from 88.4% to 96.9% and to 97.6% for ICR classes: 1 vs. 2–6; 1–2 vs. 3–6 and 1–3 vs. 4–6, respectively. Hence, the probability that a child with an ICR line with a value of three or higher, was atopic was 96.9%.

In Table 3 the results for the diagnostic accuracy of the ICR value classes 1 vs. 2–6 and also here using the specific IgE results as reference in the case where patients with at least one positive results were considered to have an allergic sensitization, are given for the three age groups 1–2, 3–5, and 6–14 yr of age respectively.

Allergen-specific identification

Dust mite was the most prevalent allergen in the study and ICR showed a high sensitivity and specificity. The low number of children sensitized to other allergens produced much less precise estimations of sensitivity. Furthermore, for dog, wall pellitory and mugwort the sensitivity results of the test were substantially lower than for the other allergens (Table 4).

Relationship between ImmunoCAP® Rapid test results and specific IgE levels

The ROC curves allowed for evaluating the diagnostic performance of the six possible values

Table 2. Number of children and the diagnostics performance of ImmunoCAP® Rapid, Phadiatop Infant and Total IgE together in comparison with laboratory specific IgE results

Lab. specific IgE	ImmunoCAP® Rapid						Phatiatop Infant®		Total IgE	
	ICR (2–6)*		ICR (3–6)		ICR (4–6)					
	Pos	Neg	Pos	Neg	Pos	Neg	Pos	Neg	Pos	Neg
Pos	99	10	95	14	83	26	108	1	92	17
Neg	13	93	3	103	2	104	5	100	43	63
Sensitivity	90.8 (83.9–94.9)		87.2 (79.6–92.2)		76.1 (67.3–83.2)		99.1 (95.0–99.8)		84.4 (76.4–90.0)	
Specificity	87.7 (80.1–92.7)		97.2 (92.0–99.0)		98.1 (93.4–99.5)		95.2 (89.3–97.9)		59.4 (49.9–68.3)	
P-LR	7.4 (4.4–12.4)		30.8 (10.1–94.2)		40.4 (10.2–59.9)		20.8 (8.8–49.0)		2.1 (1.6–2.7)	
N-LR	0.1 (0.1–0.2)		0.1 (0.1–0.2)		0.2 (0.2–0.3)		0.0 (0.0–0.1)		0.3 (0.2–0.4)	
PPV†,‡	88.4 (81.1–93.1)		96.9 (91.4–99.0)		97.6 (91.8–99.4)		95.6 (90.1–98.1)		68.1 (59.9–75.4)	
NPV†	90.3 (83–94.6)		88.0 (80.9–92.7)		80.0 (72.3–86.0)		99.0 (94.6–99.8)		78.8 (68.6–86.3)	

P-LR, positive likelihood ratio; N-LR, negative likelihood ratio; PPV, positive predictive value; NPV, negative predictive value. Values are expressed in % and its 95% CI.

*For ImmunoCAP® Rapid, the following three situations were evaluated: (i) ICR value 1 vs. value 2–6; (ii) ICR value 1–2 vs. value 3–6; (iii) ICR value 1–3 vs. value 4–6;

†Calculated according to the 52.5% of prevalence;

‡PPV is equal to positive post test probability.

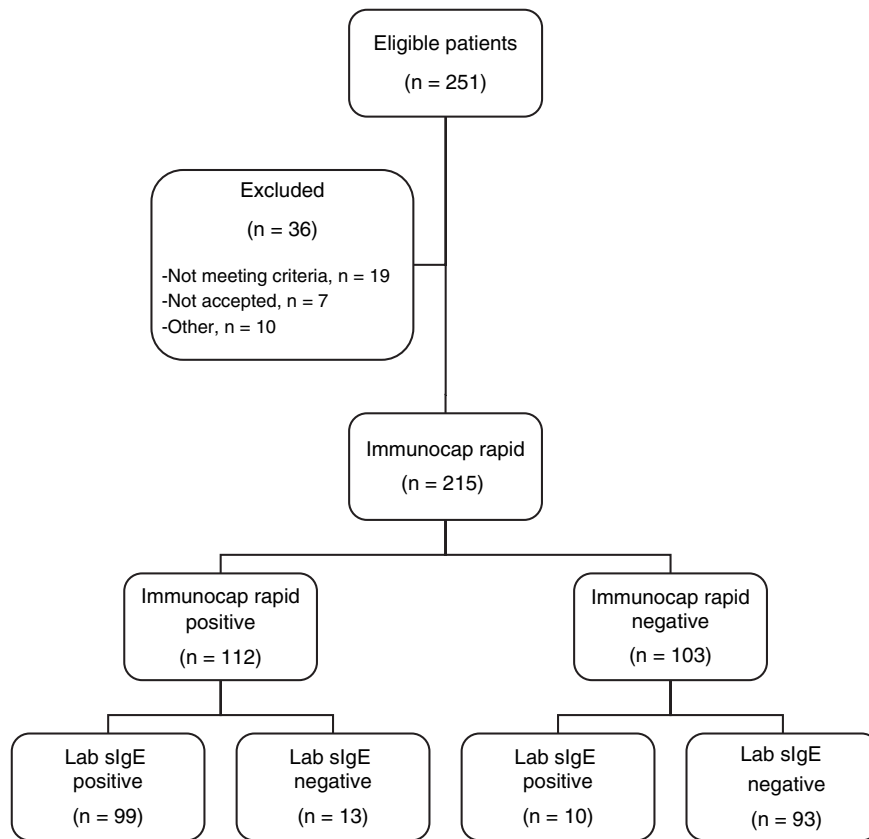


Fig. 2. Flow chart of study patients.

Table 3. Number of children and the diagnostics performance of ImmunoCAP® Rapid in three age groups in comparison with laboratory specific IgE results

Lab. specific IgE	ImmunoCAP® Rapid*					
	Age: 1–2 yr		3–5 yr		6–14 yr	
	Pos	Neg	Pos	Neg	Pos	Neg
Pos	12	2	17	5	70	3
Neg	4	35	3	31	6	27
Sensitivity†	85.7 (60.1–96.0)		77.3 (56.6–89.9)		95.9 (88.6–98.6)	
Specificity	89.7 (76.4–95.9)		91.2 (77.0–97.0)		81.8 (65.6–91.4)	
PPV	75.0 (50.5–89.8)		85.0 (64.0–94.8)		92.1 (83.8–96.3)	
NPV	94.6 (82.3–98.5)		86.1 (71.3–93.9)		90.1 (74.4–96.5)	

*For ImmunoCAP® Rapid, the following situation were evaluated: ICR value 1 vs. value 2–6.

†Values are expressed in % and its 95% CI.

of ICR according to the positiveness criterion of the specific IgE used (Fig. 3).

On the one hand, the AUC increases as the specific IgE positiveness criterion rises which involves the greater ability of ICR to detect higher blood levels of specific IgE. However, the test already provides adequate results from 0.35 kU_A/l (AUC = 0.84).

On the other hand, it is shown that value 2 of ICR (any color intensity) maximizes the diagnostic performance and generates few errors. In practical terms, any coloration of an ICR line

should be considered positive, reflecting the ability of the test to detect low specific IgE levels.

On the basis of the 2134 individual observations of the study, a relationship between higher levels of color intensity of ICR and higher levels of specific IgE have been found (Fig. 4).

Discussion

This study shows that ICR is a reliable test, which identifies most atopic children and shows a good correlation in allergen-by-allergen identifi-

Table 4. Diagnostic accuracy, allergen by allergen, of ImmunoCAP® Rapid

Allergen	Sensitivity (95% CI)	Specificity (95% CI)	Prevalence (%)
Cat	88.9 (65.3–98.6)	97.4 (94.1–99.2)	8.4
Silver birch	57.1 (18.4–90.1)	97.6 (94.4–99.2)	3.3
Mugwort	42.9 (17.7–71.1)	98.5 (95.7–99.7)	6.6
Timothy	52.4 (29.8–74.3)	99.0 (96.3–99.9)	9.9
Dog	28.6 (11.3–52.2)	97.9 (94.8–99.4)	9.9
Olive	76.2 (52.8–91.8)	98.4 (95.5–99.7)	9.9
Wall pellitory	36.4 (10.9–69.2)	97.0 (93.6–98.9)	5.2
Dust mite	90.5 (82.1–95.8)	88.5 (81.7–93.4)	39.3
White egg	66.7 (38.4–88.2)	95.5 (91.5–97.9)	7.0
Milk	58.8 (32.9–81.6)	92.3 (87.7–95.7)	8.0

cation. Determination of levels of allergen-specific IgE in serum or by skin-prick testing is a useful tool in diagnosing allergy. For example, in primary care situations the percentage of allergic patients correctly diagnosed according to medical history and physical examination is only 30–65%. With the addition of IgE antibody tests this figure increases to 85–97% (16, 17). However, today neither IgE nor skin-prick testing is used frequently in a primary care context. Often a skin-prick test has to be performed by an allergist and determination of serum IgE has to be done in a laboratory environment which is often regarded as lengthy and expensive by the primary care setting. We believe that the advent of the ICR test could help physicians to both diagnose and manage patients suffering from allergic diseases. Ease of use, rapidity and low cost contrast with the waiting time, referrals for

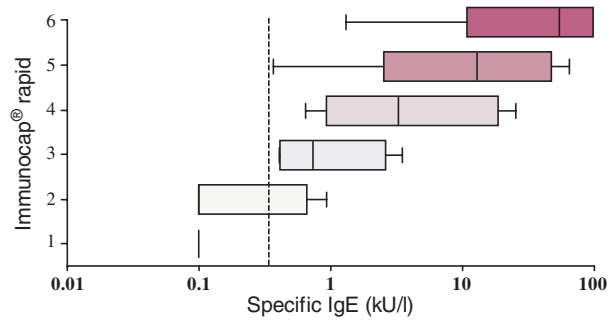
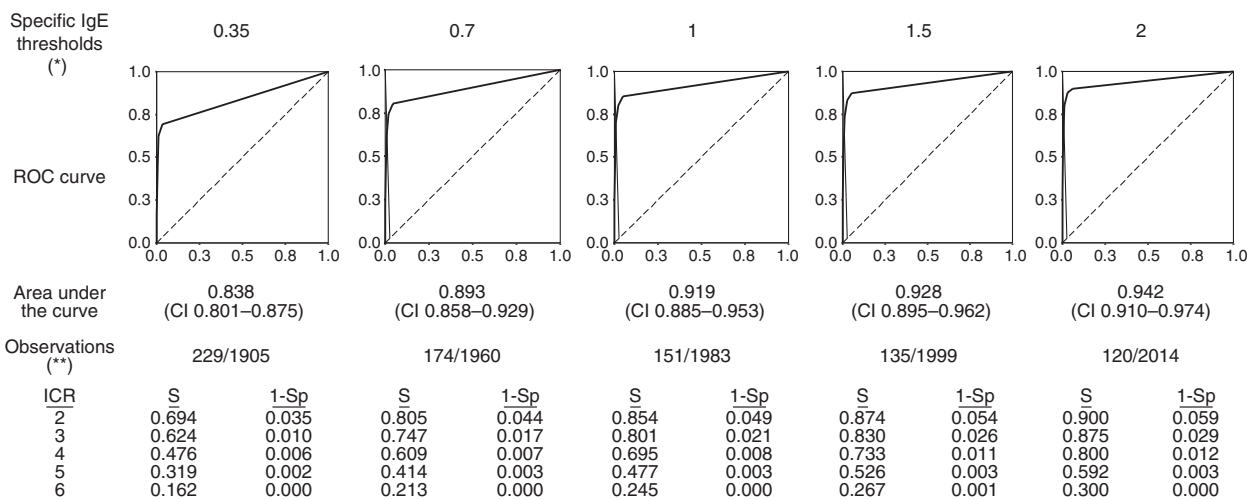


Fig. 4. Relationship between sIgE level and ICR value. The image shows the median and interquartile range. On the basis of the 2134 individual observations of the study, a relationship has been found between higher levels of color intensity in ICR and higher levels of specific IgE. Median in ICR value 2 coincides with the 25th percentile. The dotted line shows the 0.35 ku/l value.

laboratory and skin-prick tests and new appointments associated with already established methods. However, in order to become a first-choice alternative for primary care physicians, the performance of ICR must at least correspond to that of established IgE diagnostic methods.

Our findings showed that the post-test probability for ICR, when utilized as an atopy test (at least one allergen positive), was 20.3% better than the total IgE test but 7.2% poorer than Phadiatop Infant. The increased diagnostic gain for ICR shown in the 3–6 and 4–6 color intensity groups towards the level for Phadiatop Infant lowered, at the same time, the sensitivity of the



(*) kU_A/l

(**) Number of positive and negative observations determined with specific IgE

ICR: ImmunoCAP rapid value

S: Sensitivity

Sp: Specificity

Fig. 3. ROC curves of ICR for different specific IgE level.

test with 3.7% units and 14.7% units respectively, which has to be considered when using ICR as a semi-quantitative test.

The overall sensitivity and specificity (90.8% and 87.7%) obtained for ICR in this study was somewhat lower (8–9%) than for Phadiatop Infant, but higher than for total IgE. Regarding the performance of the ICR in the three different age groups it was shown that the sensitivity for the age 6–14 yr, based on 73 children, was around 19% units above the sensitivity in the age 3–5 yr (22 children), and finally 10% units above the sensitivity in the lower age group 1–2 yr (14 children). This quite large difference indicates that new studies with more children should be performed to establish whether there is an age effect on the performance of the ICR device or not. The results for specific allergen sensitivity were determined within a wide range, i.e. 28.6% for dog to 90.5% for house dust mite. Concerning the relatively low values for the allergens for dog, wall pellitory and mugwort, they would probably benefit from the manufacturer's test improvement. The results for the specificity of individual allergens were higher and less variable (88.5–99.0%). The value of the reference cut-off (same for all 10 allergens) was chosen to correspond to the established cut-offs for the reference test. To evaluate the diagnostic performance of ICR at other levels of cut-offs, visualization in non-parametric receiver operating characteristic plots showed that the AUC was increased from 83.5% to 94.2% when the cut-off level was increased from the 0.35 kU_A/l level to the 2 kU_A/l level. Thus, the detection level of ICR should be somewhat higher than that of the specific IgE test as used as a reference in the study. It has to be emphasized that the performance of the ICR was calculated on an overall level and optimal individual allergen cut-off values will be different. Consequently, as house dust mite was the most dominating allergen in the study, the performance of the ICR for this allergen dominated the overall ICR results.

In the study it was shown that the level of sensitization, i.e. the amount of specific IgE present, correlates with the color intensity in the ICR results. These results suggest that the color intensity also correlates with the degree of atopy which then can help the physician to better classify patients according to their allergic status.

The visual reading of the color scale results was performed by two independent pediatric nurses and each reading was considered subjective. In the study, the high intraclass correlation (0.98) and kappa coefficient (0.91) showed that our reading results can be reliable. These

results are also in accordance with other results based on double reading of colorimetric scale results (18).

To our knowledge there are currently no studies related to allergic tests which evaluate color scales visually compared to a gold standard. However, there are some studies performed on visual color scale tests for other applications. Metheny, for example (19), published the validation of a strip to measure bilirubin content and the pH of aspirate fluid to verify the proper position of the feeding tube in critically sick adults. For the five values on the colorimetric scale of bilirubin the agreement was 0.93 and for the dichotomic parameter yes–no the kappa coefficient was 0.86, which is somewhat lower than our results. Castellote et al. (20) analyzed the validity of the leukocyte esterase strip for the diagnosis of spontaneous bacterial peritonitis in cirrhotic patients with ascites, using a colorimetric scale from 0 to 4 and analyzing the results by taking into account stainings from 3 to 4 and from 2 to 4, the former more specific, and the latter more sensitive, in a similar way to our study. A study for the detection of free and total prostate specific antigen (PSA) using a technique similar to ICR (lateral flow based on gold-antiPSA) has shown that the color intensity of the lines was dependent on PSA concentrations, enabling a semi-quantitative assessment of results (21). On the other hand, other studies found in the literature point to difficulties in reading color scales. Some examples are the attempt to apply colorimetric analysis in the diagnosis of anemia (22), the assessment of the Doppler color to distinguish malignant pelvic tumors (23) and the identification of *Helicobacter pylori* (24).

Concluding remarks

The results from this study suggest that ICR could be useful in primary care as a tool for the firstline evaluation of children with recurrent wheezing. With reliable test results provided in less than within 20 min the selection of appropriate management strategies could be initiated. However, the allergen-by-allergen analysis was limited by the low number of children included in the study sensitized to several of the allergens, except for the house dust mite. There are probably also some weak allergens represented in ICR that would benefit from improvement, e.g. dog and wall pellitory. Therefore, to be able to show the usefulness of ICR in a general setting, further tests are needed in, for e.g. different age groups, different geographical areas,

and populations with other prevalence levels and patients with different allergy-like symptoms such as rhinitis and eczema.

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