ORIGINAL CONTRIBUTION

Numeric score and visual analog scale in assessing seasonal allergic rhinitis severity*

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SUMMARY **Background:** Allergic rhinitis (AR) is characterized by symptoms whose severity can be difficult to quantify due to the patient's subjective perception. The aim of this study was to compare two methods for assessing the severity of allergic rhinitis, a Symptomatic Global Score (SGS) and a Visual Analog Scale (VAS), respectively. Methods: A large study was carried out on more than 36,000 patients with a diagnosis of a noncomplicated and non-treated seasonal allergic rhinitis (SAR) between May and August 2004 over all the metropolitan France. For each patient, a physician had to assess the severity of the AR calculating a score corresponding to the intensity of the symptoms as felt by the patient but also using an analog scale. Results: SAR severity differed according to the used method: 18.94% of the patients were classed severe according to the SGS and 23.58% according to the VAS. Moreover, among the 35,126 people for which the two measures were available, 23.86% were classed severe according to one but not according to the other. These patients differ from those classed in the same manner by SGS and VAS in age, gender, type of doctor and geographical area. SGS and VAS correlated each other (p = 0.4895; p < 0.0001). Principal prescribed drugs for SAR were antihistamines and local steroids. Conclusion: Severity assessment varied according to the used method. Key words: allergic rhinitis, assessment, severity, Symptomatic Global Score, Visual Analog Scale

INTRODUCTION

Previously classified according to symptoms length into seasonal and perennial rhinitis, allergic rhinitis (AR), which constitutes a major risk factor for asthma development ⁽¹⁾, can also have an important impact on the quality of life, sleep ⁽²⁾ and absenteeism ^(3,4). That is why the new ARIA (Allergic Rhinitis and its Impact on Asthma) classification, takes into account symptoms length and severity but also patient's quality of life. Thus, a new distinction is made between intermittent and persistent AR and between mild and moderate/severe AR ⁽⁵⁾.

AR severity has been assessed in many ways: calculating symptom scores, measuring nasal obstruction (with peak inspiratory flow mea surements for example), assessing reactivity to nasal provocation ⁽⁶⁾. Scores offer the advantage to be computed from a standardised questionnaire.

In an epidemiological survey carried out in 2004, severity of sea-

sonal AR was assessed on more than 36,000 patients with the Symptomatic Global Score (SGS), a numeric score based on the intensity of AR symptoms as evaluated by the physician during the visit and more originally with a Visual Analog Scale (VAS) which analogically objectivises patient's perception ⁽⁷⁾. The aim of our work is to compare these two methods and to study modalities of AR management too.

MATERIALS AND METHODS

Study design

An epidemiological observatory was constituted in France with the aim to investigate the impact of airborne pollen counts on severity of seasonal AR after taking into account outdoor air pollution level. About 9,000 specialist and liberal general practitioners were enrolled throughout France. Each physician had to recruit the five first patients who came in the consultation with an established untreated and non-complicated seasonal AR. The study took place between the beginning of May and the end of August 2004, which corresponds to pollination period of grass pollen and trees in metropolitan France. The collected data, using a patient questionnaire and an investigator questionnaire filled in by the physician ⁽⁸⁾, included the date of the visit, sex, age, urban or rural localization of the place of residence, antecedents (rhinitis, conjunctivitis, asthma, atopic dermatitis, food allergy, hives) of the patients.

Measures for assessing the severity of allergic rhinitis

For each patient, the physician had to assess during the visit the presence and the intensity of AR symptoms (nasal congestion, nasal obstruction, rhinorrhea, sneezes and nasal pruritus), general symptoms (headaches, tiredness, lack of appetite and irritability), ocular symptoms (watering and pruritus) and atriolaryngeal symptoms (sore throat, cough, atriopalatin pruritus and ear aches) as well as AR impact on daily life activity and sleep. A numeric score, the Symptomatic Global Score (SGS), was then calculated according to subjects' answers to the physician's questions on four nasal symptoms (nasal obstruction, rhinorrhea, sneezes and nasal pruritus) and an ocular symptom (ocular pruritus). For each symptom, the score could take values between 0 and 4 depending on intensity felt by the patient (0 = absence, 1 = mild, 2 = moderate, 3= severe, 4 = very severe), so SGS could vary between 0 and 20. A second assessment of AR severity was defined using a Visual Analog Scale (VAS). Indeed, the physician had also to indicate AR severity through the VAS by putting a trait on a 10 cm line. At left end of the line (0 cm) severity was equal to zero and at right end (10 cm) it was maximal. Such a quantitative measure has also been used for other diseases (9,10,11) and enables to better objectivise the severity. Contrary to SGS which took into account exclusively nasal and ocular symptoms, VAS took into account also other criterions gathered during the patient's visit such as the antecedents of allergy, quality of life.

To compare individuals with a severe AR and those without, SGS and VAS were dichotomized depending on the third quartile of the total assessable population distribution. Subjects with a SGS (VAS respectively) strictly higher than the third quartile were classed as severe. A second dichotomy was realized in the same way to define patients very severe: a patient was classed as very severe according to SGS (VAS respectively) if his/her score was strictly higher than the third quartile of the SGS distribution (VAS respectively) made upon severe patients. Lastly, to study differences between SGS and VAS to define AR severity, patients were grouped together according to three groups: a group with the patients classed in the same manner by the two measures, a group with the patients classed as severe by SGS but as non severe by VAS and a last group with the patients classed as non severe by SGS and as severe by VAS.

AR management

The investigator questionnaire filled out by each physician allowed also evaluating modalities of management of patients suffering from seasonal AR and characteristics of their practice. The principal data collected concerning physicians were general data like sex, birth year, work place, number of patients seen in the clinic, percentage of children and adults seen in the clinic for seasonal AR, drugs categories as prescribed in the first and second intention, sick note or schooling prescription frequency, local data (meteorology, daily pollen counts or air pollution level), principal symptoms considered for assessing severity.

Statistical analysis

The analysis was performed with SAS version 8.2 software. Comparisons between the different groups were realized with Wilcoxon and Kruskal-Wallis tests for continuous variables because of the hypothesis of normality and/or variance equality which were not verified, and with χ^2 tests in the case of contingency tables of categorical variables. Correlation between the two measures of AR severity was also tested with a Pearson χ^2 . For each test realized, the type I error (the error of rejecting the null hypothesis when it is true) considered was 5%.

RESULTS

Total assessable population

Out of the 45,000 subjects planned at the beginning of the study, 36,397 were included because they satisfied inclusion criteria (seasonal allergic rhinitis non-complicated and untreated) and the date of their visit ranged between the May 3, 2004 and August 29, 2004. Among them, 35,426 patients had data available for the computation of a SSG value and 36,004 for a VAS value. The final number of patients, for which both a SGS and VAS were available, totalled 35,126.

Characteristics of the physicians

In this study 8,143 physicians participated. Their average age was 48.1 years old (\pm 7.68) and the proportion of women was 17.3%. In rural milieu, 21.9% practiced, 55% in urban milieu and the others were in a 'semi-urban' milieu. General practitioners represented 83.55% of the sample, otorhinolaryngologists 9.34%, pediatricians 4.39%, allergists 2.69%, psychiatrists 0.02% and lung specialists 0.01%. On average, 12.8 (\pm 10.2) patients were seen for a seasonal AR out of 124.8 (\pm 46.9) patients seen per week.

Characteristics of the patients

Among the 36,397 assessable patients, 52.5% were women. Children (between 6 and 11 years old) represented 2.41% of the consultations, adolescents (between 12 and 20 years old) 17.26%, adults (between 21 and 64 years old) 75.74% and seniors (over 65 years old) 4.59%. Of the subjects 57.4 % lived in a town. In total 93.4% reported to have suffered from rhinitis, 70.2% from conjunctivitis, 25.2% from asthma, 16% from atopic dermatitis, 7% from food allergy and 18.8% from hives.

Symptomatic global score

The mean SGS was 9.52 (\pm 3.35) in the total assessable population (Table 1) ranging to 14.40 (\pm 1.55) in severe patients to 8.37 (\pm 2.53) in non-severe patients. Its value is the same in men and women but differs significantly depending on age

Numeric score and VAS for SAR

Table 1. Severity of allergic rhinitis according to the mean SGS and the mean VAS and repartition of the subjects.

	SGS m (± SD)	p value	Severe according to	p value	VSA (mm) m (± SD)	p value	Severe according to	p value (χ^2)
	n = 35,426	(1)	SGS	(χ^2)	N = 36,004	(1)	VAS	
Assessable Patients		$9.52 (\pm 3.35)$	NA	6.712 (18.94)	NA	53.57 (± 19.19)	NA	8.490 (23.58)
NA		,()		-,, ()				-,
Sex		NS		NS		*		*
Man	9.52 (± 3.35)		3,138 (18.79)		53.75 (± 19.25)	4,123 (24.32)	
Woman	9.52 (± 3.35)		3,525 (19.15)		53.41 (± 19.14)	4,295 (22.94)	
Age (years)		***		***		***		***
6-11	9.13 (± 3.55)		136 (16.29)		49.46 (± 19.51)	158 (18.52)	
12-20	9.66 (± 3.29)		1,203 (20.04)		52.87 (± 19.20)	1,381 (22.62)	
21-64	9.57 (± 3.36)		5,107 (19.36)		54.09 (± 19.13)	6,525 (24.36)	
more than 65	8.59 (± 3.20)		178 (11.21)		50.59 (± 19.12)	293 (18.06)	
Antecedents								
Rhinitis		***		***		***		***
With	9.59 (± 3.33)		6,330 (19.42)		53.89 (± 19.13)	7,971 (24.06)	
Without	8.56 (± 3.45)		302 (13.14)		49.59 (± 19.61)	417 (17.87)	
Conjunctivitis		***		***		***		***
With	10.09 (± 3.31)	1	5,525 (23.37)		$55.43 \pm (18.89)$)	6,298 (26.25)	
Without	8.34 (± 3.06)		999 (9.92)		$50.06 \pm (19.28)$)	1,868 (18.30)	
Asthma		***		***		***		***
With	10.13 (± 3.34)	1	1,945 (23.72)		$57.93 \pm (18.87)$)	2,589 (31.13)	
Without	9.42 (± 3.31)		4,271 (17.51)		$52.64 \pm (19.05)$)	5,295 (21.42)	
Atopic dermatitis		***		***		***		***
With	10.08 (± 3.35)	1	1,173 (22.89)		$55.87 \pm (18.86)$)	1,384 (26.64)	
Without	9.51 (± 3.33)		4,943 (18.39)		$53.54 \pm (19.19)$)	6,305 (23.16)	
Food allergy		***		***		***		***
With	10.07 (± 3.38)	1	502 (22.65)		$56.69 \pm (18.69)$)	611 (27.21)	
Without	9.56 (± 3.33)		5,540 (18.80)		$53.70 \pm (19.20)$)	7,012 (23.50)	
Hives		***		***		***		***
With	10.02 (± 3.31)	1	1,355 (22.50)		$56.47 \pm (18.71)$)	1,652 (27.02)	
Without	9.50 (± 3.33)		4,758 (18.30)		53.32 ± (19.22)	6,045 (22.96)	
Localization		***		NS		**		*
Rural	9.59 (± 3.37)		2,859 (19.42)		$53.94 \pm (19.16)$)	3,626 (24.22)	
Urban	9.47 (± 3.34)		3,692 (18.62)		53.28 ± (19.19)	4,646 (23.08)	
Geographical region		***		***		***		*
Southwest	9.58 (± 3.35)		997 (19.41)		$54.12 \pm (18.86)$)	1,261(24.10)	
Southeast	9.69 (± 3.33)		1,427(20.49)		$54.26 \pm (19.25)$)	1,736(24.62)	
Northwest	9.41 (± 3.36)		838(18.16)		$53.15 \pm (19.09)$)	1,068(22.75)	
West	9.30 (± 3.35)		717(17.07)		$53.13 \pm (18.79)$)	953(22.34)	
East	9.72 (± 3.31)		852(20.27)		$53.61 \pm (19.68)$)	1,036(24.24)	
Centre	9.56 (± 3.30)		457(18.85)		$54.33 \pm (18.82)$)	605(24.55)	
Ile de France	9.40 (± 3.40)		1,155(18.17)		53.06 ± (19.52)	1,494(23.12)	

SGS: Symptomatic Global Score VAS: Visual Analog Scale

m: mean SD: Standard Deviation n: number of patients

(1) Wilcoxon-Mann-Whitney and Kruskall-Wallis tests NA: Not applicable NS: Non-significant *: p < 0.05 **: p < 0.01 ***: $p < 0.00_1$

(p < 0.0001). It was 9.13 (± 3.55) in children, 9.66 (± 3.29) in adolescents, 9.57 (± 3.36) in adults and 8.59 (± 3.20) in seniors. The mean SGS differs also depending on localization (urban or rural), geographical areas and presence or not of antecedents in patients.

According to the SGS, 6,712 (18.94%) subjects of the assessable patients were classed severe. Based on χ^2 test, the percentage of subjects with a severe AR did not differ significantly depending on sex and localization but differs significantly according to age, presence or not of antecedents and region (p < 0.0001).

The number of patients with a very severe AR is 1,381, i.e., 20.6% of the severe patients.

Visual Analog Scale

The mean VAS was 53.57 (\pm 19.19) mm for all assessable patients (Table 1). In severe patients 77.61 (\pm 7.17) and 46.14 (\pm 15.25) in non-severe patients. Of the assessable patients 23.58% were classed severe according to the VAS.

Contrary to the SGS, the repartition according to the VAS between patients with severe AR and those without differed significantly depending on sex (p = 0.0022) and localization

Table 2. Severity of allergic rhinitis: frequency of the severe patients according to the SGS and the VAS (n = 35,126).

Frequency						
% total		Severity accord	Total			
% line		Severe	Non severe			
% column		(VAS > 68)	$(VAS \le 68)$			
Severity	Severe	3,283	3,367	6,650		
according	(SGS > 12)	9.35	9.59	18.93		
to the SGS		49.37	50.63			
		39.58	12.55			
	Non severe	5,012	23,464	2,8476		
	(SGS≤12)	14.27	66.80	81.07		
		17.60	82.40			
		60.42	87.45			
Total		8,295	26,831	35,126		
		23.61	76.39	100		

Table 3. Description of the VAS according to the SGS ($n = 35, 126$).
Visual Analog Scale ($0 = non$ severe, $100 = very$ severe)

			U	· ·	· · · ·	•
Symptomatic						
Global Score						
(0-20)	n	Mean	SD	Median	Min	Max
0	40	31.05	21.73	29.50	0.00	82.00
1	113	29.14	18.53	26.00	0.00	84.00
2	320	31.97	19.70	27.00	1.00	95.00
3	682	35.61	18.83	32.00	0.00	95.00
4	1166	36.69	17.87	34.00	1.00	97.00
5	1735	40.90	17.85	38.00	0.00	97.00
6	2518	43.79	17.83	43.00	0.00	95.00
7	3207	46.59	17.60	46.00	0.00	100.00
8	3842	49.23	17.17	49.00	1.00	100.00
9	4156	52.23	17.16	53.00	0.00	100.00
10	4054	55.17	16.36	57.00	2.00	100.00
11	3519	57.95	16.33	60.00	0.00	100.00
12	3124	60.95	16.18	63.00	3.00	100.00
13	2462	63.41	15.26	65.00	8.00	100.00
14	1704	66.22	15.18	67.00	1.00	100.00
15	1121	69.36	14.45	70.00	13.00	100.00
16	656	70.37	14.89	71.00	4.00	100.00
17	349	73.20	14.35	74.00	3.00	100.00
18	202	75.44	14.55	76.00	10.00	100.00
19	101	79.41	13.23	80.00	39.00	100.00
20	55	79.56	11.56	80.00	52.00	100.00
N: number of patients		SD: Sta	SD: Standard Deviation			

Min: Minimum

Max: Maximum

(p = 0.0133) as well as age, antecedents and region. In total 1,976 subjects, i.e. 23.3% of the severe patients, were classed very severe with the VAS.

Relation between SGS and VAS

The proportion of subjects classed severe was not the same depending on the method of severity assessment used. Indeed, only 18.94% of the patients were classed severe according to SGS against 23.58% according to VAS. Among the 35,126 patients for whom the two measures were available, only 9.35% were simultaneously

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classed severe according to SGS and VAS while 23.86% were classed severe according to one but not according to the other (Table 2). Although there was a large values' dispersion of the VAS for each value of the SGS (Table 3), results show a VAS trend to increase when the value of the SGS rises (Figure 1). Calculation of the Pearson's correlation coefficient between the two measures of the severity of the seasonal AR made on 35,126 subjects produced a result equal to 0.4895. This positive correlation confirms that the VAS increases (assessment more and more severe) when the SGS rises.

Characteristics of the patients whose severity differs according to the measure used

Of the assessable population, 9.35% was simultaneously classed severe according to SGS and VAS while 23.86% was classed severe according to one but not according to the other. More in detail, there was 9.59% of the patients who were classed severe according to the SGS and non-severe according to the VAS and 14.27% who were classed non-severe according to the SGS but severe according to the VAS. Observation of the patients for whom SGS and VAS gave a different result concerning severity, shows that they contrasted on several points. Indeed, the group of the patients severe according to the SGS and non-severe according to VAS differed significantly from the group of the patients classed in the same way by the two measures in the repartition between the age groups (more adolescents, fewer seniors), the geographical areas (more subjects who come from South, fewer patients from Ile de France) and the type of physician (fewer general practitioners and more allergists consulted) (Table 4).

Compared to patients classed in the same way by SGS and VAS, patients who were severe according to the VAS but non-severe according to the SGS were characterized by a significant difference in the repartition of age (more adults, fewer adolescents), sex (more men) and the type of physician consulted (more general practitioners) (Table 4).



Figure 1. Mean VAS according to the SGS (n = 35,126).

Numeric score and VAS for SAR

Table 4. Repartition of the individuals depending on the SGS and the VAS results (n = 35,126).								
	Group 1: patients classed	Group 2: patients classed	Group 3: patients classed	р	р			
	in the same way by	severe by the SGS and non	non severe by the SGS	Value (1)	Value (1)			
	the SGS and the VAS (%)	severe by the VAS (%)	and severe by the VAS (%)	(group 2 vs.	(group 3 vs.			
	(n = 26,747)	(n = 3,367)	(n = 5,012)	group 1)	group 1)			
Sex				NS	**			
Man	47.35	46.38	49.73					
Woman	52.65	53.62	50.27					
Age (years)				***	***			
Children (6 - 11)	2.56	2.11	1.83					
Adolescents (12 - 20)	17.34	18.89	15.67					
Adults (21 - 64)	75.32	75.87	78.22					
Seniors (more than 65)	4.78	3.13	4.28					
Geographical areas				*	NS			
Southwest	14.89	16.24	15.76					
Southeast	20.28	22.16	21.00					
Northwest	13.81	12.84	13.11					
West	12.48	11.88	12.38					
East	12.45	12.69	11.92					
Centre	7.20	6.64	7.39					
Ile de France	18.89	17.55	18.44					
Physician				***	***			
Allergist	2.49	4.58	2.47					
General practitioner	83.72	81.93	85.75					
Otorhinolaryngologist	9.37	9.66	8.37					
Other specialties	4.42	3.83	3.41					
(pediatrician, psychiatrist								
and lung specialist)								

SGS: Symptomatic Global Score

VAS: Visual Analog Scale

(1) χ^2 tests NS: Non-significant *: p < 0.05 **: p < 0.01 ***: p < 0.001

Modalities of AR management

In first intention, 93% of the physicians very often prescribed antihistamines, 31.2% local steroids and 7.9% local decongestants. The average proportion of the patients for whose absenteeism (at work or school) was prescribed by the doctor was 5.6% (\pm 7.7). As a mean, the patients were absent 3.1 days (\pm 2.6).

Factors that physicians took into account for the therapeutic management of patients with seasonal AR very often or often include airborne pollen counts (42.6%), weather forecast (38.0%) and air pollution level (28.0%). Like in another study carried out with general practitioners in France (12), the symptoms retained and quoted at first by physicians to assess clinical severity of AR were the nasal obstruction (37.3%) and nasal congestion (33.7%). The symptoms quoted successively were the rhinorrhea (28%) and sneezes (29.8%) followed by ocular pruritus (34.8%). Impact on activity, quoted by 3,403 doctors, was the most important symptom for 1,005 of them, i.e. 29.5%. Among the 8,143 physicians participating in the study, 20.4% declared to use the national or international recommendations for seasonal AR management.

DISCUSSION

To assess severity of allergic rhinitis (AR), ARIA advises to take into account severity of the symptoms as well as its impact on quality of life. However, severity of AR can be difficult to be classified as shown by our findings drawn from a large sample of over 35,000 patients in which severity of seasonal AR was measured with a numeric score (SGS) concerning the intensity of nasal and ocular symptoms and with a visual analog scale (VAS) and according to which the prevalence of severe rhinitis was more elevated when using the visual analog scale.

Our data indicate that although severity of AR is certainly characterized by symptoms, the subjective perception of the patient as well as additional criteria among which co-morbidity with other allergic diseases might be also of relevance. VAS has already been used $^{\left(7,13,14\right) }$ but has been compared directly to the more classical severity score based on symptoms only once ⁽¹³⁾ and this with the aim of separating the patients without improvement from those with improvement after treatment. However, in one study ⁽¹⁴⁾, the use of VAS for assessing the nasal obstruction appeared clinically relevant once compared to rhinomanometry.

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Other studies as ours were interested in severity of AR in France, but none concerned a similar number of subjects. Thus in the French survey INSTANT ⁽¹⁵⁾, among the 601 patients suffering from an AR, 44 % of them suffered from a moderate to severe persistent AR, 6% a mild persistent AR, 43.5% a moderate to severe intermittent AR and at last 6.5% a mild intermittent AR. In the French study DREAMS ⁽¹⁶⁾, among the 591 patients, 10% of the subjects suffered from a moderate to severe intermittent AR, 17% from a moderate to severe intermittent AR and 59% from a moderate to severe persistent AR. All these investigations have taken into account only symptoms to define the severity of the condition. Our study having used also a visual analog scale underlines a difference between the tools that need to be clarified.

In our study, the percentage of patients classed severe differed significantly depending on age, geographical area and presence of antecedents for the two measures, and according to the employed method. It was equal to 18.94% for the SGS and to 23.58% for VAS. Furthermore, only 9.35% of the assessable population was simultaneous classed severe according to the SGS and the VAS. Of the subjects 9.59% were classed severe according to the SGS and non-severe according to VAS and 14.27% were classed severe according to VAS and non-severe according to the SGS. The study of the patients whose severity differed depending on the assessment method shows that their repartition varied significantly according to age, sex, type of physician consulted and geographical area.

However, our study shows that the two measures were positively correlated with each other even if the correlation coefficient between the SGS and the VAS was only equal to 0.4895. Moreover, there was a very large dispersion of the VAS for each value of the SGS. Correlations of the same order were identified by precedent studies ^(7,13), between the VAS and a score obtained from a questionnaire on the quality of life during a rhino-conjunctivitis episode ($\rho = 0.46$) and between the VAS and a symptoms score of the rhinitis ($\rho = 0.45$).

Although the SGS, which uses clinical criterions, gets closer to ARIA's recommendations concerning the severity assessment of AR, the VAS, which does not require calculations, could better represent severity of rhinitis through a better translation of the patients' perception and quality of life ⁽⁹⁻¹¹⁾, as well as of other criteria. It is also more rapid and easy to use for physicians and patients. In addition, it is important to note that the SGS does not take into account the systemic symptoms (headaches, tiredness, irritability), the atriolaryngeal symptoms as well as, contrary to what ARIA recommends, the impact on the quality of life of the patients which can be associated to rhinitis.

Such as in other surveys ^(12,17,18) and as expected, the study presented here shows that the drugs which are the most prescribed in first intention by physicians during a SAR episode are anti-histamines and local steroids. However, even though the SAR management is similar to the one of the ERASM survey ⁽¹⁸⁾, where oral antihistamines were prescribed for 92.4% and local steroids for 45.2% of the patients, it strongly differs from the results of the practices and uses of nasally corticotherapy $^{(12)}$ in which the proportion is equal to 44.7% for antihistamines and 58.8 % for local steroids.

Two strong points of our study are worth being underlined: the important size of the sample both in terms of patients and physicians, and the diagnostic confirmation of the allergic rhinitis by a doctor, which is rare in observational studies. The large geographical coverage was also noticeable.

In conclusion, our data show important variations in the determination of the severity of allergic rhinitis according to the assessments used. VAS seems to be rewarding compared to the measure based only on objective symptoms. SGS seems to under-estimate severity of AR compared to VAS, probably because the latter incorporates various dimensions of the conditions. Recognition of a patient's subjective perception, taking of clinical factors related to allergic rhinitis with the quality of life seem all important criteria in AR severity assessments. Other investigations are required to support our results.

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AUTHORSHIP CONTRIBUTION

AD, PD, RJ, JMK and IAM initiated the study and contributed to the design of the study. IAM was responsible for data collection. SR and IAM were responsible for data management and statistical analysis, planned the data and wrote the paper. SR, AD, PD, RJ, JMK and IAM contributed to interpretation of findings. All authors provided critical comments to the paper and gave final approval of the version to be published.

CONFLICT OF INTEREST

AD declares to have received fees in 2009 for scientific advice and symposiums participation from the following pharmaceutical companies: AstraZeneca, GSK, Shering-Plough, MSD, Stallergènes, ALK and Novartis. The others declare no conflict of interest.

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