



Letter

Persistent specific nasal reactivity to occupational allergens after removal from exposure

The outcome of occupational rhinitis (OR) confirmed by specific inhalation challenge (SIC) after removal from exposure is unknown. Paralleling occupational asthma (OA), it is plausible that some subjects continue manifesting rhinitis symptoms despite removal from exposure whereas others may become asymptomatic.¹ Besides, whether loss of specific nasal reactivity occurs with time after cessation of exposure is unknown. Presumably, further occupational exposure in sensitized subjects may exacerbate rhinitis symptoms.

SIC is regarded as the gold standard for confirming the diagnosis of OR. However, there is some concern about its value as diagnostic tool because the methodology to assess nasal responses during challenge lacks standardization.² In this clinical case series, we assessed the persistence of specific nasal reactivity after removal from exposure as well as the ability of SIC to reproduce nasal responses over time by examining the nasal congestive response to SIC on 2 occasions, namely, at the time of diagnosis and after a mean follow-up of 28 months. The study group consisted of 5 patients (4 males) with a confirmed diagnosis of allergic OR, aged 36 to 58 years at follow-up investigation. All subjects were nonsmokers or ex-smokers. All were atopic, defined as at least 1 positive reaction to common inhalants as well as a positive reaction to the agent causing OR. After initial diagnosis, all subjects stopped exposure to causal agents because most of them (4 subjects) had associated OA, and 1 subject retired from working. Informed consent was obtained from all subjects.

On both occasions, subjects underwent standardized SIC as previously described with control and specific agents on consecutive days.³ The first day they were exposed to a sham substance (lactose) and the next day to flour (4 patients) and to tea (1 patient) by recreating working conditions in an isolated exposure chamber according to international recommendations.⁴ The total exposure time was 30 minutes on both days. Total nasal volume and nasal symptoms were measured before and serially for 6 hours after exposure by acoustic rhinometry and a visual analog scale, respectively. Nasal response was recorded as the greatest decrease in total nasal volume between 2 and 5 cm into the nose (Vol_{2-5}) (eMethods). It was expressed as a percentage of the baseline Vol_{2-5} (nasal response = fall in Vol_{2-5} /baseline Vol_{2-5} × 100). For the interpretation of SIC results, a decrease in Vol_{2-5} of 30% or more from baseline values represented a clinically significant nasal congestive response.^{3,5}

At follow-up, subjects reported significant improvement of rhinitis symptoms, and they were not taking medications for nasal symptoms. As shown in eTable 1, prechallenge values of Vol_{2-5} were lower at follow-up compared with those at diagnosis in all subjects. On both occasions, the challenge with the control agent did not induce nasal symptoms or clinically significant changes in Vol_{2-5} in all subjects (Fig 1A). By contrast, the challenge with the causal agent induced clinically significant changes in nasal volume in both occasions manifested by a percentage fall in Vol_{2-5} from baseline values of at least 30% in all subjects (Fig 1B and eTable 1). For the whole group, the average maximum percent (standard deviation) decrease in Vol_{2-5} from baseline values at diagnosis and follow-up was –42% (13%) and –38% (11%), respectively. Individual results are shown in Figure 1B.

At diagnosis, all subjects experienced isolated immediate rhinitis reactions after challenge. At follow-up, 3 subjects experienced immediate reactions, and 2 showed isolated late reactions (eTable 1).

Reduction or avoidance of exposure to occupational allergens remains a key objective in the management of OR.² The outcome of OR after removal from exposure has not been specifically investigated. There is some evidence from follow-up studies involving OA patients with associated work-related rhinitis symptoms showing that the severity of rhinitis symptoms improves after reduction of exposure to platinum salts⁶ and latex.⁷ However, to our knowledge, no study has been conducted examining the outcome of specific nasal reactivity to occupational allergens after removal from exposure. This study showed persistence of specific nasal reactivity 2 years or more after removal from exposure in 5 patients with allergic OR. The study also showed that the SIC method with occupational allergens repeated over time is reproducible in sensitized OR patients.

Similar studies have not been conducted to make comparisons. However, a comparable study conducted in our hospital assessing the outcome of specific bronchial reactivity to high-molecular-weight agents in OA patients showed persistence of specific bronchial reactivity (estimated as the duration of exposure that induced a 20% decrease in forced expiratory volume in 1 second) to these agents in most but not all subjects.⁸ In our study, we observed persistence of specific nasal reactivity several years after removal from exposure in all subjects. However, because of the small numbers of patients, we cannot speculate about potential differential physiologic responses between the upper and lower airways. Likely the SIC investigation of larger number of patients with OR may identify cases without persistence of specific nasal reactivity.

We believe that the observed results during both visits are accurate. The ability to accurately reproduce the challenge exposure conditions on both occasions was a key feature to achieve the

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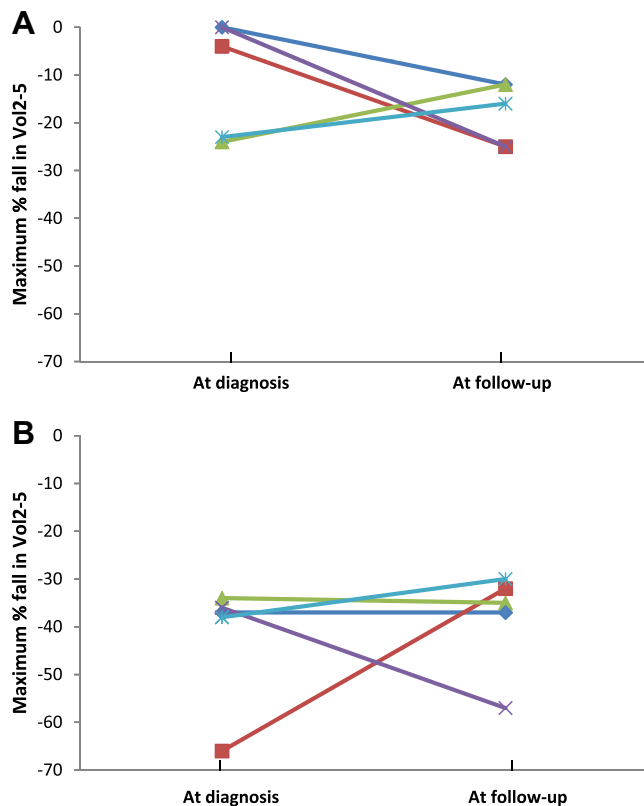


Figure 1. Individual data showing the maximum percentage fall in Vol_{2.5} from baseline values after challenge with the control (A) and the specific causal agent (B) at the time of diagnosis and at follow-up visit.

objectives of the study. The SIC method has been proposed as the gold standard tool to investigate occupational respiratory diseases^{2,9,10} because it reproduces working exposure conditions and besides, the means to assess the nasal congestive response during SIC including acoustic rhinometry have recognized validity and reproducibility. However, no study has assessed its utility to reproduce the nasal response to an occupational allergen in the long term. Based on our results, we believe that it can be further recommended as a useful tool to investigate the causes of OR. Finally, this study highlights the importance of recommending reduction or avoidance of exposure to subjects with OR attributable

to high-molecular-weight agents even if they no longer complain of symptoms. Also, larger studies are necessary to confirm our observations as well as to assess the outcome of specific nasal reactivity among subjects with nonallergic OR.

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Supplementary Data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.anai.2013.04.007>

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eMethods

SIC procedures

The suspected offending agent was identified from a detailed occupational history, a review of the material safety data sheets, and the results of specific skin prick tests. Specific inhalation challenges were carried out in challenge rooms equipped with an exhaust ventilation system and a small fan to ensure air mixing. The challenge exposure to the control and active agents was produced by tipping the agent from 1 tray to another (“realistic way”). The monitoring by acoustic rhinometry consisted of

a prechallenge assessment and 9 subsequent postchallenge assessments. On arrival of the subject (at 7:30 AM), a baseline assessment was done after a 20-minute resting period. Then the subject was challenged with the control or causal agent, and after the total exposure time (30 minutes), nasal measurements were performed at 15, 30, and 60 minutes and then each hour for the subsequent 6 hours. Subjective monitoring of nasal responses was performed by recording clinical symptoms (nasal congestion, rhinorrhea, itching) on a 100-mm-length visual analog scale. These recordings were obtained before each acoustic rhinometry measurement.

eTable 1

Changes in total nasal volume (Vol₂₋₅) from baseline values after challenge with the active agent causing OR

No	First SIC (at Diagnosis)				Second SIC (at Follow-up)				
	Vol ₂₋₅ (cc) Baseline	Vol ₂₋₅ (cc) Maximum Fall	Vol ₂₋₅ % Fall from Baseline	Time of Maximum Fall (min)	Vol ₂₋₅ (cc) Baseline	Vol ₂₋₅ (cc) Maximum Fall	Vol ₂₋₅ % Fall from Baseline	Time of Maximum Fall (min)	Time between SICs (months)
1	2.89	1.81	37	60	1.19	0.74	37	30	30
2	4.07	1.36	66	30	3.11	2.13	32	300	48
3	3.82	2.51	34	120	2.71	1.76	35	30	30
4	4.76	3.03	36	30	3.31	1.42	57	15	30
5	3.88	2.40	38	60	2.59	1.81	30	180	2