

An Effective Strategy for Diagnosing Occupational Asthma

Use of Induced Sputum

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Monitoring airway inflammation by means of induced sputum cell counts seems to improve the management of asthma. We sought to assess whether such monitoring at the end of periods at and away from work combined with the monitoring of PEF could improve the diagnosis of occupational asthma. We enrolled subjects suspected of having occupational asthma. Serial monitoring of PEF was performed during 2 weeks at and away from work. At the end of each period, induced sputum was collected. Specific inhalation challenge was subsequently performed. PEF graphs were interpreted visually by five independent observers. Forty-nine subjects, including 23 with positive specific inhalation challenge, completed the study. The addition of sputum cell counts to the monitoring of PEF increased the specificity of this test, respectively, by 18 (range [r] 13.7–25.5) or 26.8% (r 24.8–30.4) depending if an increase of sputum eosinophils greater than 1 or 2% when at work was considered as significant. The sensitivity increased by 8.2% (r 4.1–13.4) or decreased by 12.3% (r 3.1–24.1) depending on the cutoff value in sputum eosinophils chosen (greater than 1 or 2%, respectively). The addition of sputum cell counts to PEF monitoring is useful to improve the diagnosis of occupational asthma.

Keywords: eosinophils; induced sputum; occupational asthma; peak expiratory flow; specific inhalation challenge

Occupational asthma (OA) is defined as “a disease characterized by variable airflow limitation and/or airway hyperresponsiveness due to causes and conditions attributable to a particular occupational environment and not to stimuli encountered outside the workplace” (1). It is often difficult to distinguish it from preexisting asthma worsened by the workplace. The diagnosis of OA can be difficult to confirm objectively. The current gold-standard method is to perform a specific inhalation challenge (SIC) (2) with the suspected agent, but this test is expensive and time consuming, and it is available in only a few specialized centers worldwide. The alternative method is by serial PEF monitoring during periods at work and away from work (2–4). Unfortunately, PEF can be difficult to interpret, does not have optimal sensitivity and specificity, and has a number of pitfalls, such as low compliance, potential falsification of results, and underestimation of changes in airway caliber (5). The addition of serial measures of airway responsiveness to methacholine or histamine has also been advocated to document work-related changes (6).

The introduction of another measurement to the monitoring of PEF might improve the diagnostic validity. One such measurement is that of induced sputum cell counts (7). These have shown that sputum eosinophils increase during periods at work and resolve after periods away from work only in subjects with OA (8). Sputum eosinophils have also been shown to increase after positive SICs (9, 10). Therefore, we hypothesize that the analysis of induced sputum cell counts may facilitate the investigation of OA. We undertook a multicenter prospective study to assess whether adding sputum cell counts at the end of periods at work and away from work to serial monitoring of PEF and airway responsiveness could improve the diagnostic validity of OA.

Some of the results of this study have previously been reported in the form of abstracts (11, 12).

METHODS

The methods and analysis of the data are described in further detail in the online supplement.

Subjects

The study included subjects older than 18 years who had been referred to four Canadian OA reference centers for possible OA.

Concurrent treatment with inhaled corticosteroids (ICS) and long-acting β_2 -agonists was kept the same during the investigation, but long-acting β_2 -agonists were stopped 72 hours before methacholine challenge and SIC. Short-acting inhaled β_2 -agonist was used only when needed. Subjects exposed to seasonal common inhalants to which they were sensitized during the study period, and subjects who had experienced an upper or lower respiratory infection within the 4 weeks before the first visit were not enrolled.

The study was approved by the research ethics committee of each participating center. All subjects gave their written consent.

Study Design

The study was of prospective crossover design with periods of 2 weeks at work and 2 weeks away from work. The subjects were seen within 48 hours after the end of each period or whenever there was an exacerbation of symptoms. On the first occasion, subjects' characteristics were documented. On all occasions, respiratory symptoms were scored according to a Borg scale from 0 (no symptoms) to 10 (worst symptoms ever) (13). Daily use of short-acting β_2 -agonists were also recorded, and spirometry, methacholine challenge, and sputum induction were performed. PEF was monitored serially during a 2-week period at work and a 2-week period away from work. SIC in the laboratory or at the workplace was subsequently performed to confirm the diagnosis of OA, and was considered the gold standard for the diagnosis.

Procedures

Spirometry was performed according to American Thoracic Society standards (14). Methacholine challenge tests were performed as previously described (15). In our center, a change in the concentration of methacholine provoking a 20% decrease in FEV₁ (PC₂₀) between two values is considered as significant when there is at least a 3.2-fold difference between the measurements. This corresponds to the limit of reproducibility of the test in our laboratory (16). However, the experts

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who interpreted the methacholine challenge tests did not receive any specific guidance for the interpretation of changes in PC₂₀, but, instead, were asked to reproduce the protocol used in their clinical practice, where they may not necessarily follow rigid rules. Sputum was induced using inhalations of increasing concentrations (3, 4 and 5%) of hypertonic saline (17), selected from the expectorate, and processed and examined for non-squamous cell counts, as previously described. (7). The changes in sputum eosinophil counts between periods at and away from work achieving the best sensitivity and specificity compared with SIC were first identified by using a receiver operating characteristic curve. There is a high repeatability between sputum eosinophil counts performed on two occasions in subjects with asthma; (intraclass correlation coefficients from 0.85 [18] to 0.94 [7]) have been reported. Furthermore, in a previous study in which we studied subjects with asthma without OA in stable conditions on two separate occasions before and after exposure to occupational agents (19), the median change in sputum eosinophils was 0.15% (interquartile range 1.7). In that same study, a change in sputum eosinophils greater than 2% was associated with a positive SIC. Therefore, although no specific cutoff value has been defined to consider a change in sputum eosinophil count as being clinically significant, a change greater than 2% in sputum eosinophils is likely to exceed the spontaneous variability of the test in subjects with asthma. We considered the sensitivity and specificity of various changes in sputum eosinophil counts within subjects between periods at work and away from work. Skin-prick tests were performed with 12 common inhalants (20). A subject was considered to be atopic if at least one test was positive. SICs were performed as previously described (21).

PEF Monitoring

The subjects were asked to blow into a Mini-Wright peak flow meter (Clement Clarke Intl., Harlow, UK), and to record the values in a diary (22). PEF graphs were drawn and interpreted using direct visual analysis by five observers in a double-blind fashion as previously described (3). The observers did not receive any guidance to interpret PEF graphs. They were asked to interpret the graphs as they would do it in their clinical practice. We also employed a computerized approach, using the software Oasys-2 (<http://www.occupationalasthma.com>) to analyze PEF monitoring (23). PEF monitoring was considered to be suggestive of OA if the score produced by applying Oasys-2 to PEF was greater or equal to 2.51, as previously suggested (23).

Data Analysis

The paired *t* test and Wilcoxon rank test were used to compare the changes between periods at work and away from work in normally and nonnormally distributed data.

Randomized PEF graphs both including and excluding PC₂₀ values after periods at and away from work were analyzed visually by five independent experts blinded to the results of the SIC. They estimated the probability of OA for each subject by indicating yes, no, or doubtful. Sensitivity and specificity were assessed for changes in sputum eosinophil counts, interpretation of PEF graphs, and a combination of both.

RESULTS

We assessed 94 subjects who had been referred for possible OA and were potentially eligible for the study. Forty-five subjects were excluded because of nonproduction of sputum (*n* = 7), inability to complete 1 of 2 periods off work and away from work (*n* = 18), inability to perform SIC (*n* = 9), occurrence of an exacerbation of their asthma related to other allergenic exposure or change in the asthma medication during the investigation (*n* = 7), or protocol violation (*n* = 4). Forty-nine subjects completed the study (Table 1); however, one of them did not produce an adequate sputum sample and three subjects did not have interpretable PEF.

We did not find any significant differences between the baseline characteristics of the subjects included and excluded from the study in terms of age (*p* = 0.9), sex (*p* = 0.6), atopic status (*p* = 0.5), smoking habits (*p* = 0.3), type of agents to which they were exposed (high molecular weight agents versus low

molecular weight agents) (*p* = 0.2), total duration of exposure to the occupational agent (*p* = 0.9), medication (*p* = 0.1), and FEV₁ when away from work (*p* = 0.6). However, the subjects who did not complete the investigation showed a higher PC₂₀ when away from work (11.2 [95% confidence interval {CI}: 4.8–25.7] mg/ml) than did the subjects who completed the study (4.25 [CI: 2.5–7.2] mg/ml) (*p* = 0.05). The characteristics of the subjects included and excluded could not be compared when at work due to the numerous missing variables in the group who did not complete the investigation.

Forty-five subjects completed all the steps of the study. Twenty-three had a positive inhalation challenge. Immediate (*n* = 13), late (*n* = 8), dual (*n* = 1), and immediate prolonged (*n* = 1) asthmatic reactions were encountered. Twenty-six patients had a negative SIC. There were no differences in the baseline characteristics between the two groups or in the type of sensitizers to which the subjects were exposed.

Comparison of the Clinical and Functional Changes between Periods at Work and away from Work between Subjects with Positive and Negative SICs

There was a similar and significant decrease in the symptom score and in the use of short-acting β_2 -agonists during periods away from work compared with periods at work in both groups (Table 2). There was a similar slight but significant improvement in FEV₁ and PC₂₀ during periods away from work compared with periods at work in both groups.

Comparison of the Inflammatory Changes between Periods at Work and away from Work between Subjects with Positive and Negative SICs

Only in the group with positive SICs did the median percentage of sputum eosinophils significantly increase after periods at work compared with periods away from work (*p* = 0.002) (Table 2). Among the 26 subjects who had a negative challenge, only six subjects (24%) had an increase in their eosinophil count greater than 1% when at work compared with periods away from work, whereas 15 (65%) out of 23 had such an increase in the group with positive SICs. Only four subjects (two in the group with positive SICs and two in the group with negative SICs) had a decrease in their sputum eosinophil count greater than 1% when at work compared with periods away from work (Figure 1).

The increase in sputum eosinophils observed during periods at work among the subjects with positive SIC was greater in the five subjects who were not being treated with inhaled corticosteroids (median sputum eosinophils 4.2%, interquartile range: 15.7) than in the 17 subjects who were being treated (1.2%, interquartile range: 5.5) (*p* = 0.04). It was only in the group with negative SIC that the median percentage of sputum neutrophils increased after periods at work compared with the period away from work (*p* = 0.003).

Receiver Operating Characteristic Curves

Using receiver operating characteristic curves, we identified that an increase in sputum eosinophils greater than 1% during periods at work compared with periods away from work achieved the most satisfying sensitivity (65.2%, CI: 44.8–81.2) and specificity (76.0%, CI: 56.6–88.5) for predicting a positive SIC (Figure 2). We also considered alternative cutoffs, as the magnitude of the changes in sputum eosinophils that can be considered as clinically significant is likely to be greater than 2%. An increase in sputum eosinophils of 2% when at work achieved a 52% (CI: 33.0–70.7) sensitivity and an 80% (CI: 60.9–91.1) specificity. An increase of 6.4% in sputum eosinophils when at work was identified

TABLE 1. BASELINE CHARACTERISTICS OF SUBJECTS WITH NEGATIVE OR POSITIVE SPECIFIC INHALATION CHALLENGES

	Negative SIC (n = 26)	Positive SIC (n = 23)
Age, yr	40.2 ± 11.9	40.6 ± 11
Sex, M/F	12/14	18/5
Atopy	17A	19A
Smoking, S/exS/NS	5/12/9	7/11/5
Pack-years	9.6 ± 15.1	13.4 ± 12.8
Agent, HMW/LMW/U	3/13/10	7/11/6
	Flour (n = 2), latex (n = 1), isocyanates (n = 6), metals (n = 2), glutaraldehyde (n = 1), formaldehyde (n = 1), wood (n = 1), triethanolamine (n = 1), persulfate (n = 1)	Flour (n = 4), licorice (n = 1), protease (n = 1), cat (n = 1) isocyanates (n = 8), red cedar (n = 1), heated polyethylene (n = 1), chloramine (n = 1)
Total duration of exposure, yr	9.2 ± 8.9	13.8 ± 12.2
Asthma duration, yr	7.5 ± 10.6	5.2 ± 7.2
No. of subjects treated with ICS	14 (53.8%)	18 (78.3%)
No. of subjects treated with LABA	6 (23.1%)	5 (21.7%)
Period off work, d	16.1 ± 5.5	15.5 ± 3.5
Period at work, d	20.3 ± 16	16.8 ± 8.4

Definition of abbreviations: exS = ex-smoker; HMW = high molecular weight; ICS = inhaled corticosteroids; LABA = long-acting β_2 -agonists; LMW = low molecular weight; NS = non smoker; S = current smoker; SIC = specific inhalation challenge; U = unknown agent.

Data are presented as means ± SD.

No specific agent could be identified with certainty when the specific challenges were performed at the workplace. However, in the group with negative SIC, the subjects who underwent SIC at their workplace were exposed to flour (n = 1), metals (n = 1), poultry (n = 1), wood dusts (n = 3), tobacco (n = 1), pork (n = 1), formaldehyde (n = 1), or cereals (n = 1), whereas in the groups with positive challenges subjects were exposed to tobacco (n = 1), flour (n = 1), resins (n = 1), plastic (n = 1), or pork (n = 1).

by the receiver operating characteristic curve to have a high specificity (92.0%, CI: 75.0–97.8) with a low sensitivity (26.1%, CI: 12.6–46.5).

PEF Monitoring and Sputum Cell Count Analysis

The analysis of PEF monitoring by the computerized approach Oasys 2 achieved a sensitivity of 34.8% (CI: 18.8–55.1) and a specificity of 65.2% (CI: 44.9–81.2). The addition of sputum cell counts (considering an increase in sputum eosinophils greater than 1 or 2% as clinically significant) to the PEF monitoring improved the sensitivity to 50 (CI: 23.6–76.3) or 36.4% (CI: 15.2–64.6), respectively, and the specificity to 75 (CI: 50.5–89.8) or 80% (CI: 54.8–93.0), respectively. In 21 and 22 cases, respectively, there was discordance between the results of the two tests.

We examined the visual analyses of the PEF monitoring including or excluding the PC₂₀ values by the five experts (Table 3). The agreement between the PEF interpretation of the different experts (yes, no, doubtful) was moderate (Cohen's Kappa varied between 0.4 and 0.6, $p < 0.01$). When adding the results of sputum cell counts, with an increase in sputum eosinophils greater than 1% considered as clinically significant, to the interpretation of PEF monitoring alone or to the combination of PEF and PC₂₀ monitoring, the sensitivity of these tests increased, respectively, by 8.2 (range [r]: 4.1–13.4) and 7.9% (r: 4.1–11.4), and the specificity increased, respectively, by 18 (r: 13.7–25.5), and 27.4% (r: 18.1–38.2) among the experts. The results of the PEF and PEF/PC₂₀ monitoring and sputum cell count results were not in accordance in an average of 13.4 and 12.6 cases, respectively. When considering an increase in sputum eosinophils

TABLE 2. CHANGES IN CLINICAL, FUNCTIONAL, AND SPUTUM CELLULARITY BEFORE AND AFTER THE AT-WORK/OFF-WORK PERIODS IN SUBJECTS WITH NEGATIVE AND POSITIVE SPECIFIC INHALATION CHALLENGES

	Negative SIC (n = 26)		Positive SIC (n = 23)	
	Off Work	At Work	Off Work	At Work
Symptoms score	4.6 ± 5.6	14.7 ± 9.8*	4.5 ± 4.6	18.0 ± 12*
β_2 -agonist (puff/d) used	0.4 ± 0.7	1.2 ± 1.6*	0.3 ± 0.6	1.8 ± 1.9*
FEV ₁ , % pred	88.2 ± 16.9	82.4 ± 20.6†	90.8 ± 17.2	84.6 ± 22.3†
PC ₂₀ , mg/ml	6.0 ± 5.2	3.5 ± 3.0†	2.9 ± 2.3	1.6 ± 1.2†
TCC, 10 ⁶ /ml	1.8 (2.4)	2.3 (2.7)	1.8 (4.3)	2.5 (4.3)
Neutrophils, %	37.7 (32.3)	59.5 (41.6)*	35.3 (43.0)	33.2 (41.2)
Eosinophils, %	0.8 (1.5)	1.0 (3.6)	0.5 (3.0)	2.8 (9.1)*

Definition of abbreviations: PD₂₀ = change in provocative concentration of histamine aerosol causing a 20% decrease in FEV₁; pred = predicted; TCC = total cell count.

Symptom score, β_2 -agonist use, and FEV₁ are expressed as mean ± SD. PC₂₀ is expressed as geometric mean. TCC, neutrophils, and eosinophils are expressed as median (interquartile range).

* $p \leq 0.01$.

† $p \leq 0.05$.

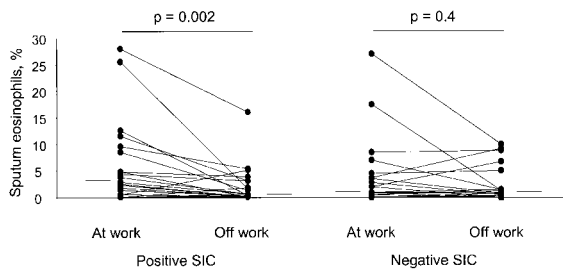


Figure 1. Changes in sputum eosinophils at work and away from work in subjects with positive (left panel) and negative (right panel) specific inhalation challenges. SIC = specific inhalation challenge.

greater than 2% when at work as significant, the sensitivity of the combination PEF/sputum and PEF/PC₂₀/sputum decreased by 12.3 (r: 3.1–24.1) and 14.6% (r: 5.3–32.0), respectively, and the specificity increased by 26.8 (r: 24.8–30.4) and 30.6% (r: 19.4–45.5) compared with PEF monitoring alone or with the combination of PEF and PC₂₀, respectively. The results of the PEF, PEF/PC₂₀ monitoring, and sputum cell count results were not in accordance in an average of 15.0 and 11.2 cases, respectively. The combination of sputum cell counts with PEF or PEF/PC₂₀ monitoring with an increase in sputum eosinophils greater than 6.4% considered as significant increased further the specificity, but lowered the sensitivity compared with PEF or PEF/PC₂₀ monitoring alone (data not shown).

DISCUSSION

This study has shown that most workers with positive SICs had higher sputum eosinophil counts when at work that decreased when they were removed from work, whereas most subjects with negative SICs did not show such changes in their sputum eosinophil counts. Also, the addition of the analysis of induced sputum cell counts to the monitoring of PEF and PC₂₀ during periods at and away from work improved the specificity of these tests compared with SIC.

Interestingly, we found that subjects who had a negative SIC had more sputum neutrophils when at work, a finding that has

not been described before to the best of our knowledge. Mechanisms of this neutrophilic inflammation are unclear, but it may be due to an irritant effect of agents in the workplace, as happens with many stimuli, such as repeated inhalation of hypertonic saline (24) or atmospheric pollutants, such as ozone (25). Exposure to swine confinement (26), or grain dust (27) also induce a neutrophilic inflammation. Some occupational agents may also induce asthma-like symptoms and neutrophilic inflammation through the same mechanism. For those subjects who experience increased symptoms of asthma combined with a neutrophilic type of inflammation, the long-term consequences of remaining in the workplace are unknown and need to be evaluated.

The sensitivity and specificity of PEF monitoring interpreted with the Oasys-2 software were lower than in a previous study (23). In this study, the interpretation of PEF monitoring by Oasys-2 was compared with several diagnostic methods independent of PEF investigation, such as SIC, changes in PC₂₀ at work and away from work, and positive IgE with a suggestive history of OA. In the present study, we used a unique reference test, SIC, which could explain at least partly this discrepancy. Nevertheless, the sensitivity and specificity of serial PEF monitoring interpreted visually in our study were also lower than those reported in previous studies (3, 4). In those studies, the sensitivity and specificity of PEF monitoring was estimated by pooling the interpretation of several experts (3), and by considering the diagnosis of OA when there was an agreement between the majority (4) or all (3) of the readers. However, such an analysis does not reflect clinical practice, where a single physician has to make a diagnosis and tends to overestimate the sensitivity and the specificity of the test.

The previous studies that evaluated the sensitivity and specificity of PEF compared with SIC were performed in the early nineties. It is possible that at this time a minority of subjects were treated with inhaled corticosteroids. By contrast, the majority of our subjects were taking this medication. This most likely influenced the intensity of sputum eosinophilia, which was lower than expected (8), as well as the PEF variability observed during periods at work. Indeed, the subjects who were not taking inhaled corticosteroids had a greater increase in sputum eosinophilia at work than those who were treated with this medication. This is consistent with previous studies showing that inhaled steroids reduce significantly sputum eosinophilia (28, 29) at baseline and after allergen challenge (30, 31). Indeed, a single dose of inhaled steroids can decrease sputum eosinophilia by 25% of the baseline value (32). Hence, when a patient is away from work and has clinically improved, consideration should be given to withdrawing corticosteroid treatment and following the response over 2 to 4 weeks before returning him/her to work. Eleven subjects were also taking long-acting β_2 -agonists during the investigation. This treatment is also likely to have had a suppressive effect on the PEF variability. When it is possible to achieve an adequate asthma control without this medication, the PEF interpretation is likely to be easier if the patient is switched to short-acting β_2 -agonists during the period of investigation.

It is likely that the enrollment of patients without inhaled steroids or long-acting β_2 -agonists would have maximized the changes observed in sputum and PEF monitoring between periods at work and away from work. However, the results of such a study would not have been applicable to clinical practices, where the majority of patients are taking these medications and cannot be weaned without impairing their asthma control. The strength of our study is that it was performed in real-life conditions. Hence, its results can be applied to other clinical settings.

The evaluation of any diagnostic tool has to be done in comparison with a gold standard. We compared the results of PEF monitoring and sputum induction with those of SIC. Although

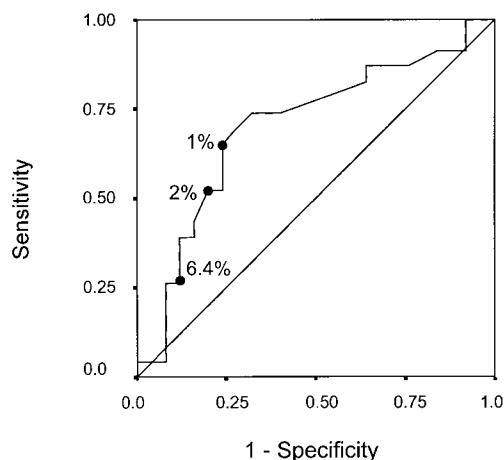


Figure 2. Receiver operating characteristic curve built to determine the most relevant difference in sputum eosinophil percentage between periods at work and away from work for predicting the positivity of specific inhalation challenges.

TABLE 3. SENSITIVITIES AND SPECIFICITIES OF PEAK EXPIRATORY FLOW MONITORING WITH AND WITHOUT THE ADDITION OF SPUTUM CELL COUNTS ACCORDING TO THE DIFFERENT EXPERTS

	Expert 1	Expert 2	Expert 3	Expert 4	Expert 5
PEF					
Sensitivity, %	63.1	78.9	82.3	77.7	86.6
Specificity, %	61.9	52.9	55.0	47.6	50.0
Doubtful cases, n	6	10	9	7	17
PEF-sputum1/PEF-sputum2					
Sensitivity, %	72.7/60.0	83.8/71.4	90.9/66.6	81.8/66.6	100.0/62.5
Specificity, %	81.8/92.3	66.6/77.7	69.2/80.0	72.7/75.0	66.0/76.4
Discrepancy between PEF and sputum	17/17	11/13	12/15	16/18	11/12
PEF/PC ₂₀					
Sensitivity, %	65.2	60.0	87.5	72.2	63.1
Specificity, %	61.9	36.8	44.4	47.6	42.8
Doubtful cases, n	2	7	11	7	13
PEF-PC ₂₀ -sputum1/PEF-PC ₂₀ -sputum2					
Sensitivity, %	71.4/52.9	71.4/52.6	91.6/55.5	81.8/56.2	71.4/57.8
Specificity, %	80.0/81.3	75.0/82.3	75.0/76.4	69.2/71.4	71.4/75.0
Discrepancy between PEF/PC ₂₀ and sputum	16/12	12/9	10/11	14/15	11/9

The sensitivity and specificity for the combination of PEF and sputum or PEF-PC₂₀ and sputum were calculated with a difference greater than 1% (sputum1) and 2% (sputum 2) in sputum eosinophil counts between periods at work and away from work.

SIC tests are reliable, they can be falsely negative when they are performed with the wrong agent, or when the subjects have been away from exposure for a long period (33). Therefore, it is possible that some patients were misdiagnosed in our study. Indeed, at least two subjects with negative SICs had a high increase in sputum eosinophil counts when at work in addition to suggestive PEF and PC₂₀ monitoring, suggesting that the SICs were falsely negative.

The analysis of sputum cell counts may be used only after the first steps of OA investigation—the clinical history, performance of relevant skin-prick tests, and measurement of airway responsiveness—have been completed (34).

The use of this strategy has a number of limitations, as do other assessments based on serial PEF and PC₂₀ monitoring (5). Indeed, it cannot be performed in a substantial number of patients in real life, as shown by the large number of subjects who had to be excluded from our study. Any exposure to a common allergen to which the subjects are sensitized, the occurrence of a respiratory infection, or the modification of treatment during the period of investigation precludes a reliable interpretation of the data. The inability to return to the workplace or to be removed from the workplace during the investigation prevents the assessment. Moreover, some subjects may be too sick for specific challenge testing, whereas others may not follow instructions for PEF monitoring. In the present study, sputum production and examination was successful in all but 7.5% of attempts, which is consistent with previous data (35). However, although the analysis of induced sputum is becoming more and more common, it is not yet widely available.

In this study, we found that changes greater than 1% in sputum eosinophils between periods at work and away from work gave the best compromise between specificity and sensitivity, and increased both the sensitivity and specificity when added to the PEF and PC₂₀ monitoring. However, this change in sputum eosinophils is minimal and may not be clinically significant. Considering an increase in sputum eosinophil count greater than 2% when at work in addition to the PEF monitoring will improve the specificity of the test but not its sensitivity. Clinically significant changes in sputum eosinophils that occur between periods at work and away from work need to be defined to facilitate the future interpretation of this test in the investigation of OA.

In conclusion, the analysis of induced sputum cell counts

during periods at work and away from work is a valuable tool, which, when added to investigation by PEF monitoring, improves the specificity of this test compared with specific inhalation challenges. When the monitoring of PEF and sputum cell counts are both highly suggestive of OA, it may constitute an alternative to the performance of SIC unless the etiological agent needs to be identified. Alternatively, when there is discordance between the monitoring of PEF, PC₂₀, and sputum cell counts, the investigation may be pursued by performing SICs, or by returning the patient to the workplace, with a reduction of the medication if possible, to perform PEF, PC₂₀, and sputum cell-count monitoring at work and away from work.

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