

Case Report

The Use of Fractional Exhaled Nitric Oxide In Investigation of Work-Related Cough in a Hairdresser

Gianni Pala, MD,* Patrizia Pignatti, PhD, and Gianna Moscato, MD

Background Occupational and environmental factors may be a cause of nonasthmatic eosinophilic bronchitis (NAEB). The diagnosis of occupational NAEB requires evidence of sputum eosinophilia. Nevertheless, a minority of patients are not able to produce suitable sputum specimens.

Methods This case report describes a 25-year-old woman, working as a hairdresser since the age of 20 years and handling ammonium persulfate, who came under our observation for work-related rhinitis and cough.

Results A specific inhalation challenge with ammonium persulfate elicited dry cough, without any significant change in forced expiratory volume in 1 s (FEV₁). Sputum induction was unsuccessful both pre- and after specific inhalation challenge. Fractional exhaled nitric oxide (FeNO) values significantly increased after specific inhalation challenge, suggesting a diagnosis of occupational NAEB due to ammonium persulfate.

Conclusions From this observation we suggest that FeNO measurement should be added to the investigation of work-related cough during specific inhalation challenge, and may be considered as an alternative to induced sputum to evaluate bronchial inflammation when sputum collection is unavailable or unsuccessful. Am. J. Ind. Med.

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KEY WORDS: occupational asthma; eosinophilic bronchitis; induced sputum; persulfate salts; fractional exhaled nitric oxide

INTRODUCTION

Nonasthmatic eosinophilic bronchitis (NAEB) is defined as a chronic cough in patients with no symptoms or objective evidence of variable airflow obstruction, normal airway hyperresponsiveness and sputum eosinophilia [Brightling,

2006]. Occupational and environmental factors may be a cause of persistent cough and NAEB is one of the possible causes [Tarlo, 2006]. When it occurs under occupational conditions, it can be considered as a variant of occupational asthma [Quirce, 2004]. Few cases of occupational NAEB have been described [Quirce, 2004], most due to high-molecular weight (HMW) agents. Ammonium persulfate is a low-molecular weight (LMW) agent well known as a cause of occupational rhinitis and asthma in hairdressers [Moscato et al., 2010], but no case of occupational NAEB due to this compound has been reported to date. The diagnosis of occupational NAEB requires evidence of increase in sputum eosinophils related to exposure to the offending agent [Quirce, 2004]. Nevertheless, nearly one-third of patients with respiratory allergy to ammonium persulfate are not able

Allergy and Immunology Unit, Fondazione 'Salvatore Maugeri', Institute of Care and Research, Scientific Institute of Pavia, Pavia, Italy

*Correspondence to: Gianni Pala, Allergy and Immunology Unit, Fondazione 'Salvatore Maugeri', Institute of Care and Research, Scientific Institute of Pavia, Via Maugeri 10, Pavia, Italy. E-mail: giannipalass@libero.it

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to produce suitable induced sputum specimens [Moscato et al., 2010], limiting our ability to investigate the possible inflammatory status of lower airways.

It is now possible to assess airway inflammation in asthma patients by measuring the fractional exhaled nitric oxide (FeNO) during an office visit [ATS/ERS, 2005]. Although there is international consensus regarding the testing methodology, nevertheless there are still questions to be answered regarding the clinical interpretation of FeNO findings in specific situations [Lim and Mottram, 2008].

In this report we propose FeNO measurement as an alternative to induced sputum for confirming a diagnosis of occupational NAEB due to ammonium persulfate.

CASE REPORT

This case report describes a 25-year-old woman, a mild smoker, referred to us with work-related rhinitis and cough. She had been working as a hairdresser since the age of 20 years. Two years after commencing work she developed nasal obstruction and itching and dry cough only while at work when handling hair-bleaching products containing ammonium persulfate salts. The workplace was provided with a ventilation system and extractor fans. Symptoms improved with oral corticosteroid intake (betametasone) prescribed by a general practitioner and by complete work exposure avoidance during weekends and holidays.

METHODS

The patient was admitted to our hospital free of any therapy and was asked to avoid smoking during the whole examination period. She underwent the common diagnostic pathway for the investigation of occupational respiratory allergy (duration of the whole examination period: 7 days—Table I). On the day of admission (Day 1) basal spirometry, a methacholine challenge test [performed by means of a nebulizer (MEFAR, Brescia, Italy) connected to a dosimeter], skin prick tests to common allergens and to ammonium persulfate, patch tests (FIRMA, Florence, Italy) and serum determination of IgE were performed. On Days 2 and 3 patient lung function was monitored by hourly measurement of peak expiratory flow rate. On Day 4 FeNO measurement [ATS/ERS, 2005] [performed with NIOX-MINO[®] (Aerocrine AB, Solna, Sweden) at a constant flow rate of 50 ml/s] [Lim and Mottram, 2008], sputum induction [Quirce et al., 2010; Moscato et al., 2010] and nasal secretion collection [Moscato et al., 2010; Pignatti et al., 2010] were performed. On Day 5 a control challenge test with ethanol was performed and the day after (Day 6) the patient underwent the specific inhalation challenge with ammonium persulfate (240 min cumulative exposure in a 7.46 m³ inhalation challenge room) [Moscato et al., 2010]. FeNO measurement, sputum induction, nasal secretion collection, and methacholine

TABLE I. Diagnostic Pathway for Diagnosis of Occupational Rhinitis and Asthma

Diagnostic pathway	
Day 1	Spirometry, methacholine challenge test, PEF monitoring, SPTs, patch tests, serum determination of IgE
Day 2	PEF monitoring
Day 3	PEF monitoring
Day 4	FeNO measurement, nasal secretion collection, sputum induction, PEF monitoring
Day 5	Challenge test with ethanol, PEF monitoring
Day 6	Specific inhalation challenge with ammonium persulfate, PEF monitoring
Day 7	FeNO measurement, nasal secretion collection, sputum induction, methacholine challenge test, PEF monitoring

PEF, peak expiratory flow; SPTs, skin prick tests; FeNO, fractional concentration of exhaled nitric oxide.

challenge test were repeated 24 after exposure to ammonium persulfate (Day 7). Peak expiratory flow rate was also measured during the whole examination period.

RESULTS

Basal spirometry was normal (FEV₁ 3.10 L—95% predicted) and methacholine challenge test was negative (Table II). Skin prick tests were slightly positive to *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* (mean wheal diameter 2 mm), and negative to ammonium persulfate [Moscato et al., 2010]. Patch tests were positive to nickel sulfate (light nonvesicular erythema). Total serum IgE concentration was 78.3 kU/L (normal value <120 kU/L).

No significant FEV₁ variation ($\geq 10\%$) nor nasal reaction was shown during the control challenge with ethanol. The specific inhalation challenge with ammonium persulfate elicited nasal itching, sneezing, rhinorrhea, mucosal edema (via anterior rhinoscopy) and nasal obstruction, with reduction in peak nasal inspiratory flow from 60 to 0 L/min and dry cough 240 min after the end of the exposure, without any significant change in FEV₁ values. Peak expiratory flow values were in the normal range during the whole examination period (diurnal variation <20% throughout). Methacholine challenge test performed 24 hr after specific inhalation challenge was negative (Table II). Sputum induction was unsuccessful both pre- and after specific inhalation challenge, owing to the onset of nausea during the procedure. A significant increase in FeNO values was registered 24 hr after exposure to ammonium persulfate (from 35 ppb at baseline to 143 ppb after specific inhalation challenge). An increase in nasal secretion eosinophils [from 78.9% ($12.6 \times 10^4/\text{ml}$) to 84.9% ($16.1 \times 10^4/\text{ml}$)] and peripheral blood eosinophils [from 7.2% ($0.34 \times 10^9/\text{L}$) to

TABLE II. Results of the Tests Performed Before and After Specific Inhalation Challenge (SIC)

	Before SIC	After SIC
FEV ₁	2.82 L—88% predicted	2.79—87% predicted
PEF	400 L/min	370 L/min
PNIF	60 L/min	0 L/min
PD ₂₀ FEV ₁ ^a	>1,976 µg	>1,976 µg
FeNO ^b	35 ppb	143 ppb
Nasal eosinophilia ^c	78.9% (12.6×10^4 /ml)	84.9% (16.1×10^4 /ml)
Blood eosinophilia ^d	7.2% (0.34×10^9 /L)	8.2% (4.34×10^9 /L)

FEV₁, forced expiratory volume in 1 s; PEF, peak expiratory flow; PNIF, peak nasal inspiratory flow.

^aPD₂₀FEV₁: provocative dose of methacholine causing a 20% fall in FEV₁ (normal value >1,600 µg).

^bFeNO: fractional concentration of exhaled nitric oxide (normal value ≤35 ppb) [Oh et al., 2008].

^cCut-off for the increase of eosinophils after challenge: 4% eosinophils and/or 1.0×10^4 eosinophils/ml [Pignatti et al., 2010].

^dNormal range 1–4%.

8.2% (4.34×10^9 /L)] was also registered (Table II). A diagnosis of occupational rhinitis was made [Moscato et al., 2008]. In addition, the clinical history of work-related dry cough, the induction of cough in the absence of any significant functional change and the increase in FeNO values during the specific inhalation challenge strongly suggested a diagnosis of occupational NAEB due to ammonium persulfate exposure [Quirce, 2004].

DISCUSSION

The importance of a correct diagnosis of NAEB is underscored by some recent reports suggesting that this condition is rarely self-limiting [Brightling, 2006] and that the risk of developing asthma should be considered, particularly in the absence of adequate treatment and monitoring. That is particularly relevant in the occupational setting since occupational asthma is a cause of disability and has a significant socio-economic impact. In the present case the failure to collect a proper induced sputum sample could have led to an incomplete diagnosis.

The level of FeNO is correlated with sputum eosinophilia, mucosal eosinophilia, and bronchoalveolar lavage eosinophilia [Lim and Mottram, 2008]. In the nonoccupational setting some studies have shown its usefulness in the investigation of chronic cough, and its high negative predictive value for NAEB [Oh et al., 2008]. In our case FeNO values markedly increased after exposure to ammonium persulfate during the specific inhalation challenge. All factors possibly influencing FeNO increase [ATS/ERS, 2005] were ruled out. The low FeNO levels measured at baseline suggested that the bronchial NO measurement was not affected by the high nasal eosinophilia recorded at the same time point, and consequently by nasal NO.

The mechanism through which ammonium persulfate can induce rhinitis and asthma in exposed subjects is not completely known. An immunologic mechanism has been postulated by different authors [Muñoz et al., 2003; Diab

et al., 2009; Moscato et al., 2010], and could also be considered for NAEB, which is a variant of occupational asthma. It was inferred that NO was formed in the lower respiratory tract as a consequence of ammonium persulfate exposure, which has been demonstrated to be able to induce nasal and bronchial eosinophilia both in atopic and in non atopic exposed subjects [Moscato et al., 2010].

According to the test results and current diagnostic criteria [Quirce, 2004] we made a diagnosis of occupational NAEB due to ammonium persulfate. The present case suggests that FeNO measurement, which is non-invasive, quick, and relatively simple to perform, should be added to the investigation of work-related cough during specific inhalation challenge, and may be considered as an alternative to induced sputum to evaluate bronchial inflammation both in atopic and in nonatopic subjects with a suggestive clinical history of occupational NAEB, when sputum collection is unavailable or unsuccessful.

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