

Feasibility of monitoring nasal and exhaled nitric oxide with a handheld analyzer during specific inhalation challenge

Chemiluminescence analysis is regarded as the standard method to measure nasal nitric oxide (nNO) and exhaled nitric oxide (eNO). However, this technology has disadvantages (eg, cost, size) that limit its use in clinical practice. A portable nitric oxide (NO) analyzer has been validated for measuring eNO and nNO.^{1,2} The feasibility of incorporating this technology during specific inhalation challenge (SIC) remains unknown. Thus, we monitored nNO and eNO levels during SIC using a portable NO analyzer. We also assessed the correlation between nNO and eNO measurements.

Ten male patients (mean [SD] age, 39.1 [9.1] years) with occupational rhinitis and asthma and sensitized to wheat flour were studied. They had been removed from the workplace, and rhinitis and asthma symptoms were stable. Informed consent was obtained from all study participants. Participants underwent standardized SIC as previously described,³ with monitoring of nasal and bronchial responses on consecutive control and flour challenge days. Nasal congestion was measured by acoustic rhinometry and a visual analog scale (VAS) before and serially (at 10, 30, and 60 minutes and then hourly) for 6 hours and at 24 hours after challenge. Lung measurements included measuring forced expiratory volume in 1 second (FEV₁) before and serially (every 10 minutes for 1 hour, every 30 minutes for 2 hours, and then hourly) for 6 hours after exposure. Both nNO and eNO were measured before and at 30 minutes, 60 minutes, 6 hours, and 24 hours after challenge using a portable NO analyzer (NIOX mino; Aerocrine, Solna, Sweden). For measuring nNO, a nasal mask (Fisher & Paykel Healthcare Ltd, Laval, Canada) was connected to the mouthpiece filter of the analyzer.¹ The changes in nNO and eNO levels were analyzed with the non-parametric Friedman and Wilcoxon rank tests. Correlations between nNO and eNO measurements were analyzed using the Spearman test.

In contrast to control challenge, flour challenge induced respiratory symptoms and significant objective nasal congestion and bronchoconstriction in all study participants in the early allergic reaction. During the control day, the mean (SD) maximum percentage decrease in nasal volume from baseline was 15.0% (10.4%), whereas after flour challenge it was 38.7% (8.6%).

On the control day, the median (interquartile range) VAS rating at baseline was 0.3 (2.7), and no increase was observed after challenge. On the active challenge day, the VAS rating at baseline was 0.3 (2.3), whereas the median highest VAS rating was 3.4 (3.1) at 10 minutes

after challenge with flour. The challenge with flour induced significant changes in bronchial caliber in all patients, defined as a decrease in FEV₁ of more than 20% after allergen challenge.³ During the control day, the mean (SD) maximum percentage decrease in FEV₁ from baseline was 3.6% (4.2%), whereas after flour challenge it was 31.0% (10.4%).

Flour challenge induced a significant decrease in nNO levels at 30 minutes after challenge ($P < .05$) that was followed by a gradual increase that reached nearly significant maximum levels at 24 hours after challenge ($P = .06$) (Table 1). Flour challenge induced a gradual increase in eNO levels that was nearly significant at 6 hours ($P = .06$) and reached significant maximum levels at 24 hours after challenge ($P < .01$) (Table 1). A strong correlation between nNO and eNO measurements was found at baseline and after control and flour challenge (Table 1). However, weak, nonsignificant correlations were observed between nNO and eNO measurements and VAS scores and acoustic rhinometry measurements.

The observed early decrease in nNO levels after flour challenge is in agreement with allergen challenge studies that have monitored nNO with nonportable chemiluminescence analyzers.⁴ This decrease has been proposed to be induced by swelling of the nasal mucosa involving the sinus ostium during the early allergic reaction, thereby preventing the normal diffusion of NO from the sinuses into the nose. In agreement with the same study,⁴ we observed a gradual increase in nNO that reached maximum levels at 24 hours after challenge. In the lower airways, we observed a gradual increase in eNO that reached maximum levels at 24 hours after challenge, which is consistent with studies showing elevated eNO levels after allergen challenge at the time of the late allergic reaction.⁵ Interestingly, we found a strong correlation between nNO and eNO measurements, suggesting a parallel inflammatory response of the upper and lower airways. This finding is in accordance with the unified airways concept in cases involving exposure to occupational allergens as we have demonstrated previously.⁶

The measurement of nNO and eNO using a portable analyzer can be easily incorporated into SIC protocols and appears useful for detecting nasal and bronchial responses after allergen challenge. However, nNO kinetics during the early allergic reaction may be altered by a pronounced nasal congestive response. The portable technology may be useful to complement other diagnostic tests performed during SIC. Also, it has potential to be used at the workplace to produce serial measurements to provide evidence of exposure-related airway inflammation.

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Table 1
Levels of Nasal and Exhaled Nitric Oxide Before and After Control and Active (Flour) SIC

	Control SIC, median (IQR)			Active (flour) SIC, median (IQR)		
	nNO, ppb	eNO, ppb	r (P value) ^a	nNO, ppb	eNO, ppb	r (P value) ^a
Before challenge	35.0 (18.0)	18.0 (28.0)	0.82 (.004)	35.0 (26.0)	15.5 (19.0)	0.92 (<.001)
30 Minutes after challenge	35.5 (16.0)	21.5 (33.0)	0.81 (.005)	30.5 (21.0) ^b	14.5 (20.0)	0.81 (.008)
60 Minutes after challenge	31.0 (31.0)	19.0 (32.0)	0.72 (.02)	31.5 (11.0)	15.5 (28.0)	0.52 (.15)
6 Hours after challenge	37.0 (37.0)	17.0 (88.0)	0.73 (.03)	34.5 (29.0)	21.5 (30.0) ^c	0.58 (.08)
24 Hours after challenge	35.0 (26.0)	15.5 (19.0)	0.92 (<.001)	43.0 (20.0) ^c	41.0 (65.0) ^d	0.78 (.01)

Abbreviations: eNO, exhaled nitric oxide; IQR, interquartile range; nNO, nasal nitric oxide; SIC, specific inhalation challenge.

^aSpearman coefficient quantifying the relationship between nNO and eNO at each challenge time.

^b $P < .05$ compared with prechallenge value.

^c $P = .06$ compared with prechallenge value.

^d $P < .01$ compared with prechallenge value.

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Occupational asthma induced by exposure to lima bean (*Phaseolus lunatus*)

We report the first case of occupational asthma (OA) due to the exposure to vapors from boiling *Phaseolus lunatus* in a food processing industry. *Phaseolus lunatus*, commonly known as the lima bean or butter bean, belongs to the Leguminosae family and is native of the Central America and Andean regions.

A 41-year-old, male, former smoker was referred to our department for work-related respiratory symptoms. He had been employed in a food processing factory that produced cake dough (ie, panettoni) mainly with almonds, which were sometimes replaced by lima beans. His job consisted of boiling, mincing, and drying large amounts of lima beans (approximately 200 kg/d). The working environment, especially during cooking and cutting, was full of hot bean aerosol because the product line was only partially enclosed and exhaust fans were out of order. Furthermore, the patient wore an inappropriate protective mask. Four months after the recruitment, the patient reported the onset of dry cough, wheezing, dyspnea, and chest tightness; on 2 occasions, the dyspnea was severe enough to require hospitalization. Symptoms typically appeared a few minutes after entering the factory department and

were more severe during the cooking phase of the beans. Initially, the symptoms improved during weekends and disappeared during holidays, and after 3 months of work they became almost persistent. No similar symptoms were reported by other employees. The patient came to our observation 3 months after the onset of symptoms. He underwent the common diagnostic investigations for OA.¹ Basal spirometry results were normal (forced expiratory volume in 1 second [FEV₁], 87% predicted), and the results of skin prick tests (SPTs) to common and work-related allergens were positive for house dust mites and Leguminosae mix. Serum IgE levels were 1,168 kU/L (reference range, <120 kU/L), and peripheral eosinophil percentage was 4.1%. After 3 days from the last exposure, a methacholine challenge test revealed mild bronchial hyperreactivity (provocative dose that caused a decrease in FEV₁ of 20%, 691 µg), and bronchodilation test with salbutamol was positive, showing a 13% FEV₁ increase.² To evaluate the possible sensitization to *P lunatus*, extracts from cooked beans (taken directly in the factory) were prepared. Fifteen milligrams of homogenized beans were incubated and end-over-end mixed overnight at room temperature with 30 mL of phosphate buffer. Then the

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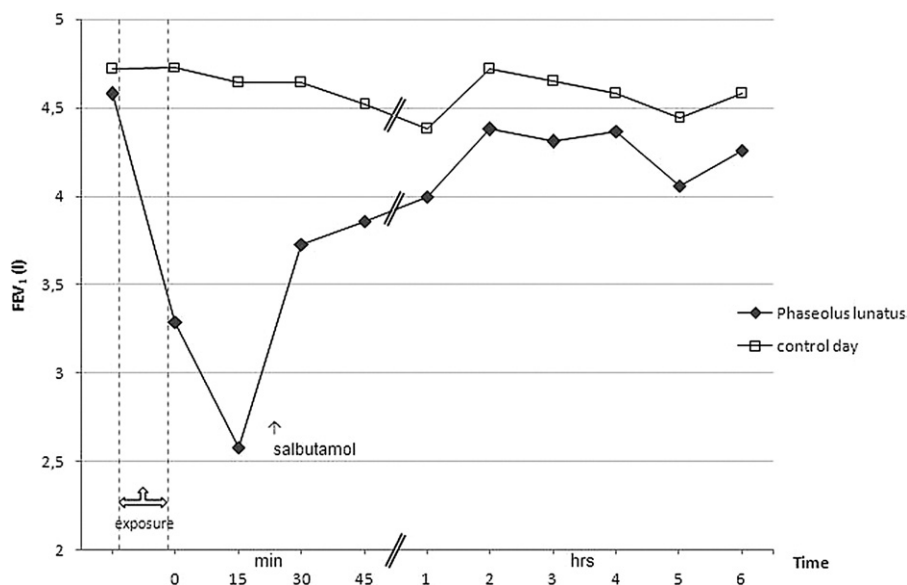


Figure 1. Specific inhalation challenge with the *Phaseolus lunatus* extract (1:100 [wt/vol]).