ORIGINAL ARTICLE

Educational Intervention in Farmers With Occupational Asthma: Long-term Effect on Exhaled Nitric Oxide

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Abstract

Background: The fraction of exhaled nitric oxide (FE_{NO}) has been found reduced 4 to 6 weeks after an educational intervention in farmers with occupational asthma.
Objective: To reveal whether long-term changes in FE_{NO} would still be detectable a year after the intervention.
Methods: We evaluated airway inflammation and obstruction at baseline and after 1 year in animal farmers with occupational asthma (n = 43, 16 women, mean [SD] age, 46.5 [8.9] years) who participated in a 1-day educational program, and in a control group of farmers without intervention (n = 15, 3 women, mean age, 44.1 [10.7] years). FE_{NO}, spirometry results, and questionnaire data were compared between measurements and between the intervention and control group.
Results: In the intervention group, geometric mean (SEM) FE_{NO} decreased from 31.5 (1.1) to 25.0 (1.1) parts per billion (ppb) (P = .001), whereas in the control group there was a slight but not statistically significant increase from 27.2 (1.2) to 30.7 (1.2) ppb. Spirometric values remained unchanged in both groups.
Conclusions: We found that FE_{NO} was still decreased 1 year after an educational intervention in farmers with occupational asthma. It would thus seem that FE_{NO}, a noninvasive marker of airway inflammation that can be easily assessed in occupational field work, may be suitable for the evaluation of both short-term and long-term effects of preventive measures in occupational asthma.

Key words: Agriculture. Educational intervention. Exhaled nitric oxide. Farming. Occupational asthma.

Resumen

Antecedentes: Se ha encontrado una reducción en la fracción de óxido nítrico en aire espirado (FE_{NO}) en agricultores con asma ocupacional 4 a 6 semanas después de una intervención educacional.
Objetivo: Revelar si los cambios a largo plazo en el FE_{NO} podrían ser detectados aún un año después de la intervención.
Métodos: Evaluamos la inflamación y obstrucción basal y 1 año después en granjeros con asma ocupacional (n = 43, 16 mujeres, media de edad [DE], 46,5 [8.9] años) que participaron en un programa de educación de 1 día, y en un grupo control de granjeros sin intervención (n = 15, 3 mujeres, media de edad, 44,1 [10.7] años). Se compararon el FE_{NO}, los resultados de espirometría, y los datos de un cuestionario entre las mediciones y el grupo de intervención y el grupo control.
Resultados: En el grupo de intervención disminuyó la media geométrica (MG) del FE_{NO} de 31,5 (1,1) a 25,0 (1,1) partes por billón (ppb) (P = ,001), mientras que en el grupo control incrementó ligeramente aunque no de forma estadísticamente significativa de 27,2 (1,2) a 30,7 (1,2) ppb. Los valores espirométricos permanecieron sin cambios entre los dos grupos.
Conclusiones: Encontramos que el FE_{NO} se encontraba disminuido 1 año después de la intervención educativa en granjeros con asma ocupacional. Este dato sugeriría que el FE_{NO}, un marcador no invasivo de inflamación de la vía aérea que puede ser fácilmente evaluado en el trabajo de campo, podría ser adecuado para la evaluación de los efectos tanto a corto como a largo plazo en las medidas preventivas en asma ocupacional.

Palabras clave: Agricultura. Intervención educacional-educativa. Óxido nítrico en espirado. Ganadería. Asma ocupacional.

Introduction

The fraction of exhaled nitric oxide (FENO) is increasingly used to assess airway inflammation in asthma [1]. FENO levels increase with allergen exposure [2] and decrease with the administration of antiinflammatory medication [1]. Elevated FENO, for example, has been found 22 hours after a latex allergen challenge in sensitized health care workers [3], while corticosteroid treatment has been shown to decrease FENO within a matter of days [4]. In addition to its use in clinical trials, FENO has been used as an outcome measure in environmental and occupational interventions to detect short-term effects within a time interval of several weeks [5-7]. However, there is a lack of data addressing the long-term sustainability of such interventions with regard to changes in FENO.

Farmers have a high risk of asthma [8], a condition associated with considerable employment disability [9]. Current guidelines recommend that workers with occupational asthma completely avoid further exposure to causal agents [10,11] but this is not always feasible in agriculture, mainly due to economic considerations. The second best option for the many farmers who continue to work despite asthma is to reduce exposure to allergens through technical or organizational means such as the use of personal protective equipment [12,13] or through hygienic measures designed to stop the transport of allergens from the stables into the house [14]. Indeed, 4 to 6 weeks after an educational intervention addressing these issues [7], we found reduced FENO levels in farmers with occupational asthma and continued exposure, mainly to cow dander and storage mites, indicating a reduction of airway inflammation. We have now extended the follow-up observation period to test whether this reduction was still detectable 1 year after continued farming exposure.

Materials and Methods

The study design, educational intervention, measurements, and short-term results have been described in detail elsewhere [7]. Here we compare baseline data with follow-up data after 1 year. In brief, 2 German statutory accident insurance institutions for the agricultural sector organized educational programs for dairy and/or swine farmers with a diagnosis of occupational asthma (n = 120). FENO, spirometry, and questionnaire data were assessed in the participants.

Ninety-one subjects returned for follow-up after 1 year (Figure 1). In order to assess only farmers exposed to occupational allergens throughout the study period, we excluded those who were not working in the stable at either baseline or follow-up (n = 26). Additionally, we excluded subjects who were smoking or had acute respiratory tract infections at either of these times (n = 22) to rule out changes in FENO values that might be related to common confounding factors [15] but not to the intervention. Thus, our final study sample consisted of 43 farmers (16 women) with a mean (SD) age of 46.5 (8.9) years. Onsite baseline measurements had also been performed in 27 farmers with occupational asthma unable to participate in the program due to organizational restraints. Of this group, 22 farmers were available for assessment after a year. After excluding farmers who were not working in the stable (n = 2) and who were smoking or had respiratory tract infections (n = 5) at baseline or follow-up, the control group comprised 15 subjects (3 women) aged 44.1 (10.7) years. Written informed consent was obtained from all the participants and the study was approved by the local ethics committee.

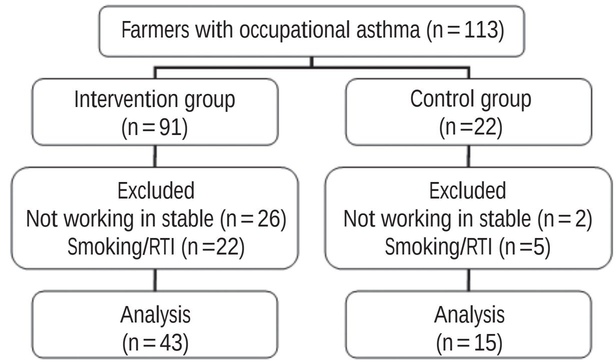

Figure 1. Flow chart of study participants. RTI indicates respiratory tract infection.

The educational intervention lasted 4 to 5 hours and comprised presentations about asthma pathophysiology, appropriate medication, and workplace-related prevention measures presented by a specialist in occupational and respiratory medicine. Practical advice was also given by a representative of the statutory accident insurance institution on technical, organizational, and personal means for allergen reduction.

Both FENO and spirometry were assessed using handheld devices (Niox Mino; Aerocrine, Solna, Sweden and SpiroPro; Jaeger, Würzburg, Germany, respectively) in accordance with international guidelines [16,17]. After FENO measurement, standard spirometric airway obstruction measures—forced expiratory volume in 1 second (FEV_1) and FEV_1/forced vital capacity (FVC)—were recorded. Information on symptoms at work (shortness of breath, wheeze), smoking habits, medication (inhaled corticosteroids, long-acting ß$_2$-agonists), daily working hours in the stable, and organizational or personal protective means employed was obtained by questionnaire.

Statistical Analysis

FENO values were log-transformed to achieve normal distribution. Depending on the nature of the data, results were presented as proportions, or as mean values (geometric where appropriate) and standard errors (SEM). For comparison of baseline data, the Fisher exact test and the unpaired *t* test were employed. Data before and after the intervention were evaluated by the McNemar test and the paired *t* test. Statistical significance was defined as $P < .05$.

Results

The groups were comparable in terms of age and gender ($P > .05$ in each case) and no significant differences were found

Table. Characteristics of Subjects at Baseline and Follow-up

	Intervention Group (n = 43)		Control Group (n = 15)	
	Baseline	Follow-up	Baseline	Follow-up
Shortness of breath[a]	12 (27.9)	16 (37.2)	3 (20.0)	3 (20.0)
Wheeze[a]	14 (32.6)	8 (18.6)	3 (20.0)	4 (26.7)
Daily working hours in the stable[b]	4.0 ± 0.3	4.0 ± 0.3	3.7 ± 0.4	3.9 ± 0.4
Use of protective measures[a]	36 (83.7)	40 (93.0)	11 (73.3)	11 (73.3)
Daily use of protective measures, h[b]	2.7 ± 0.3	3.0 ± 0.3	2.9 ± 0.7	2.4 ± 0.6
Wearing working clothes inside the home[a]	5 (11.6)	2 (4.7)	1 (6.7)	0 (0.0)
Hair wash before going to bed[a]	18 (41.9)	21 (48.8)	5 (33.3)	6 (40.0)
Bed linen change interval, wk[b]	3.1 ± 0.2	2.7 ± 0.2	2.1 ± 0.3[c]	1.9 ± 0.2
Dog inside home[a]	3 (7.0)	2 (4.7)	2 (13.3)	2 (13.3)
Cat inside home[a]	13 (30.2)	10 (23.3)	5 (33.3)	6 (40.0)
Inhaled corticosteroids[a]	24 (55.8)	23 (53.5)	6 (40.0)	6 (40.0)
Long-acting $ß_2$-agonists[a]	20 (46.5)	22 (51.2)	4 (26.7)	5 (33.3)
FE_{NO}, ppb[d]	31.5 ± 1.1	25.0 ± 1.1[e]	27.2 ± 1.2	30.7 ± 1.2
FEV_1, L[b]	3.13 ± 0.13	3.18 ± 0.13	3.38 ± 0.28	3.49 ± 0.29
FEV_1/FVC, %[b]	75.9 ± 1.4	76.0 ± 1.4	75.4 ± 2.8	74.0 ± 2.8

Abbreviations: FEV_1, forced expiratory volume in 1 second; FE_{NO}, fraction of exhaled nitric oxide; FVC, forced vital capacity; ppb, parts per billion.
[a] Data are presented as the number of subjects (%) that answered yes to the respective question.
[b] Data are presented as mean ± SEM.
[c] $P < .01$. Refers to comparison with intervention group at baseline.
[d] Owing to data distribution, geometric means (SEM) are given. The mean has to be multiplied or divided by the SEM factor.
[e] $P < .01$. Refers to comparison with same group a baseline.

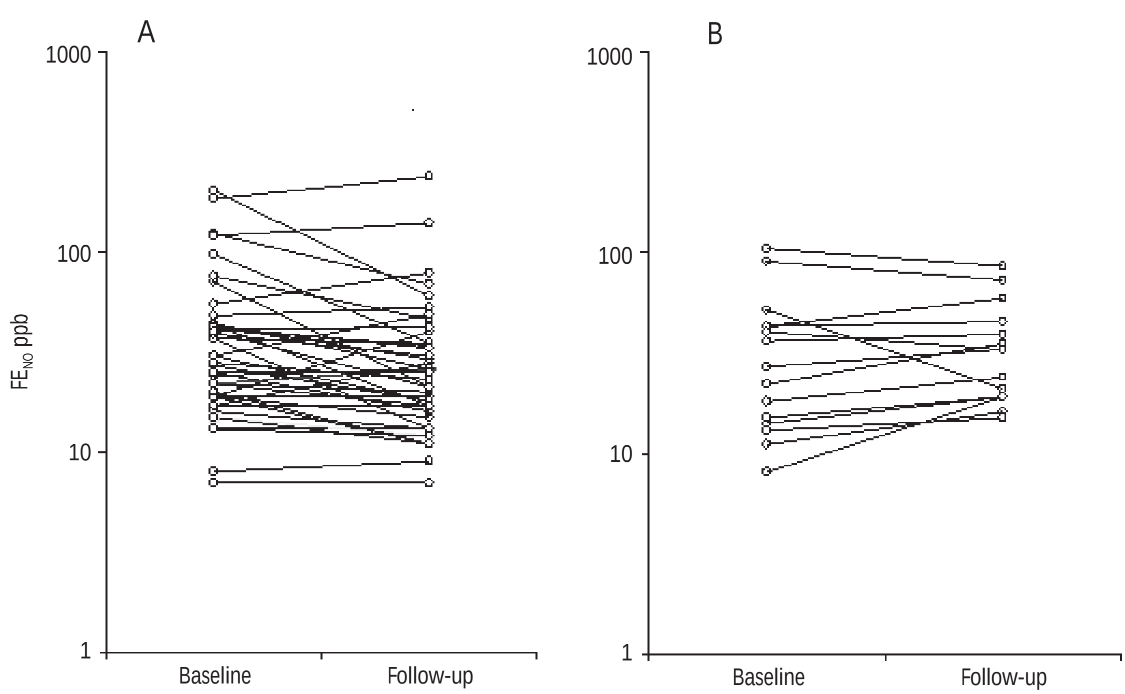

Figure 2. Fraction of exhaled nitric oxide (FE_{NO}) at baseline and follow up. A, intervention group (n = 43). B, control group (n = 15). ppb indicates parts per billion.

for either baseline FENO or spirometric indices. Subjects in the control group changed their bed linen more often than those in the intervention group ($P = .005$, Table).

In the intervention group, there was a tendency ($P = .09$) towards an increase in the duration of use of respiratory protective equipment (from 2.7 h/d to 3 h/d). Geometric mean (SEM) FENO decreased from 31.5 (1.1) to 25 (1.1) parts per billion (ppb) in the intervention group ($P = .001$), while it showed a slight but not statistically significant increase in the control group ($P = .258$, Figure 2). FEV_1 and FEV_1/FVC did not significantly change over time in either group.

Discussion

We found that FENO, a marker of allergic airway inflammation, was still significantly decreased 1 year after an educational intervention in dairy and swine farmers with occupational asthma. Previous work had already shown a decrease in FENO and respiratory symptoms 4 to 6 weeks after the intervention [7]. Thus the present observation extends and supports the previous finding. We are not aware of other published data on FENO as an objective outcome measure for educational interventions in occupational asthma.

FENO has been successfully applied to assess short-term effects in clinical trials and other intervention studies [3-6], but data assessing long-term changes of FENO are scarce. Although FENO is reproducible in the long term, diurnal or seasonal variations still have to be considered, even in healthy subjects [18]. We assessed each participant at the same time of day at baseline and follow-up. Moreover, measurements were performed in winter time to exclude interference with the pollen season.

There are, however, other potential sources of bias associated with FENO [15] that might have been active 1 year after follow-up. To avoid these, we excluded subjects who were smokers or had a respiratory tract infection at the time of the measurements. Whereas smoking was rare (n = 2), the prevalence of acute respiratory tract infections at baseline and/or follow-up in this cohort was considerable (n = 21 in the intervention group). This may have been due to the increased susceptibility of patients with airway diseases to respiratory tract infections, especially in winter. While in our study sample (n = 43) geometric mean FENO decreased from 31.5 to 25.0 ppb ($P = .001$), the respective values when subjects with respiratory tract infections were included in this group (n = 63) were 30.8 and 26.9 ppb ($P = .028$). We applied a numerical procedure designed to adjust for common interfering factors recently published by a group at our center [15] to the subjects with acute respiratory tract infections. When using the appropriate correction factor (1.235) for respiratory tract infections, mean FENO decreased from 29.6 to 25.8 ppb ($P = .034$). This means that a significant difference in FENO would also have been detected had we used all 63 subjects, either with or without the application of the correction factor. However, the increased variability due to infection was reflected by the fact that changes were less pronounced in comparison to the 43 subjects without respiratory tract infections. As we had previously found a decrease in FENO 4 to 6 weeks after the intervention [7], we wished to check whether this reduction would also be detectable using the stricter inclusion criteria applied in the second follow-up study, ie, in the group of subjects working in the stable, not smoking, and free of respiratory tract infection at baseline and both follow-up visits (n = 38). Using this sample, we found that the geometric mean (SEM) FENO at baseline (33.9 [1.1] ppb) had decreased significantly after 4 to 6 weeks (29.0 [1.1] ppb, $P = .005$) and 1 year (25.9 [1.1] ppb, $P = .001$). There was no statistically significant difference between the first and second follow-up values.

Respiratory symptoms were not significantly altered 1 year after the intervention. It is noteworthy that the percentage of subjects reporting wheeze while working in the stable decreased from 32.6% to 18.6%; the sample was too small, however, to detect any statistically significant differences. Since no significant changes in airway obstruction measures such as FEV_1 or FEV_1/FVC were observed, it would seem that FENO is the most sensitive outcome measure for asthma follow-up. It should be noted that the use of small portable devices for FENO and lung function measurements provided an easy, viable means of objectively evaluating the intervention in asthma patients in an epidemiological field setting. The approach, therefore, may be useful for future occupational and environmental intervention studies.

In contrast to the intervention group, the control group showed a slight but not significant increase in FENO from baseline (27.2 ppb) to follow-up (30.7 ppb). Due to the strict inclusion criteria employed, the control group was rather small but its primary purpose was to check for the long-term repeatability of measurements and not to discover additional factors that might influence FENO.

As often encountered with multimodal intervention or educational programs, no single factors underlying the reduction in FENO were discernible. Among others, exposure reduction, behavioral changes, and better compliance with medication may have contributed to the reduction. As our focus was on changes in FENO as an integrative outcome parameter, we did not aim to trace single causes in our limited sample of participants. Individual trends, however, were noticeable in subjects with large reductions in FENO. The most pronounced decrease (203 ppb to 60 ppb) was found in a subject who had reduced the amount of time spent in the stable from 3 to 1.5 hours a day, started using a respirator after the baseline measurement, and reduced the bed linen change interval from 5 to 2 weeks. The second largest decrease (98 ppb to 35 ppb) was found in a participant who had increased the amount of time he wore respiratory protective equipment in the stable from 80% to 100%, started to wash his hair before going to bed every day, and reduced the bed linen change interval from 4 to 2 weeks. Reduced exposure is likely to have contributed to the decrease in FENO levels in these patients and suggests that the educational intervention had been remarkably successful. This highlights the fact that, even though causative factors could not be singled out in the group, FENO seems to be a useful tool for the long-term monitoring of occupational asthma.

In conclusion, FENO levels were reduced 1 year after an educational intervention in dairy and swine farmers with occupational asthma, as found previously 4 to 6 weeks after the intervention, thus indicating that the education program was also a success in the long term. Therefore, FE_{NO}, which can be easily and quickly assessed in the field, should be considered for short-term and long-term evaluations in intervention studies dealing with occupational asthma.

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