

FeNO levels increase with degree of sensitisation in apprentices at risk of occupational asthma

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SUMMARY

BACKGROUND: Atopy has emerged as a major determinant of airway inflammation.

OBJECTIVE: To examine whether early markers of occupational asthma increase with degree of sensitisation.

METHOD: This study was a prospective follow-up study of apprentices in baking, pastry-cooking and hairdressing during their 2-year apprenticeship. Four visits were conducted to administer a standardised questionnaire, a methacholine challenge test to assess bronchial hyperresponsiveness (BHR) and to measure fractional exhaled nitric oxide (FeNO). Degree of sensitisation was estimated based on the number of positive skin prick tests (SPTs) for 12 common allergens. Mixed-effect models were applied to examine the association between the degree of sensitisation and FeNO levels, BHR and

eosinophilic status (more than 3% of cells in nasal lavage fluid).

RESULTS: Of the 441 apprentices who agreed to take part in the study, 417 had at least one SPT session providing usable results. Degree of sensitization was related to BHR and FeNO levels. Compared to non-sensitised subjects, FeNO levels were 83% higher ($P < 0.01$) in highly sensitised subjects and 30% higher ($P < 0.01$) in weakly sensitised subjects. However, the degree of sensitisation was not predictive of the evolution of these markers.

CONCLUSION: Degree of sensitisation is related to early markers of airway inflammation.

KEY WORDS: sensitisation; atopy; eosinophilic inflammation markers; bronchial hyperresponsiveness; occupational epidemiology

OCCUPATIONAL ASTHMA (OA) is the most frequently reported work-related lung disease in industrialised countries.¹ Bronchial hyperresponsiveness (BHR) has been shown in several circumstances to be predictive of OA.² Eosinophil count in nasal lavage and fractional concentration of exhaled nitric oxide (FeNO)³ are both higher in subjects with OA or BHR. The FeNO test is characterised by good reproducibility,⁴ and is validated as a non-invasive surrogate marker of eosinophilic airway inflammation.⁵ Although the added value of FeNO in diagnosing OA remains controversial,^{6,7} increased levels of FeNO have been repeatedly observed in occupationally exposed populations,^{8,9} and increases in FeNO have been shown to be predictive of BHR in our study population of baking, pastry making and hairdressing apprentices.¹⁰ However, FeNO depends on a number of modifying factors, in particular atopic status.¹¹

Studies in adults have revealed that atopy is one of the most important risk factors for the development

of OA and occupational rhinitis, especially when these diseases are immunoglobulin E (IgE) mediated.¹² ‘Atopy’ is a term used to describe a familial or personal tendency to develop allergen-specific IgE on exposure to environmental allergens, a constitutional trait¹³ that is commonly considered a qualitative trait. Only a few studies have considered this trait as possibly quantitative, and shown that it is related to wheezing and reduced lung function.^{14–17}

In the present paper, sensitisation to common pneumoallergens measured using the skin prick test (SPT) is used as a surrogate of atopy.^{18,19} We hypothesised that the number of common allergens to which a subject is sensitised differentially predicts the appearance of early markers of airway inflammation (FeNO levels and eosinophilic cells in nasal lavage), development of BHR and sensitisation to specific occupational agents. We examined these hypotheses in a cohort of non-asthmatic apprentices in occupations at risk of OA (baking, pastry making

and hairdressing) followed throughout their 2-year apprenticeship period.

METHODS

An in-depth methodological description of the study design has been provided elsewhere.²⁰ Briefly, the study comprised prospective follow-up of apprentice bakers, pastry makers and hairdressers over their 2-year apprenticeship period. Subjects who reported previous exposure to substances known to induce OA or who suffered from physician-diagnosed asthma were excluded.

The study was approved by the local ethics committee, and the apprentices (or parents of underage trainees) gave their written consent. An initial inclusion examination (visit 1 [V1]) was undertaken within 3 months of the start of each apprentice training programme, and three follow-up examinations were performed 6 (V2), 12 (V3) and 15 (V4) months after V1.

Questionnaires and clinical examination

Symptoms were assessed at each examination using a standardised questionnaire covering demographic information, known past and current allergies, past respiratory diseases and symptoms and a detailed passive and active smoking history.²¹

FeNO and BHR

FeNO concentrations were measured using the NIOX[®] chemiluminescence analyzer (Aerocrine AB, Solna, Sweden) in compliance with American Thoracic Society/European Respiratory Society recommendations,⁵ and was expressed in parts per billion (ppb). BHR was assessed using an abbreviated methacholine challenge test (MCT) with three cumulative successive doses (0.5, 3.0 and 8.0 μ mole). A linear two-point dose-response slope (DRS) in %/ μ mole was then calculated, as described in a previous paper.²² DRS values were normalised as NDRS = $1/(\text{slope} + 2.5)$.¹⁰ BHR and FeNO levels were measured at each examination.

Eosinophil count in nasal lavage fluid

Hilding's method was applied to perform nasal lavage.³ The absolute number of cells was counted and the percentage of eosinophils was calculated from this number. Subjects were considered as eosinophilic if the eosinophil count exceeded 3%.

Skin prick tests and sensitisation status

Sensitisation to common pneumoallergens and to workplace-specific allergens was assessed using SPT performed on the forearm at V1 and V4. Sensitisation status was assessed with a standard battery of 12 common allergens (Stallergènes, Antony, France) including acarians, animal danders, storage mites,

pollens and moulds (Table 1). Bakers and pastry makers were submitted to SPT for six specific occupational allergens (Stallergènes France): wheat, rye, oat and barley flours, alpha amylase and baker's yeast. As persulfate salts are the major agents involved in OA,²³ apprentice hairdressers were tested with a 1% solution of ammonium persulfates prepared daily by the pharmacological laboratory of the clinical trials centre at the local university hospital. A 10% histamine solution was used as a positive control and a phenolated 4% isotonic solution as a negative control. The largest wheal diameter was assessed after 20 min. An SPT was considered positive if the wheal diameter was 3 mm larger than that of the negative control. Degree of sensitisation was defined based on the number of positive reactions to common, i.e., non-specific, allergens. The maximum number of positive SPT between V1 and V4 was selected if the subject took part in two SPT sessions. Subjects were then classified into three groups: no positive SPT = non-sensitised, 1–2 positive SPT = weakly sensitised, ≥ 3 positive SPT = highly sensitised.

Statistical analyses

FeNO measurements expressed in ppb were log-transformed. Longitudinal models with subject-specific random intercepts were applied to assess changes in log-transformed FeNO, NDRS levels and eosinophils during follow-up as a function of the degree of sensitisation at an independent variable. As these statistical models are specific to longitudinal data, any difference between two time points will only be based on subjects providing data for both. All models included terms for examination, training track and sex. With regard to FeNO, the model was further adjusted for subject height and smoking status.¹¹ As the population was uniform with respect to age, this was never taken into account. The main outcomes of these models were the main effects and interactions of sensitisation, training track and visit.

We performed the same analyses based on allergen families (mites, pollens, animal danders and moulds) to account for possible cross-sensitisation. Subjects were then classified according to the number of allergen families to which they were sensitised: none, 1–2 families and 3–4 families.

RESULTS

Of the 441 apprentices who agreed to take part in the study, 417 had at least one SPT session that gave usable results. Table 1 shows the characteristics of this population at inclusion and during follow-up. Overall, the number of positive SPTs for common allergens stayed constant between V1 and V4 (Table 2). The number of subjects newly sensitised at V4 was

Table 1 Population characteristics

	Bakers <i>n</i> (%)	Pastry makers <i>n</i> (%)	Hairdressers <i>n</i> (%)
Subjects, <i>n</i>	150	106	161
Male	141 (94.0)	84 (79.3)	12 (7.5)
Female	9 (6.0)	22 (20.8)	149 (92.6)
Age at start of training programme, years, mean $\pm$ SD	16.9 $\pm$ 1.4	16.8 $\pm$ 1.2	17 $\pm$ 1.5
Methacholine tests per subject, <i>n</i> , mean $\pm$ SD	3.1 $\pm$ 0.99	3.3 $\pm$ 0.8	3.4 $\pm$ 0.7
DRS at inclusion, %/ μ mole methacholine, mean $\pm$ SD	1.45 $\pm$ 5.13	1.06 $\pm$ 2.22	0.97 $\pm$ 1.20
FeNO measurements per subject, <i>n</i> , mean $\pm$ SD	3.1 $\pm$ 0.96	3.2 $\pm$ 0.9	3.3 $\pm$ 0.8
FeNO measurements at inclusion, ppb, mean $\pm$ SD	21.0 $\pm$ 23.1	19.8 $\pm$ 17.3	15.5 $\pm$ 15.0
Nasal lavage per subject, <i>n</i> , mean $\pm$ SD	2.9 $\pm$ 1.17	3.0 $\pm$ 1.2	3.3 $\pm$ 0.8
Number of lavages with eosinophils >3% at inclusion	16 (12)	16 (17)	15 (10)
SPT sessions per subject, <i>n</i> , mean $\pm$ SD	1.5 $\pm$ 0.5	1.6 $\pm$ 0.4	1.7 $\pm$ 0.5
SPT positive response to common allergens			
Any common allergen	59 (39.3)	45 (42.5)	51 (31.7)
<i>Dermatophagoides farinae</i>	35 (23.33)	29 (27.36)	24 (14.91)
<i>Dermatophagoides pteronyssinus</i>	47 (31.33)	30 (28.30)	32 (19.88)
12 grass pollens	28 (18.67)	19 (17.92)	30 (18.63)
Cat	19 (12.67)	13 (12.26)	8 (4.97)
Dog	10 (6.67)	5 (4.72)	3 (1.86)
Storage mites	8 (5.33)	1 (0.94)	4 (2.48)
4 cereal pollens (corn, wheat, barley, oat)	27 (18)	17 (16.04)	23 (14.29)
Herbaceous pollens	7 (4.67)	2 (1.89)	5 (3.11)
Tree pollens	5 (3.33)	2 (1.89)	8 (4.97)
<i>Betulacea</i> pollens (alder, birch, hornbeam, hazel tree)	11 (7.33)	8 (7.55)	9 (5.59)
<i>Alternaria tenuis</i>	7 (4.67)	7 (6.60)	7 (4.35)
<i>Aspergillus mix</i>	2 (1.33)	1 (0.94)	3 (1.86)
Degree of sensitisation (number of positive responses)*			
Non-sensitised (no positive response to common allergens)	91 (60.7)	61 (57.6)	110 (68.3)
Weakly sensitised (1 or 2 positive response/s to common allergens)	27 (18)	22 (20.8)	31 (19.3)
Highly sensitised (>2 positive responses to common allergens)	32 (21.3)	23 (21.7)	20 (12.4)

* Maximum number of positive SPTs between examination 1 and examination 4 in the 250 subjects who took part in two SPT sessions. SD = standard deviation; FeNO = fractional exhaled nitric oxide; DRS = dose-response slope; SPT = skin prick test.

close to the number of subjects whose V1 sensitisation had disappeared at V4.

Table 3 compares sensitisation with workplace-specific allergens at V1 and V4. Among bakers and pastry makers, highly sensitised subjects seemed more likely to be sensitised to bakery-specific allergens than non-sensitised subjects at either V1 or V4. However, irrespective of the training track, there was no relationship between sensitisation status and new sensitisation to occupational allergens at V4. In particular, the apparent difference between highly sensitised bakers and pastry makers was not significant.

The Figure presents predicted values per examination and sensitisation status based on mixed-effect

regression models for the main clinical outcomes including examination $\times$ sensitisation status interactions. No interaction was significant, except for FeNO (upper left graph). The evolution by exami-

Table 3 Sensitisation to workplace-specific allergens at V1 and V4 according to the degree of sensitisation to common allergens in subjects who took part in both SPT sessions (*n* = 250)

	Bakers (<i>n</i> = 81) <i>n</i> (%)	Pastry makers (<i>n</i> = 64) <i>n</i> (%)	Hairdressers (<i>n</i> = 105) <i>n</i> (%)	Total (<i>n</i> = 250) <i>n</i> (%)
Non-sensitised				
0-0*	46 (96)	36 (97)	64 (94)	146 (95)
1-1	0	0	1 (1)	1 (1)
1-0	0	0	0	0
0-1	2 (4)	1 (3)	3 (5)	6 (4)
Total	48 (100)	37 (100)	68 (100)	153 (100)
Weakly sensitised				
0-0	15 (88)	15 (100)	21 (100)	51 (96)
1-1	0	0	0	0
1-0	1 (6)	0	0	1 (2)
0-1	1 (6)	0	0	1 (2)
Total	17 (100)	15 (100)	21 (100)	53 (100)
Highly sensitised				
0-0	7 (44)	10 (83)	14 (88)	31 (70)
1-1	5 (31)	2 (17)	2 (12)	9 (20)
1-0	1 (6)	0	0	1 (3)
0-1	3 (19)	0	0	3 (7)
Total	16 (100)	12 (100)	16 (100)	44 (100)

* 0-0 = no sensitisation at both SPT sessions; 1-1 = sensitisation at both SPT sessions; 1-0 = sensitisation at V1 but not at V4; 0-1 = new sensitisation at V4. V = visit; SPT = skin prick test.

* 0-0 = no sensitisation at both SPT sessions; 1-1 = sensitisation at both SPT sessions; 1-0 = sensitisation at V1 but not at V4; 0-1 = new sensitisation at V4. V = visit; SPT = skin prick test.

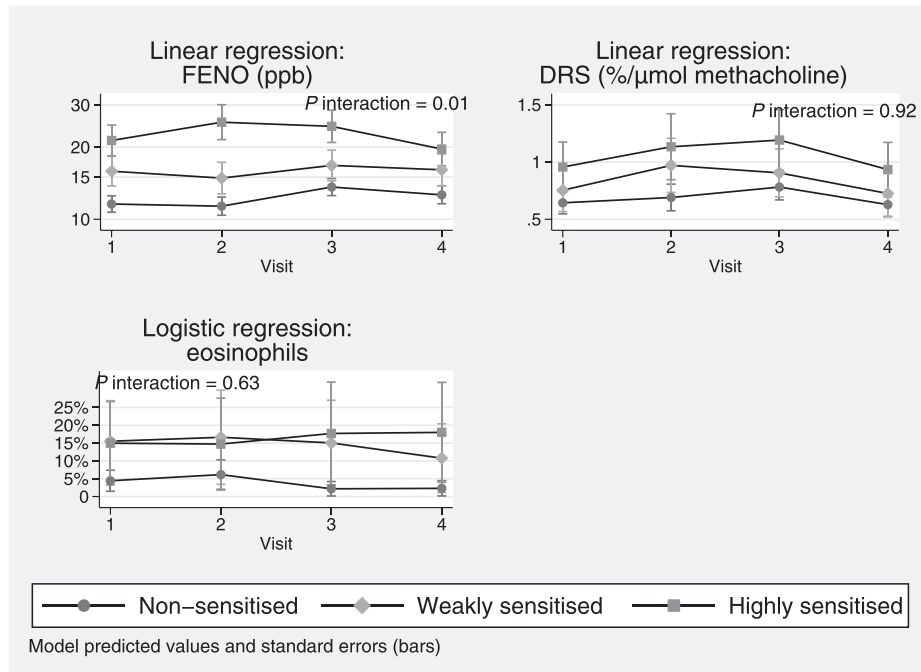


Figure Model of predicted values of FeNO, DRS from the methacholine challenge test and eosinophilic status according to examination and degree of sensitisation to common allergens. FeNO = fractional exhaled nitric oxide; ppb = parts per billion; DRS = dose-response slopes.

nation of FeNO levels differed significantly with respect to degree of sensitisation (test for interaction $P = 0.01$): the FeNO values increased significantly between V1 and V2 among highly sensitised subjects, although they seemed to decrease at V3 and V4.

Table 4 presents the results of the analyses, ignoring these interactions. Overall FeNO concentration increased with degree of sensitisation, and the pairwise comparisons of the three groups were all highly statistically significant ($P < 0.001$). The same feature was observed for the DRS from the methacholine challenge test, although pair-wise comparisons between weakly sensitised and non-sensitised cases and between highly sensitised and non-sensitised cases were just above the 5% significance level. Positive eosinophilic status (eosinophils in nasal fluid $>3\%$) was more frequent among the highly sensitised ($P < 0.001$) and among the weakly sensitised ($P <$

0.001) than among the non-sensitised; however, no difference between the highly sensitised and the weakly sensitised was found ($P = 0.69$).

Similar results and trends were observed using SPT data from V1 only. In particular, FeNO levels remained significantly different when comparing sensitisation status (highly sensitised vs. non-sensitised, $P < 0.001$ /weakly sensitised vs. non-sensitised, $P < 0.001$ /highly sensitised vs. weakly sensitised, $P = 0.001$, data not shown).

Table 5 shows these outcomes as a function of training track and its interaction with the degree of sensitisation. FeNO concentrations increased significantly with the degree of sensitisation, and its interaction with training track is borderline significant on the whole ($P = 0.07$). The increase in FeNO in the highly sensitised was significantly more marked in bakers and pastry makers than in hairdressers ($P = 0.02$).

Table 4 Results of the mixed-effect regression model for FeNO, NDRS from the methacholine challenge test and presence of eosinophils* according to degree of sensitisation

	Weakly sensitised vs. non-sensitised		Highly sensitised vs. non-sensitised		Highly sensitised vs. weakly sensitised
	Coefficient (95%CI)	P value	Coefficient (95%CI)	P value	P value
log FeNO*	0.26 (0.13 to 0.40)	<0.001	0.60 (0.46 to 0.74)	<0.001	<0.001
NDRS†	0.014 (−0.001 to 0.028)	0.066	0.032 (0.017 to 0.047)	<0.001	0.052
More than 3% eosinophils‡	1.36 (0.79 to 1.94)	<0.001	1.49 (0.90 to 2.01)	<0.001	0.689

* Linear mixed-effect model of log-transformed FeNO, adjusted for training track, sex, height, examination and smoking status.

† Linear mixed effect model of the NDRS from the methacholine challenge test adjusted for training track, sex and examination.

‡ Logistic mixed-effect model of the presence of $>3\%$ eosinophils adjusted for training track and examination.

FeNO = fractional exhaled nitric oxide; NDRS = normalised dose-response slopes; CI = confidence interval.

Table 5 Results of the mixed-effect linear regression model for FeNO and NDRS from the methacholine challenge test according to training track and degree of sensitisation

	log FeNO: mixed-effect linear regression model*		NDRS: mixed-effect linear regression model†	
	Exponentiated coefficient (95%CI)	P value	Coefficient (95%CI)	P value
Training track: bakers and pastry makers vs. hairdressers	1.14 (0.94 to 1.39)	0.17	0.005 (−0.02 to 0.03)	0.64
Degree of sensitisation				
Weakly sensitised vs. non-sensitised	1.23 (0.99 to 1.53)	0.06	−0.01 (−0.04 to 0.01)	0.23
Highly sensitised vs. non-sensitised	1.42 (1.10 to 1.83)	<0.01	−0.01 (−0.04 to 0.02)	0.47
Global test		0.01		0.43
Training track × degree of sensitisation interaction				
Baker and pastry maker vs. hairdressers × weakly sensitised	1.09 (0.83 to 1.44)	0.52	0.000 (−0.03 to 0.03)	0.98
Baker and pastry maker vs. hairdressers × highly sensitised	1.44 (1.06 to 1.95)	0.02	−0.03 (−0.06 to 0.001)	0.06
Global test for interaction		0.07		0.15

* Adjusted for examination ($P < 0.001$), sex ($P = 0.27$), height ($P = 0.008$) and smoking status ($P < 0.001$).

† Adjusted for examination ($P = 0.003$) and sex ($P = 0.97$).

FeNO = fractional exhaled nitric oxide; NDRS = normalised dose-response slopes; CI = confidence interval.

Interaction between training track and degree of sensitisation on DRS values was not significant ($P = 0.15$). However, degree of sensitisation tended to have more effect among bakers and pastry makers than among hairdressers ($P = 0.06$). There was no interaction ($P = 0.78$) between training track and degree of sensitisation on eosinophilic status (data not shown).

The three-way interaction between degree of sensitisation, training track and examination was marginally significant for FeNO ($P = 0.06$; Appendix*) but not for NDRS ($P = 0.75$).

DISCUSSION

Degree of sensitisation, defined as the number of positive SPTs for common allergens, is related to BHR and markers of bronchial eosinophilic inflammation in a cohort of young and initially asymptomatic apprentices at risk of OA. However, the degree of sensitisation is not found to be predictive of variations in these markers. Moreover, the difference in FeNO levels between highly sensitised and non-sensitised participants is significantly higher among bakers and pastry makers than among hairdressers.

The relationship between BHR and the number of SPTs positive for common allergens was reported to be significant in five, albeit cross-sectional, studies.^{24–28} Three^{25–27} were conducted in children and two^{24,28} in young adults, but none in an occupational setting.

In the present paper, the clearest relationship with degree of sensitisation was obtained in the case of FeNO levels which, to our knowledge, has only been reported once, in a recent paper by Scott et al.²⁹ in a non-occupational population. It must be stressed that while the sensitisation profile affects FeNO levels,

eosinophilic status and BHR, it does not seem to affect their variations in time. However, this result holds only for our relatively short follow-up, and longer prospective studies are required to confirm our findings. It should be noted that a recent study with a longer follow-up of apprentices appears to be in line with our findings.³⁰

Finally, the effect of high sensitisation on FeNO levels is significantly greater among bakers and pastry makers than among hairdressers. This is consistent with the fact that bakers and pastry makers are exposed to flour dust, which is known to cause IgE-mediated OA, whereas the immunological mechanisms of OA are still not fully understood for hairdressers.²³ This supports the hypothesis that the type of allergen to which the individual is sensitised and the number of skin reactions to common allergens are factors that may interact to increase the risk of BHR or bronchial eosinophilic inflammation.²⁵ The slight differences between bakers and pastry makers might be due to greater exposure in bakers.³¹

These results should be interpreted in the light of the strengths and weaknesses of our study. Although not all subjects had two SPTs, we showed that the SPT data remained the same at V1 and V4 for most subjects. This suggests that SPTs positive to common allergens remained constant over a 15-month period and can therefore be considered a valid, repeatable method for assessing degree of sensitisation.

Not all the allergens used for SPT belonged to today's standard battery of allergens,³² and our study is therefore not reproducible. However, our main finding is the existence of a relationship between the degree of sensitisation and airway inflammation. We hypothesise that this remains valid irrespective of the battery of allergens used.

At present, there is no standard method of quantifying sensitisation to common allergens.³³ It

* The appendix is available in the online version of this article, at <http://www.ingentaconnect.com/content/iuatld/ijtd/2017/00000021/00000011/art00017>

could be argued that quantifying sensitisation according to the number of SPTs positive for common allergens may underestimate the sensitisation status of subjects who react strongly, but only to a few allergens. We believe that expressing sensitisation profiles in terms of the number of different allergens to which one is sensitised is more relevant. Similar results were obtained using the sum of total wheal sizes (data not shown).

In line with the European Academy of Allergy and Clinical Immunology position paper,² we found sensitisation to workplace-specific allergens to be related to sensitisation to common allergens among subjects with at least three positive reactions to common allergens. However, the number of sensitised subjects was very low, and we could not find any link between new sensitisation to occupational allergens and sensitisation to common allergens. For hairdressers, this might also be due to a relatively low concentration of persulfates. Given the lack of standardisation of the extracts used, our results for occupational allergens should be interpreted with caution. The procedures required to obtain consent from the volunteer apprentices and/or their parents meant that 85% of the subjects could not be initially examined before 3 months after the start of the training programme. This would explain why some subjects (mostly the highly sensitised) were already sensitised to occupational allergens at the first SPT session, although the time required to acquire sensitisation to occupational allergens, particularly to high-molecular-weight allergens, is longer than 3 months.³⁴

A major strength of this study is the sample of a non-asthmatic, exposed population. The relationships uncovered were therefore not due to pre-existing asthmatic conditions, which could be the case in cross-sectional studies. Our findings thus support the hypothesis that BHR and eosinophilic status in fact precede potential occurrence of asthma symptoms.

CONCLUSION

Our findings give support to the idea that testing sensitisation to common allergens in workers subject to early exposure to agents known to cause OA could help detect those who are at greater risk of developing OA, especially when exposed to IgE-mediated allergens.

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Conflicts of interest: none declared.

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APPENDIX

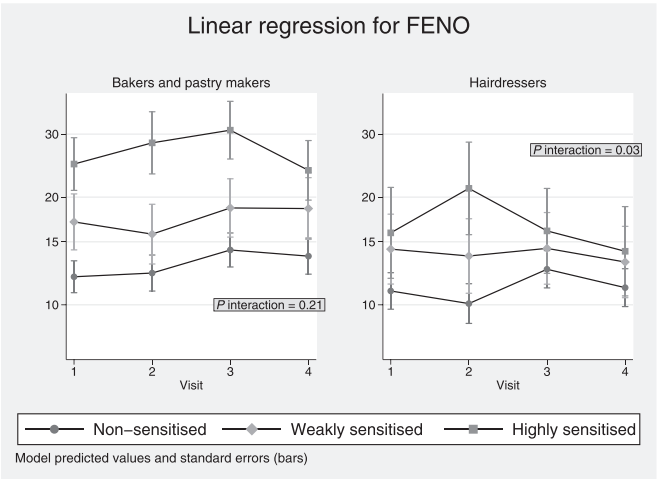


Figure A Predicted values of FeNO by visit, degree of sensitisation and training track.

RESUME

CONTEXTE : L'atopie est reconnu comme un des déterminants majeurs de l'inflammation bronchique.

OBJECTIF : Examiner si des marqueurs précoces de l'asthme professionnel augmentent avec le degré de sensibilisation.

MÉTHODES : Cette étude était fondée sur une étude prospective d'apprentis boulangers, pâtisseries et coiffeurs pendant leurs 2 ans d'apprentissage. Ce suivi a inclus quatre visites avec un questionnaire standardisé, un test de provocation bronchique (BRH) à la méthacholine et la mesure de l'oxyde nitrique exhalé (FeNO). Le degré de sensibilisation a été évalué par le nombre de prick test cutanés positifs (SPT) pour 12 allergènes communs. Des modèles mixtes ont été utilisés pour examiner l'association entre le degré de

sensibilisation d'une part et les niveaux de FeNO, le BRH et le statut éosinophilique (>3% des cellules d'un liquide de lavage nasal) d'autre part.

RÉSULTATS : Sur les 441 apprentis qui ont accepté de participer, 417 avaient au moins un SPT utilisable. Le degré de sensibilisation était lié au BRH et aux niveaux de FeNO. Ce dernier était plus élevé de 83% ($P < 0,01$) chez les sujets fortement sensibilisés et de 30% chez les sujets faiblement sensibilisés ($P < 0,01$) comparé au groupe des sujets non-sensibilisés. Cependant le degré de sensibilisation n'était pas prédictif de l'évolution de ces marqueurs.

CONCLUSION : Le degré de sensibilisation est lié aux marqueurs précoces de l'inflammation bronchique.

RESUMEN

MARCO DE REFERENCIA: La atopía ha surgido como un determinante mayor de la inflamación de las vías respiratorias.

OBJETIVO: Investigar si los marcadores tempranos del asma profesional aumentan en función del grado de sensibilización.

MÉTODO: El estudio se fundamentó en un seguimiento prospectivo de los aprendices en panadería, pastelería o peluquería durante los 2 años de su período de aprendizaje. Se realizaron cuatro consultas, que incluían un cuestionario normalizado, una prueba de provocación con metacolina a fin de examinar la hiperreactividad bronquial (BRH) y mediciones de la fracción exhalada de óxido nítrico (FeNO). El grado de sensibilización se evaluó según el número de resultados positivos a las pruebas cutáneas por punción (SPT) para 12 alérgenos frecuentes. Se aplicó un modelo de efectos fijos a fin de examinar la asociación entre el grado de

sensibilización y las concentraciones de FeNO, la BHR y el estado eosinofílico (más de 3% de las células en el líquido del lavado nasal).

RESULTADOS: Aceptaron participar en el estudio 441 aprendices, de los cuales 417 presentaron por lo menos una sesión de SPT con resultados utilizables. El grado de sensibilización se relacionó con la BHR y la concentración de FeNO. En comparación con las personas no sensibilizadas, la concentración de FeNO fue 83% más alta en las personas altamente sensibilizadas ($P < 0,01$) y 30% más alta en las personas con una baja sensibilización ($P < 0,01$). Sin embargo, el grado de sensibilización no permitió pronosticar la evolución de estos marcadores.

CONCLUSIÓN: El grado de sensibilización guarda relación con los marcadores tempranos de inflamación de las vías respiratorias.
