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Methacholine responsiveness, respiratory symptoms and pulmonary function in aluminium potroom workers

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ABSTRACT: The relationship between nonspecific bronchial reactivity and work-related asthmatic symptoms was examined in a cross-sectional study of 337 aluminium potroom workers by a shortened method of continuous methacholine nebulization. The provocative concentration producing a 20% fall in forced expiratory volume in one second (FEV_1) (PC_{20}) was ≤8 mg·ml⁻¹ (hyperresponsiveness) in 17 workers (5%), whilst minor responsiveness (8 mg·ml⁻¹ < PC_{20} <32 mg·ml⁻¹) was present in 24 subjects (7%). The prevalence of work-related asthmatic symptoms was 9%. Female sex, ex-smoker and airflow limitation were significant predictors of methacholine responsiveness ($p<0.05$). In a multiple logistic regression analysis the odds ratios (OR) for work-related asthmatic symptoms was 10.8 (95% confidence interval: 2.9–40.6) for hyperresponsiveness and 4.4 (95% confidence interval: 1.2–16.4) for minor responsiveness. The sensitivity, specificity and predictivity of PC_{20} <32 mg·ml⁻¹ for work-related asthmatic symptoms were 35, 92 and 35%, respectively, whilst the agreement, when adjusted for the by chance expectation, was 0.27 (95% confidence interval: 0.10–0.54). Although a significant association was found between bronchial reactivity and work-related asthmatic symptoms, the usefulness of the methacholine test as a tool for detection of work-related asthmatic symptoms appears to be of limited value due to its low sensitivity.
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Nonspecific bronchial challenge has been suggested as a more objective method than questionnaires to assess the prevalence of asthma and related conditions in epidemiological surveys [1, 2]. Measurement of bronchial reactivity has therefore gained usage in epidemiological studies of asthma, and has also been applied in the diagnosis and surveillance of occupational asthma. Although the sensitivity in asthmatics has been claimed as good [3–5], there is increasing evidence that nonspecific bronchial challenge is not a fully sensitive test for asthma [6, 7]. Dodge [6] refers to several studies where nonspecific bronchial responsiveness has been reported as normal in diagnosed occupational asthma or has returned to normal after persons have left their work.

Occupational asthma related to aluminium potroom exposure was reported as early as 1936, and later studies have confirmed the original observation [8]. Also, the presence of nonspecific bronchial reactivity has been reported in potroom workers with occupational asthma [9, 10]. The pot emissions consist of known respiratory irritants such as hydrogen fluoride (HF) and sulphur dioxide (SO_2). The airborne dust contains alumina, cryolite, carbon and aluminium fluoride with minor amounts of vanadium, chromium and nickel. About 40% of the airborne dust is in the respirable range. Polycyclic aromatic hydrocarbons are also present. There are no definite respiratory sensitizers as major constituents of the pollutants. However, chemical workers exposed to aluminium fluoride have been shown to develop asthma, which improves away from exposure, and increased bronchial reactivity [11]. The metal elements vanadium, nickel and chromium are known sensitizers [12]. It is not known whether exposure sufficient to cause disease occurs in the potroom.

The aims of the present study were firstly to describe the prevalence of methacholine responsiveness, secondly to assess the correlation between methacholine responsiveness and respiratory symptoms as well as pulmonary function, and thirdly to evaluate the methacholine challenge as a tool for detection of work-related asthmatic symptoms in a cross-sectional study.

Materials and methods

The present cross-sectional survey was a supplement to a longitudinal study of methacholine responsiveness in potroom workers at Årdal aluminium plant in Western Norway. The smelter had three potroom departments, all with their own working staff. There was one Soderberg, one prebake with automatic alumina delivery (without lifting the pot covers) and one prebake with alumina delivery from a circulating vehicle. Dry scrubbed, recovery alumina was used on the prebake pots, whilst pure alumina was used on the pots in the Soderberg department. The average levels of exposure during the year of the study as measured by personal samplers are shown in table 1. Methacholine challenge was carried out in September and October 1988. The local union and management agreed with the project which was approved by the Regional Ethical Committee. Informed consent was obtained from all participants.

Table 1. – Geometric mean levels of exposure from personal samplers worn over the whole workshift from major job groups in the potrooms studied

	Total particulates HS 5.0 mg·m^{-3}			Total fluorides HS 1.0 mg·m^{-3}		
	Prebake		Soderberg	Prebake		Soderberg
	1	2	3	1	2	3
Pot operator	4.0	1.4	1.8	0.7	0.4	0.3
Pot service	7.3	-	1.6	0.8	-	0.3
Vehicle driver	4.3	0.9	1.8	0.8	0.2	0.2
Foreman	0.5	0.2	1.2	0.2	0.2	0.2

HS: hygienic standards.

Subjects

All potroom workers, female and male (aged 18–67 yrs), were invited to take part in the study. Of the 380 workers registered as potroom employees, 370 subjects (97%) were available at the time of the examination by questionnaires and spirometry. A control group of 59 new employees with no history of potroom exposure were included.

Of the 370 exposed workers only four subjects (1%) had forced expiratory volume in one second (FEV_1) <60% of predicted and were excluded from the methacholine testing. Twenty nine subjects (8%) refused to attend the methacholine challenge; thus, 337 workers (91%) had this test. There were no significant differences between challenged workers and those who refused challenge with regard to smoking habits and occurrence of symptoms, whilst median age was highest in the latter group (41 *vs* 32 yrs). The unexposed workers underwent a methacholine challenge after passing the usual pre-employment examination and before they started work.

Questionnaires

Respiratory symptoms (dyspnoea, wheezing and cough) during the last year, presence of familial asthma, asthma prior to potroom employment, use of airway protection and smoking habits were recorded by a self-administered questionnaire [13]. In a second stage, a standardized interview questionnaire was administered by trained interviewers [13]. This questionnaire was partly based on the questionnaire prepared by the British Medical Research Council [14], and was supplemented by questions on frequency of symptoms, on the occurrence of symptoms on workdays, on rest-days and on longer vacations.

Spirometric measurements

FEV_1 was measured on a dry bellow spirometer (Jones Pulmonaire, Jones Medical Instruments Co., Oak Brook, Illinois). FEV_1 and forced vital capacity (FVC) were normally taken as the highest values from the first three technically satisfactory forced expirations. The FVC value chosen should not exceed the next highest by more than 0.3 *l*. Measurements were converted to body temperature and pressure saturated (BTPS). Spirometry testing was conducted with the subject standing and without a noseclip as only forced expiratory volumes were registered. The testing procedure followed the recommendations of The American Thoracic Society with a few modifications [15]. Measurements were converted to BTPS. The prediction equations estimated from a general population in Norway were used to define levels as percentage of predicted [16]. Standardized residuals of FEV_1 ($SFEV_1$) were obtained by dividing the absolute residual (recorded FEV_1 - predicted) by the residual standard deviation (RSD) taken from the regression equations used to predict lung function [16]. Standardized residuals have the same scale for all lung function indices and are normally distributed around the mean, hence avoiding the age and height bias introduced by the percentages of predicted values [17].

Methacholine provocation test

The tests were carried out by trained nurses and a plant physician during the first 4 h of a day-shift and within the first 3 days of a working week. Subjects were asked not to smoke in the 2 h before their appointment. Theophyllines and antihistamines, or inhaled bronchodilator were not to be taken within 24 and 6 h, respectively, prior to the test. None of the subjects used corticosteroids in any form. Subjects whose baseline FEV_1 was ≥ 60% of predicted, had a methacholine challenge test, using a modification of the method of Cockroft *et al.* [18]. The procedure for inhalation of methacholine was carefully standardized. The reproducibility of nebulizer output, one of the most important technical factors, has been thoroughly examined in this industrial setting [19]. Subjects reporting wheezing and dyspnoea or FEV_1 within the range of 60–70% of predicted were given a starting dose of 0.125 $mg \cdot ml^{-1}$ methacholine, otherwise the first dose was 2 $mg \cdot ml^{-1}$. Unless FEV_1 decreased by > 10% from one concentration to the next, or was < 85% of the pretest value, fourfold increments of the dose with 2 min of inhalation at each concentration were given. Otherwise, a doubling of the dose was given. Saline control was omitted to further shorten the procedure. FEV_1 was measured 30 and 90 s after each dose. If the FEV_1 declined by more than 10% from one concentration to the next, a doubling of the dose was given. The challenge was stopped if a maximum concentration of 32 $mg \cdot ml^{-1}$ was reached, or the FEV_1 decreased by >20% from the baseline value.

The PC_{20} was estimated by linear interpolation on a logarithmic scale on the basis of data from the last two points on the noncumulative dose-response curve.

Methacholine challenge proved to be feasible in this industrial setting. On average the test was carried out in 23 (SD 6) min and no unpleasant symptoms were experienced by the subjects.

Skin tests

Immunological identification of atopy was made by skin prick testing. Registration of the wheal was done 15 min after application of dog epithelium, common silver birch, timothy grass, mugwort and house mite, with saline and histamine as controls (Phazet skin prick test, Nyegaard & Co.). The wheal diameters were measured in mm, as the mean of the long axis and its perpendicular.

Exposure measurements

During the year of the study measurements of total airborne dust and total fluorides (fluorides in gas and particulate form) had been regularly performed from personal samplers with filters to absorb dust and fluoride. Sampling was done during 4 to 8 h and time-weighted average exposures were calculated. The amounts of trace elements (vanadium, chromium and nickel) were not available for the present survey, but in another Norwegian plant were reported to be far below the hygienic standards for the respective elements [20]. Ninety percent of the workers reported that they regularly wore airways protection (Racal airstream helmet or 3-M disposable mask) in order to reduce inhalation of pollutants.

Definitions

The following classification on smoking habits was used: never smokers were lifelong nonsmokers; ex-smokers were those who stopped smoking at least one year prior to the study; whilst all other subjects were classified as current smokers.

Cough was defined as chronic or episodic cough apart from colds; work-related asthmatic symptoms as dyspnoea and wheezing apart from colds with improvement on rest-days or vacations and absence of asthma before employment. Symptoms should have been present within the previous 12 mths.

Normal methacholine responsiveness was defined as a < 20% decrease in FEV_1 from baseline value at a methacholine concentration of 32 $mg \cdot ml^{-1}$. Subjects defined to have abnormal methacholine responsiveness were divided into two groups: minor responsiveness as PC_{20} between 8.1 and 32 $mg \cdot ml^{-1}$ and methacholine hyperresponsiveness as PC_{20} ≤8 $mg \cdot ml^{-1}$.

Atopy was defined according to the wheal of the skin test and scored as follows: Negative = no different from the saline control; Equivocal = larger than 1 mm but less or equal to the histamine wheal; Positive = larger than the histamine wheal.

Data analysis

Agreement between work-related asthmatic symptoms and methacholine responsiveness was expressed by the kappa value which takes into account the by chance agreement [21]. Associations between respiratory symptoms and methacholine responsiveness were also analysed by multiple logistic regression using symptoms as dependent variables and responsiveness as a categorical, independent variable. Furthermore, the relationships between methacholine responsiveness and certain personal characteristics were analysed by multiple logistic regression with methacholine responsiveness as the dependent variable. The logistic model included the interaction terms smoking *$SFEV_1$, sex*smoking and sex*$SFEV_1$. The principal model was constructed using the Generalized Linear Interactive Modelling (GLIM) system [22]. Associations in contingency tables were studied with Chi-squared values. One way analysis of variance was applied to examine differ ences in group means of $SFEV_1$. Differences in age between groups were assessed by the nonparametric Kruskal-Wallis' test using The Statistical Package for The Social Sciences (SPSS-PC) [23].

Results

Of the 337 potroom workers tested, 17 (5%) had a PC_{20} ≤8 $mg \cdot ml^{-1}$, while 24 (7%) were minor responders (table 2). In 59 subjects unexposed to the potroom atmosphere, only one had a PC_{20} < 8 $mg \cdot ml^{-1}$ and 3 (5%) ≤ 32 $mg \cdot ml^{-1}$.

Table 2. – Characterisitcs of unexposed controls and of exposed aluminium potroom workers by degree of bronchial responsiveness to methacholine

		Responsiveness mg·ml⁻¹				
		≤8 n=17	8.1–32 n=24	>32 n=296	Total n=337	Unexposed n=59
Age yrs	Median	40	37	31	32	24
	LQ	31	25	24	24	21
	UQ	47	46	44	44	29
Gender						
Male	n	12	18	269	299	59
Female	n	5	6	18	38	0
Smoking status						
Lifetime NS	n	2	2	79	83	11
Past	n	3	5	22	30	1
Current	n	12	17	195	224	47
Atopy						
Negative	n	13	17	222	252	21
Equivocal	n	2	1	38	41	17
Positive	n	2	6	36	44	19
Familial asthma						
Present	n	4	9	49	62	7
Absent	n	13	15	247	275	52
Airway protection						
Yes	n	16	23	267	306	-
No	n	1	1	29	31	-
$SFEV_1$	Mean	-1.23	-1.40	-0.62	-0.70	-0.84
	SD	0.93	0.74	0.87	0.89	0.88

LQ: lower quartile; UQ: upper quartile; FEV_1: forced expiratory volume in one second; $SFEV_1$: standardized FEV_1 residual *i.e.* (observed FEV_1 - predicted)/RSD (from the regression equation of the predicted values taken from GULSVIK [16]); lifetime NS: lifetime nonsmoker; RSD: residual standard deviation; n: number.

Methacholine responsiveness and personal characteristics

Exposed subjects with abnormal methacholine responsiveness were older than subjects with a normal methacholine reactivity, although the differences did not reach statistical significance (p=0.08, Kruskal-Wallis' test) (table 2). The percentage of workers with abnormal bronchial responsiveness was significantly higher among females (29%) than among males (10%) (p<0.01). The prevalence of methacholine responders was higher in ex-smokers (27%) and current smokers (13%), than in lifetime nonsmokers (5%), whilst only the difference between lifetime nonsmokers and ex-smokers was statistically significant (p<0.01). A positive skin prick test (atopy) and use of airway protection were unrelated to methacholine responsiveness, whilst the prevalence of abnormal responsiveness was significantly higher in subjects with a family history of asthma (21%) compared to those without (10%). $SFEV_1$ was significantly lower in responders than in non-responders (p<0.001).

The controls were younger than the exposed workforce, whilst the prevalence of smokers (80%) and subjects with a positive skin test (32%) was higher than seen in the exposed workers, 66 and 11%, respectively, (table 2). No significant differences in $SFEV_1$ were present between exposed and unexposed workers.

Table 3. – Adjusted odds ratios (OR) for methacholine responsiveness (PC_{20} ≤32 mg·ml⁻¹) by some characteristics of aluminium potroom workers, using multiple logistic regression

	OR	95% CI
Sex (females *vs* males)	5.7	2.2–14.8
Age*	1.3	1.0–1.8
Smoking habits		
ex *vs* nonsmoker	6.4	1.5–28.4
current *vs* nonsmoker	2.3	0.8–7.1
Atopy (present *vs* absent)	1.4	0.8–2.3
Familial asthma		
(present *vs* absent)	1.2	0.7–2.2
$SFEV_1$	0.3	0.2–0.5
Airway protection		
occasional and always *vs* never	1.6	0.3–7.7

95% CI: 95% confidence interval; *: age is grouped in intervals of 10 yrs; PC_{20}: provocative concentration producing a 20% fall in forced expiratory volume in one second. For further abbreviations see legend to table 2.

Table 4. – Prevalence of respiratory symptoms in unexposed controls and by degree of bronchial responsiveness in exposed aluminium potroom workers

		Responsiveness ($mg \cdot ml^{-1}$) in exposed workers				
		≤8 n=17	8.1–32 n=24	>32 n=296	Total n=337	Unexposed n=59
No symptoms	n (%)	7 (3)	13 (5)	222 (92)	242	53
Dyspnoea*	n (%)	10 (14)	8 (11)	53 (75)	71	4
Wheezing*	n (%)	8 (13)	9 (15)	44 (72)	61	4
Coughs*	n (%)	6 (14)	5 (12)	32 (74)	43	2
WASTH*	n (%)	6 (19)	5 (16)	20 (65)	31	-

*: distribution of bronchial responsiveness in exposed subjects significantly different from that in subjects with no symptoms ($p<0.01$, Chi-squared); WASTH: work-related asthmatic symptoms; n=number.

Table 3 shows the results from a multiple logistic regression analysis with methacholine responsiveness as the dependent variable and age, sex, smoking status, atopy, familial asthma, airway protection and $SFEV_1$, as independent variables. Adjusted odds ratios (OR) were significantly higher in females (OR=5.7; 95% confidence interval, 2.2–14.8) compared to males,and in ex-smokers (OR=6.4; 95% confidence interval, 1.5–28.4) *versus* lifetime nonsmokers. Decreased $SFEV_1$ was a strong risk factor for a positive methacholine test (OR=0.3; 95% confidence interval, 0.2–0.5). Age, current smoking, use of airway protection, atopy and familial asthma were not significantly related to non-specific bronchial responsiveness.

Table 5. – Odds ratios for presence of respiratory abnormalities by methacholine responsiveness controlled for age, sex, smoking habits, allergy, familial asthma, airflow limitation ($SFEV_1$) and use of airway protection

Dependent variables	Responsiveness $mg \cdot ml^{-1}$ >32	8.1–32	≤8
Dyspnoea	1.0	1.9	5.2*
Wheezing	1.0	2.4	4.0*
Cough	1.0	1.5	4.1*
WASTH	1.0	4.4*	10.8*

*: odds ratios significantly different from one ($p<0.05$). For further abbreviations see legend to tables 2 and 4.

Methacholine responsiveness and respiratory symptoms

The prevalence of respiratory symptoms is shown in table 4. Abnormal bronchial responsiveness was present in 11 of 31 subjects with work-related asthmatic symptoms (35%), whilst the prevalence of abnormal reactivity was higher in subjects with weekly work-related asthmatic symptoms (50%) than in subjects with more infrequent symptoms (24%). The prevalence of responders in subjects with dyspnoea (25%), wheezing (28%) and cough (26%) was higher than observed in subjects with no respiratory symptoms (8%).

In a multiple logistic regression analysis, controlling for age, sex, smoking habits, atopy, familial asthma, $SFEV_1$ and use of airway protection, the likelihood of respiratory symptoms for different levels of methacholine responsiveness was estimated by their odds ratios (table 5). Hyperresponsiveness was significantly related to all symptom groups, and the odds ratio (OR) for work-related asthmatic symptoms was 10.8 (95% confidence interval, 2.9–40.6). Minor responsiveness significantly associated with work-related asthmatic symptoms, OR=4.4 (95% confidence interval, 1.2–16.4) but not with other symptoms.

The validity of methacholine challenge was estimated with work-related asthmatic symptoms as the reference, and subjects without symptoms (n=242) as the contrast. The sensitivity of methacholine responsiveness with a cut-off point of 32 $mg \cdot ml^{-1}$ was 35%, whereas specificity and the predictive power of a positive test (the probability of having work-related asthmatic symptoms given a positive test) were 92 and 35%, respectively, (see appendix). If the cut-off point for a positive test was set to 8 $mg \cdot ml^{-1}$ the sensitivity decreased to 19%, while specificity and predictivity increased to 97 and 46%, respectively. The agreement (kappa value) between work-related asthmatic symptoms and methacholine responsiveness was 0.27 and 0.22 for PC_{20} ≤32 and 8 $mg \cdot ml^{-1}$, respectively.

Interaction

As shown in table 6, the odds for ex-smokers for a positive methacholine test was independent of lung function and the odds ratio for ex-smokers (lifetime nonsmokers OR=1) was highest in subjects with the best lung function (OR=11.7). This observation was responsible for a significant interaction in the logistic model induced by the interaction term smoking*$SFEV_1$, and the interaction disappeared when ex-smokers were excluded from the model. The logistic model was, however, unable to converge with ex-smokers alone in the model and separate, adjusted odds ratios for ex-smokers were impossible to achieve. Nevertheless, exclusion of ex-smokers from the logistic analysis did not change the estimates of the other variables, and ex-smokers were allowed to be included in the final model to obtain an adjusted odds ratio for ex-smokers also. No interaction was found by the cross-product terms sex*smoking (current and lifetime non) and sex*$SFEV_1$.

Table 6. – Crude odds for a positive methacholine provocation test according to smoking habits, stratified by lung function ($SFEV_1$)

	$SFEV_1$ ≤-1.5		$SFEV_1$ >-1.5	
	Odds	OR	Odds	OR
Lifetime NS	0.13	1.0	0.03	1.0
Ex-smoker	0.40	3.1	0.35	11.7
Current smoker	0.64	4.9	0.07	2.3

OR: odds ratio; Lifetime NS: lifetime nonsmoker. For further abbreviations see legend to table 2.

Discussion

Methacholine responsiveness was more closely associated with work-related asthmatic symptoms than with any other respiratory abnormality in the present work-force. Nevertheless, the sensitivity of the test was too low to make the test appropriate as a tool for detecting work-related asthmatic symptoms in a cross-sectional study. Female sex, ex-smoking and airflow limitation were the most important predictors of abnormal responsiveness.

Prevalence of methacholine responsiveness and respiratory symptoms

The prevalence of abnormal methacholine responsiveness was lower than has been found in general population studies [2, 24, 25] and in other work-forces where occupational asthma has been described [26]. Als,o the prevalence of respiratory symptoms was not higher than reported from general population studies [2, 25]. VEDAL *et al.* [26] found that 20% of western red cedar workers had a PC_{20} ≤ 8 mg·ml^{-1}, whilst in our study only 5% of the workers were hyperresponsive. Nevertheless, the 59 new entrants appeared to be even healthier than the exposed workers, with a lower prevalence of abnormal reactivity as well as respiratory symptoms. Only one subject had methacholine reactivity <8 mg·ml^{-1} and he left after only one day in the potroom. Also, selection of workers out of the potroom is known to occur. Analyses of other data from our survey have shown that 8 of 12 relocated subjects (66.7%) had methacholine reactivity ≤ 8 mg·ml^{-1}. Thus, the rather low prevalences of methacholine responders and symptoms are probably a result of a strong health selection both in and out of the potrooms.

Association between methacholine responsiveness and personal characteristics

Females had a significantly higher occurrence of abnormal reactivity than males, controlling for differences in age, smoking habits, atopy, $SFEV_1$ and the use of airway protection. A higher frequency of nonspecific bronchial hyperresponsiveness in females has also been observed by others [27]. In the present industrial setting, the possibilities of alternative jobs in the community are few, especially for females. Their opportunities to change occupation are probably less than for males and, therefor,e the threshold of respiratory abnormality before they change job might be higher.

Airflow limitation was closely correlated to bronchial responsiveness as has been shown in other studies [28]. The significant relationship between familial asthma and methacholine responsiveness found in the simple stratified analysis in table 2, disappeared when other extraneous factors were controlled for in the multivariate analysis.

Also of interest was the absence of any significant relationship between PC_{20} and atopy which is in contrast to the reports from other studies [2, 24]. The prevalence of non-reactors to the skin test was 75 and 36% in the old and new employees, respectively. This could imply a stronger selection of subjects with atopy out of the potroom, which could decrease the association between PC_{20} and atopy.

Current smoking was not significantly related to methacholine reactivity, while the prevalence of responders was significantly increased among ex-smokers. One might speculate that ex-smokers gave up smoking because of respiratory symptoms, and that the increased number of methacholine responders possibly reflects severity of symptoms in ex-smokers.

Association between methacholine responsiveness and respiratory symptoms

We found a significant correlation between work-related asthmatic symptoms and methacholine responsiveness as estimated by the odds ratio for different levels of responsiveness, as well as by the kappa coefficient. The odds ratio for work-related asthmatic symptoms was 10.8 at a methacholine threshold value of 8 mg·ml^{-1}, which is in accordance with RIJCKEN *et al.* who found an OR=7.7 for asthmatic attacks in a general population in The Netherlands.

A sensitivity of 35% (PC_{20}≤32 mg·ml^{-1}) for work-related asthmatic symptoms in the present work-force was less than expected. However, hyperresponsiveness is not usually a feature of immediate asthmatic reactions, and is variable in late asthmatic reactions. BURGE [30] found that the sensitivity of PC_{20} <32 mg·ml^{-1} (methacholine) was 56% in subjects with isocyanate asthma, although misclassification of the diagnosis was reduced by specific bronchial challenge. A lower sensitivity than expected of nonspecific bronchial reactivity in asthmatics has also been reported by JOSEPHS *et al.* [7]. In several patients they found that exacerbations of asthma occurred in the absence of bronchial hyperresponsiveness.

However, the low sensitivity of methacholine challenge may rather suggest that the severely affected workers have been removed from exposure as bronchial reactivity has been shown to correlate well with the severity of asthma [31, 32]. This hypothesis is supported by the finding that workers with weekly symptoms had a higher prevalence of methacholine reactivity than workers with less frequent complaints.

Other factors leading to underestimation of sensitivity of methacholine reactivity in relation to work-related asthmatic symptoms are misclassification of symptoms and the use of a shortened test protocol. Transient bronchoconstriction has been demonstrated in healthy persons exposed to SO_2 at levels as low as 1.0 ppm without increase in bronchial responsiveness [33]. We have measured short-term SO_2 exposure as high as 10 ppm in the potrooms. It is possible that transient episodes of bronchoconstriction in connection with such exposure can be misjudged as work-related asthma when questionnaires are the only source of clinical information.

Avoidance of saline inhalation and the quadrupling of the methacholine concentrations may influence the precision and, hence, the sensitivity of the test. CHINN *et al.* [34] found that most subjects in their study (75%) increased their FEV_1 after the saline inhalation, and that the difference between the results was trivial whether they used the pre- or post-saline value as the baseline FEV_1. A fourfold increase of the dose until there is a definite change from baseline has been proposed to shorten the duration of the test [35]. In a community study in Western Norway the reproducibility of our shortened procedure was examined (P. Bakke, personal communication). PC_{20} values obtained from 20 subjects studied within 3–7 days were reproducible within one doubling dose of methacholine in all but three subjects, which is comparable with other studies [25]. Nevertheless, the omission of the lower doses in some of the subjects may reduce the sensitivity of the test.

Conclusions

A significant association between methacholine responsiveness and respiratory symptoms was found in aluminium potroom workers. Prevalence of bronchial reactivity was highest in subjects with the most frequent symptoms. Female sex, ex-smoking and decreased FEV_1 were strongly associated with methacholine responsiveness. The rather low sensitivity of methacholine challenge found in relation to work-related asthmatic symptoms indicates that methacholine challenge is of limited value as a tool to detect work-related asthmatic symptoms, although the use of a full protocol for methacholine challenge could have-increased the sensitivity of the test.

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Réponse à la methacholine, symptômes respiratoires et fonction pulmonaire, chez les travailleurs au creuset d'aluminium. J. Kongerud, V. Søyseth.

RÉSUMÉ: Les relations entre la réactivité bronchique non spécifique et les symptômes asthmatiques en relation avec l'activité professionnelle, ont été examinées dans une étude transversale chez 337 ouvriers au creuset d'aluminium, par une méthode abrégée de nébulisation continue de methacholine. La PC_{20}, c'est-à-dire la concentration de provocation qui entraîne une chute 20% du VEMS, s'est avérée égale à ou plus petite que 8 $mg \cdot ml^{-1}$ (hyperréactivité) chez 17 travailleurs (5%), alors qu'une réactivité minime (8 $mg \cdot ml^{-1}$ $\leq PC_{20} \leq 32$ $mg \cdot ml^{-1}$) existait chez 24 sujets (7%). La prévalence des symtômes asthmatiques liés au travail fut de 9%. Les facteurs significatifs d'une réactivité à la methacholine ($p<0.05$) furent le sexe féminin, les antécédents de tabagisme, et une obstruction des débits aériens. Dans une analyse de régression logistique multiple, les risques relatifs pour les symptômes asthmatiques en rapport avec le travail furent de 10.8 (intervalle de confiance à 95%: 2.9–40.6) en cas d'hyperréactivité, et de 4.4 (intervalle de confiance à 95%: 1.2–16.4) pour la réactivité faible. La sensibilitité, la spécificité et la valeur prédictive du $PC_{20} < 32 mg \cdot ml^{-1}$ à l'égard des symptômes asthmatiques en relation avec le travail, furent respectivement de 35, 92 et 35%, alors que la concordance, après ajustement pour les valeurs attendues par le hasard, était de 0.27 (intervalle de confiance à 95%: 0.10–0.54). Quoique nous ayons trouvé une association significative entre la réactivité bronchique et les symptômes asthmatiques en rapport avec le travail, l'utilisation du test à la methacholine comme instrument pour détecter les symptômes asthmatiques en relation avec le travail apparatat de valeur limitée en raison de sa faible sensibilité.

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