Relation between decline in FEV_1 and exposure to dust and tobacco smoke in aluminium potroom workers

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Abstract

***Objectives*—To investigate the relation between pulmonary function and occupational exposure in aluminium pot operators.**

***Methods*—2795 observations were obtained in 630 workers over six years of follow up. An autoregressive method of analysis was used.**

***Results*—After adjustment for FEV_1 in the three previous years, the effect of smoking *v* no smoking on FEV_1 was −43·1 ml, 95% confidence interval (95% CI) −72·3 to −13·9. Similarly, an increase in the exposure to particulates by 1 mg/m³ corresponded to a decrease in FEV_1 of −11·9 ml, 95% CI −19·9 to −3·9. Age was a significant predictor of both FEV_1 and FVC.**

***Conclusion*—Exposure to particulates in aluminium potrooms seems to increase the decline in FEV_1, thereby increasing the risk of development of chronic obstructive lung disease in pot operators.**

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Keywords: aluminium; autoregressive time series; pulmonary function; occupational exposure; tobacco smoke

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It has been found that forced expiratory volume in one second (FEV_1) is a good predictor of mortality due to chronic obstructive pulmonary disease (COPD).[1 2] Hence, in the prevention of COPD it is important to identify determinants of the annual decline of FEV_1. It is generally well accepted that smoking is associated with increased annual decline of FEV_1.[3] The relation between the development of COPD and occupational exposure to airborne pollutant is less well documented although the evidence for such an association is increasing.[4 5]

Aluminium is produced by electrolysis of alumina (Al_2O_3). Alumina is a powder with a median mass diameter of 100 μm.[6] The range of the respiratory fraction of the powder is < 2%.[6] Nevertheless, about 50% of the particles in the potroom atmosphere are < 6–15 μm.[6] As well as alumina, the work atmosphere is polluted with fluoride dust and carbon particles from the anode. Gases that act as airway irritants, such as hydrogen fluoride and sulphur dioxide, are also emitted from the pots. We have previously shown that these exposures increase bronchial responsiveness[7], and the incidence of respiratory symptoms,[8] and that the prevalence of airways obstruction increases with the duration of exposure in the potrooms.[9] An increased mortality due to COPD in aluminium potroom workers has recently been reported by Rønneberg.[10] The relation between occupational exposures and the development of airway obstruction is, however, lacking.[11]

We have performed repeated spirometries annually in potroom workers for six years at an aluminium smelter in western Norway. The objective of the study was to investigate the chronic effect of exposure to potroom pollutants on the development of lung function in pot operators.

Materials and methods

POPULATION AND THE PLANT

The study was conducted at Hydro Aluminium Plant in Årdal in 1986–92. During this period the production of aluminium has increased from 170 000 to 190 000 tonnes, whereas the emission of fluoride and sulphur dioxide to the environment has decreased from 40 kg/h to 15 kg/h and from 270 kg/h to 50 kg/h, respectively. These improvements have been achieved by introduction of new technology and better pot operation routines. The plant has three potroom departments, two prebake and one Søderberg.

All employees working in these potrooms in September 1986 or later were invited to participate in the study. Those starting work in the potrooms during the follow up were also recruited to the cohort. The workers were examined annually between 1 September and 1 November. The attendance rate was 95%–98% at each of these surveys. New employees attending the potrooms were examined before the first day at work. Those who left the potrooms were examined during the last 14 days before they finished work. Workers who temporarily left the potrooms were examined before leaving work and after returning to the potrooms.

PULMONARY FUNCTION AND QUESTIONNAIRE

Pulmonary function was measured with a dry bellow spirometer (Jones Pulmonaire, Illinois). It was calibrated monthly with a 1l syringe. The subject performed at least three expiratory manoeuvres; the two best should not differ by more than 5% or 100 ml, whichever was the largest.[12] The results were converted to body temperature, pressure, and saturation (BTPS). Three technicians (nurses) were trained to perform the test by one of us (JK)

before the start of the study and annually thereafter. Reference values were taken from an asymptomatic Norwegian urban population.[13] Information on smoking habit was obtained from a validated questionnaire.[14]

OCCUPATIONAL EXPOSURE

Since 1986 measurements of exposure to particulates and fluoride have been performed annually with personal samplers.[9] The work in the potrooms is divided into several job categories. Each year during this follow up, workers have been randomly selected to wear such samplers for eight hour shifts; 874 measurements were taken. The annual exposure in each job category was expressed as the geometric mean of these measurements.

Information on the job category in each operator who participated in the study was obtained from a questionnaire[14] at each examination. It was assumed that the workers were exposed to the estimated exposure in their job category in the time interval between the surveys. The availability of information about deviation from this assumption was limited. Consequently, we were not able to adjust exposure for absence from work, such as sickness absence and military service. Such deviations were likely to cause irregular time spacing between the examinations.

STATISTICAL ANALYSES

In this longitudinal study we chose to use an autoregressive method that has been described by Rosner and coworkers.[15] Other alternative methods of longitudinal analyses could also be considered, such as the random effects model[16] and generalised estimation equations.[17] These methods enable use of all the available data. The advantage of the method chosen is its simplicity. The data can be analysed with software that offers ordinary multiple regression methods, and no complex algorithms for non-linear calculations are required.

The limitation of this approach is the assumption that the observations must be equally spaced and that the number of excluded subjects increases as the order of the autoregression model increases. The problem of excluding subjects is of minor importance as the objective of the study was to investigate the chronic effects of exposure on lung function—that is, in the subjects who stayed at work.

Briefly, the outcome (FEV_1 or FVC) and the covariates were entered into an ordinary multiple regression model, adjusting for one or more of the previous values of the outcome. The appendix explains details about the model and how the number of previous values of the outcome were determined. The method is based on the assumption that observations are equally spaced over time.[15] Thus, only those observations that were separated by between 10 and 14 months were included in the analyses—that is, only workers who had worked in the potrooms for at least 10 months were included.

The analyses were conducted in two steps. Firstly, the number of previous values of the outcome was found (appendix). Next, height, sex, age, total fluoride, total particulates, and smoking habits were included as covariates. Two indices of smoking were used; non-smoker and current smoker, and the amount of tobacco smoked (g/week) was used as a continuous variable. Finally, the model was reduced by backward elimination by removal of covariates that did not contribute significantly to the model, provided that this removal caused < 10% change in the remaining coefficients.[18]

Results

In all, 2795 spirometries were carried out during the follow up in 630 workers. Table 1 shows the characteristics of the workers at inclusion to the cohort. It shows that 58% of the workers were excluded from the final analyses, covering 32% of the total follow up time. Hence, the final analyses covered 68% of the observation time. Except for annual decline in FEV_1 and age the differences between the subjects were neglectable.

Table 2 shows the number of examinations during the follow up. In the total workforce, a mean (SD) time lag was 12 (2) months between two examinations over 1500 observa-

Table 1 Personal characteristics at baseline of the workers who were included in the cohort and those who were available in the final analyses

	Not included in the final analyses		
	≤ 3 y follow up n = 251	*> 3 y follow up n = 114*	*Final analyses n = 265*
Sex (F (%))	32 (12·8)	21 (18·4)	29 (10·9)
Current smoking habits (%)	131 (52·2)	66 (57·9)	155 (58·5)
Age (y)	25·1 (19·2 to 57·5)	26·0 (18·8 to 48·1)	33·5 (20·1 to 51·8)
FEV_1:			
ml	4100 (2940 to 5090)	4100 (2960 to 5360)	4050 (3080 to 5060)
Predicted (%)	88·9 (73·5 to 104·0)	88·8 (71·9 to 107·7)	90·5 (77·9 to 105·2)
FVC:			
ml	5140 (3860 to 6200)	5110 (3800 to 6410)	5130 (399 to 6330)
Predicted (%)	92·7 (79·3 to 108·4)	92·4 (79·3 to 107·4)	94·8 (82·2 to 110·7)
Annual decline in FEV_1 ml/y	−35·6 (−162·2 to 152·9)*	−14·4 (−75·7 to 73·6)	−41·8 (−90·3 to 22·7)
Duration of employment (months)	0 (0 to 315)	3 (0 to 277)	70 (0 to 329)
Ended employment (%)	213 (84·9)	35 (30·7)	31 (11·7)
Particulates (mg/m³)	2·17 (0 to 6·64)	2·35 (1·24 to 6·64)	3·19 (1·70 to 6·64)
Follow up time (y)	209·5	508·2	1493

Continuous variables are medians (10th to 90th percentiles).
*Estimated in 72 workers who had three or more recordings.

Table 2 Number of spirometries that were carried out during the follow up

Number of examinations	*Year of follow up*							
	1986	*1987*	*1988*	*1989*	*1990*	*1991*	*1992*	*Sum*
1	371	83	81	41	18	16	20	630
2	1	298	100	65	38	21	8	531
3		6	243	96	47	37	19	448
4		2	5	221	77	57	31	393
5			2	14	180	90	51	337
6				4	8	164	93	269
7					4	6	161	171
8						5	9	14
9						1	1	2
Sum	372	389	431	441	372	397	393	2975

tions of 478 workers. The mean (SD) time between two successive examinations in these workers was 12·0 (0·6) months.

The exposure to fluorides and particulates decreased during the follow up (table 3). The decline in exposure seemed to be greatest between 1987 and 1989, when manual refill of alumina was replaced by automatic refilling of the prebake pots. The tobacco consumption was, however, nearly unchanged during follow up (table 3).

In the first step of the analyses, the order of the autoregressive model was settled among the 478 workers in whom the time between two consecutive examinations was within 12 (2) months (table 4). It was found that the three last measurements of the outcome were significantly related to the dependent variable. Because of this the number of observations was reduced to 658 from 265 workers available for the final analyses (tables 1 and 4). Despite the large reduction of data available for analysis, the difference between the original population and the final population did not differ in the characteristics at inclusion (table 1). The final analyses started with the full model (AR3) including height, sex, total fluoride, age, total particulates, and tobacco smoke as covariates. During the backward model reduction, height, sex, and total fluoride did not contribute significantly to the model, and removal caused only minor changes to the coefficients of the remaining variables when FEV_1 was used as the dependent variable. When smoking (dichotomised) was replaced by the amount of tobacco smoked (g/week), the coefficient was estimated to be −0·39 ml/g/week (SEM 0·18, P = 0·03). Table 5 shows the results of the final analysis of FEV_1. Age, current smoking, and exposure to particulates were the significant covariates. After adjustment for three previous measurements of FEV_1, a significant effect of age on FEV_1 was found. If FEV_1 is related linearly with age, the association between them should have the same magnitude independent of age when previous FEV_1 is taken into account. It therefore seems that the decline in FEV_1 accelerates with age. Also, the age effect expresses the association between the outcome and age conditionally on previous levels of the outcome (that are themselves dependent on age). Thus, the absolute age effect on FEV_1 is not estimated with this method.

The association between exposure to particulates and FEV_1 was investigated in non-smokers separately. An increase in exposure to particulates by 1 mg/m³ corresponded to a decline in FEV_1 of −13·4 ml (SEM 5·7, P = 0·02) in non-smokers. Modification of the effect of exposure to particulates by smoking was investigated by adding a product term between these two covariates. This product term was not significant (P > 0·05), indicating that effect of particulates was not greater in smokers than in non-smokers.

The analyses of FVC as the dependent variable showed no significant association with smoking or the occupational exposure indices (table 5). It was, however, significantly related to age.

Finally, we have used the results from table 5 to predict FEV_1 in a worker for different levels of exposure to particulates and smoking habits (figure). The models predict FEV_1 in four workers who all have the same baseline FEV_1 (4 l) at 30 years of age. After having reached 62 years, the difference in FEV_1 between a smoker who was exposed to 5 mg/m³ (the hygienic threshold level in the Norwegian aluminium industry) and a non-smoker who has had a negligible exposure to particulates, is 1518 ml. It is also indicated that the effect of exposure to particulates on FEV_1 is of the same size as the effect of smoking in this cohort (75 g/week). The decline in FEV_1 seems to accelerate with increasing age.

Table 3 Exposure to total fluorides (mg/m³), particlulates (mg/m³), and smoking habits during the follow up

Type of exposure	*Year of follow up*						
	1986	*1987*	*1988*	*1989*	*1990*	*1991*	*1992*
Total fluoride:							
Median	0·72	0·52	0·37	0·38	0·35	0·24	0·36
10th to 90th percentile	0·37 to 1·16	0·34 to 1·04	0·28 to 0·70	0·26 to 0·61	0·14 to 0·48	0·12 to 0·38	0·13 to 0·40
Total particulate:							
Median	3·19	3·05	3·43	1·31	1·56	0·99	1·47
10th to 90th percentile	1·70 to 6·64	1·64 to 4·07	1·63 to 4·36	1·01 to 2·17	0·68 to 1·87	0·60 to 1·67	1·13 to 2·10
Smoking:							
Amount (mean (SD), g/week)	74 (33)	75 (35)	78 (38)	77 (38)	73 (36)	74 (38)	75 (39)
Prev. (%)	55·8	58·0	59·2	57·4	59·4	58·1	62·7

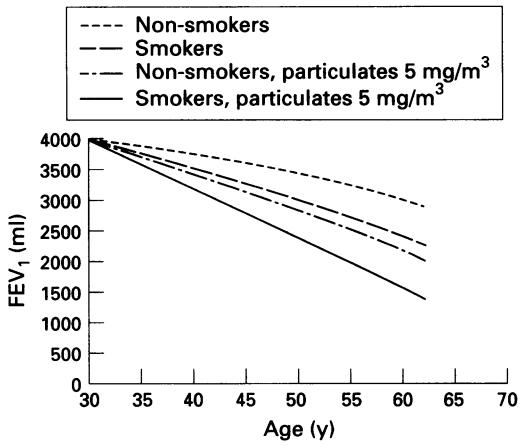
Table 4 Model (equation 2, appendix) with no covariates

L	n	r	Model parameters	Parameter estimate	SEM	P value
1	478	1500	α	76·1	28·9	0·009
			γ_1	0·971	0·007	< 0·001
2	328	1002	α	−18·3	32·4	0·57
			γ_1	0·653	0·029	< 0·001
			γ_2	0·338	0·029	< 0·001
3	265	658	α	−91·3	40·8	0·025
			γ_1	0·527	0·042	< 0·001
			γ_2	0·292	0·044	< 0·001
			γ_3	0·184	0·036	< 0·001
4	210	370	α	−97·1	53·8	0·07
			γ_1	0·545	0·055	< 0·001
			γ_2	0·220	0·064	< 0·001
			γ_3	0·181	0·056	< 0·001
			γ_4	0·055	0·048	0·25

L = the order of the autoregressive model, n = number of individuals, r = number of rows in the design matrix to fit specific models.

Table 5 Result from the autoregressive model of FEV_1 and FVC as the dependent variables

Independent variable	FEV_1 (ml)			FVC (ml)		
	Coefficient	SEM	P value	Coefficient	SEM	P value
Intercept	176·0	72·2	0·015	−271·0	308	0·38
Particulates (mg/m³)	−11·9	4·1	0·004	−8·1	5·7	0·15
Current smoking						
Yes *v* no	−43·1	14·9	0·004	−29·0	20·6	0·16
Age (y)	−2·75	0·79	0·001	−3·80	1·00	< 0·001



Prediction lines of FEV_1 in four workers with different exposures to particulates and smoking habits. All had the same baseline FEV_1 at 30 years of age.

Discussion

In this longitudinal study we have found that the decline in FEV_1 is increased in smokers compared with non-smokers, and that it increases with the amount of tobacco smoked. Furthermore, it increases with occupational exposure to particulates.

The choice of analytical methodology might be questioned, as only one quarter of the original observations were available in the final analyses. This number might have been slightly increased if a method that allows for unequally spaced observations have been used.[19] However, inclusion of more workers with unequally spaced examinations during follow up might have decreased the validity: according to the protocol, the operators should meet to do the examinations during September and October—that is, 12 (2) months apart. Those who were observed outside this range were likely to have been unexposed to potroom fumes in the period between the observations. Although about 60% of the workers were excluded from the final analyses, nearly 75% of the follow up time of the long term employees was included. Furthermore, classification of exposure in the long term workers who were periodically absent from work is likely to be incorrect causing misclassification of exposure, thereby distorting the results. The finding that they actually had a lower decline in FEV_1 supports the association between exposure and outcome. As the association between FEV_1 and particulates was found in non-smokers, the results seem not to be confounded by smoking.

There are, however, some problems with the interpretation of the coefficients. They express the effect of a covariate conditionally on the three previous measures of the outcome. Thus, they do not express the annual change of the outcome directly. Rosner and coworkers offer a formula for calculation of annual change in cases of first order regression—that is, after adjustment for the previous value of the outcome.[15] In the case of third order regression this task is much more complex. Therefore we chose to use the estimated coefficients to predict lung function for different alternatives of smoking and occupational exposure.

As the characteristics of the total work force and the subjects included in the final model were similar it seems that the results should be valid for pot operators who have worked in the potrooms for at least 10 months. Loss of information decreases the precision of the coefficients. As significant results were obtained, we regard this as a minor problem.

As the final analysis included only those who had three previous spirometries or more, the workers must have worked in the potrooms for three years or more. Thus, the results are not applicable to the short term effect of these exposures on FEV_1. Nevertheless, the development of COPD needs several years. Therefore, we think that the current analyses are relevant in this context. Furthermore, it seems to us that previous levels of FEV_1 are confounded by previous exposure, and this effect has to be taken into account in the estimation of the current effect. However, we have data on operators with short term exposure, and we plan to make a separate analysis of these data.

In previous studies we have found that respiratory symptoms and bronchial responsiveness were associated with exposure to fluoride but not the exposure to particulates.[7,8] Therefore it seems that the present results deviate from our previous results. This inconsistency has at least two explanations. Firstly, both bronchial responsiveness and respiratory symptoms are probably more related to reversible obstruction than the development of COPD. Although there is some overlap in the morphology of these entities, they represent different diseases, and they may be associated with different exposures. Next, exposure to particulates and fluoride (and exposure to other airway irritants) are closely correlated. Thus, the capability of the statistical models to differentiate between them is limited. In a follow up of a cross sectional study of aluminium pot operators, Chan-Yeung and coworkers were not able to show any increased decline in FEV_1

compared with an unexposed control group between the original and follow up surveys.[20] It should be noted that about 50% of the work force on the original survey left the industry before the follow up. It seems likely that workers who develop respiratory impairment are more prone to leave the industry than those who remain healthy. Hence, the negative result may be explained by a selective loss of follow ups.

From a preventive point of view, our results have several implications. Firstly, a significant effect of dust exposure on the development on FEV_1 was found. Therefore efforts should be made to reduce the exposure to particulates. Several alternatives should be considered, such as increase of particle diameter, decrease of contamination of the work atmosphere, and improvement of airway protection. Routine surveillance of the decline in FEV_1 in each worker, and removal of workers with increased decline from exposure as well as selective intervention against smoking, should also be considered.

Finally, the Norwegian compensation legislation has considerable consequences for the industry. It states that in a subject with a disease that might be caused by any occupational exposure, the contribution of lifestyle exposure on the disease should be ignored. Thus, the aluminium industry must be prepared to compensate for the smoking habits in workers with COPD, as smokers are more likely to develop the disease than non-smokers. It is therefore profitable to prohibit smoking in pot operators, at least at work. This is a serious problem, as more than 50% of the workforce were smokers, and the fact that neither the prevalence of smoking or the amount of tobacco smoked has decreased during the past years.

In conclusion, FEV_1 is negatively related to exposure to tobacco smoke and occupational exposure in aluminium pot operators. Great efforts should be made to decrease the occupational exposures as well as tobacco consumption.

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Appendix

The autoregressive method used in this paper allowed for inclusion of independent variables that are time dependent and fixed over time and partial use of data for people with missing data. For the ith person the outcome y_{it}(FEV_1 or FVC) at time t is expressed as

$$y_{it} = a + \sum_{l=1}^{L} \eta y_{i,t-1} + \sum_{j=1}^{J} \beta_j x_{ijt} + \sum_{k=1}^{K} \beta_k^* z_{ik} + e_{it} \qquad (1)$$

where $I = 1$ to n; $t = L$ to T; y_{it} = value of the outcome variable for the ith person at the tth examination, e_{it} is statistically independent for all i,t with common $N(0,\sigma^2)$ distribution. x_{ijt} is the jth time dependent exposure variable for ith subject ascertained at time t. The zs represent exposure variables that do not change over time. The γs represent the effect of the previous ys on the current level of y, whereas the βs and the β^*s represent the effect of the independent variables on the level of the outcome variable at time t after adjusting for the levels of the outcome variable at the previous L time points.

To find the number of previous measurements of outcome to be included, the following equation was used:

$$y_{it} = a + \sum_{l=1}^{L} \eta y_{i,t-1} + e_{it} \qquad (2)$$

L was the highest order of previous outcome that contributed significantly to the model. Table 4 shows the results of these analyses.

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