Effects within the week on forced vital capacity are correlated with long term changes in pulmonary function: reanalysis of studies on car painters exposed to isocyanate

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Abstract

Objectives—To examine if car painters who work with polyurethane paints that contain hexamethylenediisocyanate (HDI) and hexamethylenediisocyanate biuret trimer (HDI-BT) develop acute as well as chronic impairment of lung function.

Methods—In this study data were reanalysed from two earlier studies on a group of car painters to see if a decrease in lung function within the week is a marker of vulnerability in those workers. Data on changes in forced vital capacity (FVC) and forced expiratory volume in one second (FEV₁) within the week were available for 20 car painters who were also examined six years later.

Results—10 men showed a decline in FVC within the week. There were no significant differences in age, duration of employment, exposures during the follow up period, or smoking between car painters who had decline in lung function within the week and car painters who had not. A significant correlation was found between the change in FVC within the week and the long term (six year) change in FVC, standardised for the effects of aging and smoking, and adjusted for the number of peak exposures.

Conclusions—The results suggest that the decrease in FVC within the week might serve as a guide to identify car painters at risk of a further decrement in lung function above the effects of aging, smoking, and exposure.

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Keywords: forced vital capacity; deterioration of pulmonary function; diisocyanates; painters

Measurements of dynamic lung volumes such as forced vital capacity (FVC) and forced expiratory volume in one second (FEV₁) are powerful measures to examine the effects of certain exposures on lung function. In several studies we have found acute temporary effects on FVC and FEV₁ in workers exposed to irritating air contaminants.¹⁻⁵ These temporary effects were correlated with the concentration of the air contaminants. The measurement of acute effects from irritants on lung function is of value as a complement to exposure measurements. It is also of great interest to study the medical importance of acute temporary

effects. The results from a recently published study indicated that a change in FEV₁ within the week was correlated with an accelerated decline in lung function in asymptomatic wood trimmers.⁶ An accelerated decline in FVC, correlated with long term exposure, has been found in car painters,⁷ although the mean values for FVC and FEV₁ in those painters were unaltered during a working week.⁸ The effects of exposure may be difficult to find due to the normal diurnal variation in lung function.^{6,9,10} If the short term decrease during a workshift or week cannot be associated with the exposure, it is possible that subjects who show a decrease are vulnerable. By measuring lung function during a working shift or week, such subjects may be identified and measures can be taken to decrease or stop the exposure.

Polyurethane car paints contain hexamethylenediisocyanate (HDI) and hexamethylenediisocyanate biuret trimer (HDI-BT), which is a polycondensation product of HDI and water. Isocyanates belong to a group of chemicals that contain the highly reactive isocyanate group ($-N=C=O$). The respiratory effects of exposure to isocyanates include chemical bronchitis, allergic asthma, non-specific bronchial hyperreactivity, chronic deterioration in lung function, and hypersensitivity bronchial pneumonitis.¹¹ To evaluate if a decrease in lung function within the week is a marker of vulnerability in workers exposed to isocyanates, we reanalysed the data from two earlier published studies.^{7,8}

Material and methods

STUDY GROUP

Lung physiological investigations were carried out on two occasions (in 1978 and 1984) in male car painters who worked with polyurethane paints. The original group of car painters were randomly chosen from 14 garages in Stockholm, Sweden.^{7,8} In February and March 1978, the workers were examined on a Monday before work after two days of no exposure, and again on Friday in the same working week. At the follow up in October and November 1984 the workers were examined during the first three hours of a working day. Twenty eight car painters participated in all three spirometric examinations, but only those 20 car painters who had been working during the entire period 1978-84 were chosen. At the time of the follow up their mean age was 41 years. There were four never smokers, six ex-smokers and 10 current

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smokers. There were no significant differences in age, height, smoking habits, and symptom score between this group and the entire group studied in 1978 or 1984.

EXPOSURE CONDITIONS

An industrial hygienist, blinded to the medical condition of the workers, performed individual assessments of exposure to HDI and HDI-BT during 1978-84. All car painters were interviewed about their working routines and use of respirators. Hygienic standards were studied and exposure measurements were carried out at representative shops. A total of 81 measurements were performed for three different worktasks and in 25 different spray painting chambers, classified according to the number of air changes/hour. To find situations when peak exposure occurred—that is, concentrations $> 2.0 \text{ mg/m}^3$ HDI-BT for at least 30 seconds—exposure measurements with a sampling time of < 3 minutes were carried out. Peak exposure to HDI-BT occurred when, without respiratory protection of any kind, the subject was cleaning a spray gun or stayed within the spraying chamber for more than 20 seconds before it was ventilated.⁷ For the car painters studied, the calculated time weighted average exposure between 1978 and 1984 was 0.0014 mg/m^3 HDI and 0.09 mg/m^3 HDI-BT, which is lower than measured or estimated values in 1984. Median of yearly number of peak exposures to HDI-BT was 2000.

SPIROMETRY

Forced expiratory vital capacity manoeuvres were carried out with a calibrated low resistance bellows spirometer (Ohio 740). The subject was seated and was carefully instructed before the test was performed. Each man carried out three tests. The best result for each variable was chosen, even if the results were selected from different recordings.¹² In our study FVC and FEV_1 were measured.

Table 1 Mean (SD) age, duration of employment, yearly number of peak exposures, and percentages of ex and current smokers at follow up for 20 car painters with and without a decrease in FVC within the week

	With (n = 10)	Without (n = 10)
Age (y)	41 (12)	42 (8)
Duration of employment (y)	25 (13)	22 (9)
Exposure 1978-84 (peaks/y)	2573 (1719)	1785 (1410)
Ever smokers (%)	80	80

Table 2 Number of subjects with respiratory symptoms at the initial study and six years later, divided into car painters with and without a change in FVC within the week

	With (n = 10)	Without (n = 10)
1978:		
Chronic bronchitis	1	1
Cough	2	1
Dyspnoea	4	3
Wheeze	3	0
1984:		
Chronic bronchitis	1	0
Cough	3	1
Dyspnoea	3	3
Wheeze	3	3

STATISTICAL ANALYSIS

Standard statistical methods were used, in conjunction with multiple regression analyses.¹³ Change in lung function within the week in each man was calculated according to the formula:

$$\text{change} = 100 \frac{(\text{after} - \text{before})}{0.5 (\text{after} + \text{before})}$$

Lung function values obtained in 1978 were expressed as percentages of the expected values from the European summary equations.¹⁴ The values obtained at the second occasion in 1984 were standardised for the long term effects of aging and smoking found in a population.¹⁵ The long term decline in lung function between the first and the second study in each man was calculated according to the formula:

$$\text{decline} = 100 \frac{(2\text{nd} - 1\text{st})}{0.5 (2\text{nd} + 1\text{st})}$$

The absolute values obtained at the first and the second study were used in the formula. Appropriate transformations were applied to those variables found to have a distribution that diverged from normality. As the aim of this study was to evaluate if subjects who had a decrease in lung function within the week are vulnerable, the changes in FVC and FEV_1 within the week were dichotomised. A change $< 0\%$, signifying a decrease, was scored 1—that is, an effect was indicated. A change $\geq 0\%$ (no decrease) was scored 0—that is, no effect was indicated. Stated P values involved two tailed analysis; differences were considered to be significant at $P \leq 0.05$.

Results

The mean (SEM) changes in FVC and FEV_1 during a shift in 1978, were -0.6 (2.6) and -3.6 (4.1)% respectively. Age, duration of employment, yearly number of peak exposures to HDI-BT, and distribution of smoking habits did not differ significantly between the 10 car painters who showed a decrease in FVC and those who did not (table 1). There were no significant differences between the two groups in the distributions of acute or chronic respiratory symptoms in 1978 or in 1984 (table 2). A similar lack of difference was found for the 10 car painters who had and 10 who had no change in FEV_1 within the week. The changes in FVC and FEV_1 within the week were also well correlated ($r^2 = 56\%$, $P = 0.009$). The mean values of the changes for FVC and FEV_1 within the week for never smokers were 4.0 (6.9) and 5.8 (9.2)% respectively, compared with the corresponding values of -0.5 (3.5) and -5.7 (5.2)% for the 10 car painters who were current smokers in both studies ($P > 0.2$). The decline in FVC was significantly greater in current smokers (-5.9 (2.7)) than in never smokers (4.4 (3.3)). Current smokers had on average a higher yearly number of peak exposures to HDI-BT than did never smokers (2928 (454) v 762 (367), $P < 0.05$).

Car painters in the initial study who showed a decrease of FVC within the week in

Table 3 Mean (SEM) percentage of predicted lung function¹⁴ at the initial investigation and changes from 1978 to 1984 for car painters with and without decrease in FVC and FEV₁ within the week

	FVC		FEV ₁	
	With (n = 10)	Without (n = 10)	With (n = 10)	Without (n = 10)
FVC:				
Initial 1978*	112.1 (3.7)	104.6 (5.0)	113.0 (2.9)	103.7 (5.4)
Decline 1978-84†	-8.1 (2.6)‡	0.5 (2.6)	-7.4 (2.5)	-0.2 (2.9)
FEV ₁ :				
Initial 1978*	98.3 (4.9)	99.3 (6.5)	100.8 (4.2)	96.9 (6.9)
Decline 1978-84†	4.4 (6.1)	1.9 (5.0)	2.3 (6.4)	4.0 (4.6)

*Lung function at first occasion, standardised for age and height; †percentage of the change in lung function standardised for the effects of aging and smoking; ‡significantly lower compared with car painters without a decrease in FVC within the week.

1978 had a significantly greater decline in FVC from 1978 to 1984, than car painters who did not, after adjustment for smoking (table 3). There was a significant correlation between the change in FVC within the week in the first study and the decline in FVC during the six year follow up ($r^2 = 47\%$, $P = 0.005$). The six year decline in FVC was still correlated with the yearly number of peak exposures to HDI-BT, after adjustment for the effects of changes in FVC within the week ($r^2 = 32\%$, $P = 0.009$) and also to the change in FVC within the week adjusted for the effects of yearly number of peak exposures to HDI-BT ($r^2 = 32\%$, $P = 0.009$, figure).

Car painters who showed a change in FEV₁ within the week in 1978 had a tendency to a greater six year decline in FVC ($P = 0.08$, table 3). There were no significant correlations either between the change in FVC during a shift and the long term decline in FEV₁ or the change in FEV₁ within the week and the long term decline in FVC and FEV₁. The decline in FVC was not significantly correlated with the mean exposure to HDI or HDI-BT estimated during the entire follow up.

Discussion

A significant correlation was found between the changes within the week and the six year decline in FVC standardised for age and smoking, adjusted for the effects of yearly number of peak exposures to HDI-BT in car painters (figure). The distributions of respiratory symptoms were similar in those car painters who showed a decrease in FVC during a working week and those who did not (table

2). Thus the correlation between the changes within the week and a long term decline in FVC is not likely to be influenced by the presence of symptoms, which have been shown to predict a decrease in lung function.¹⁶ Changes in FEV₁ within the week have been shown to predict pulmonary impairment in wood trimmers without any respiratory illness and without any acute or chronic symptoms.⁶

In the first study, there was a slight average decrease in FVC and in FEV₁ within the week in this group of car painters. The car painters were examined before (in the morning) and after a working week (in the afternoon). The normal circadian rhythm in FVC and FEV₁ will result in higher values in the afternoon compared with morning values^{9,10} and the difference seems to be larger for FEV₁ than for FVC.¹⁷ Therefore, a numerically small non-significant decrease in FVC or FEV₁ during a working week may be of importance in the long run, as the effects of exposure may be overridden due to the normal variation in lung function. Although there were trends towards greater changes in FVC and FEV₁ within the week in current smokers, the differences when compared with the results obtained for never smokers were not significant. The distribution of smoking habits was also identical between car painters who had a decrease in FVC and those who had not. It is therefore not likely that active smoking should have resulted in a decrease in FVC within the week. This is in agreement with previously reported results.¹⁰

There was no significant correlation between the decline in FVC from 1978 to 1984 and the estimated mean exposures to HDI or HDI-BT during the entire follow up time. On the other hand there was a correlation between the decline in FVC and yearly number of peak exposures to HDI-BT also after adjustment for the effects of the change in FVC within the week. The number of peak exposures was related to each car painter's working routine and the use of protective equipment during short working operations.⁷ It is noteworthy that the current smokers on average had a significantly higher yearly number of peak exposures and also a greater decline in FVC than did the never smokers. This may indicate that car painters who smoke are less likely to use respiratory protection in highly exposed situations and therefore show a greater decline in lung function. The unadjusted decline in FVC for men who were ex-smokers and current smokers at both occasions were 72, and 91 ml/year, respectively. This is about twofold higher than the decline found in a population study standardised for the effects of aging and smoking.¹⁵ Although it may be questionable to standardise long term effects on lung function without quantification of smoking, the findings in our study may indicate additional harmful effects of yearly number of peak exposures to HDI-BT in smokers.

The main finding in this study is a correlation between the changes in FVC within the week and long term changes in FVC, after adjustment for the effects of yearly number of

Correlation in car painters between the changes in FVC (%) within the week and the long term changes in FVC (%) standardised for the effects of aging and smoking¹⁵ at the follow up six years after initial study, adjusted for the effects of yearly number of peak exposures to HDI-BT.

peak exposures to HDI-BT. If the long term exposure was representative of the exposure over the week, the observed correlation between short term and long term deterioration in lung function could be explained by differences in exposure. This could be the case in a population with specialised work or workers from different workplaces with very different exposure conditions. It cannot be entirely excluded that the average long term exposure is representative of the exposure during one week. We think, however, that the exposures vary too much in the long term for us to obtain the results observed. Another explanation could be that smoking is a confounder related to both short and long term impairment of lung function and also to HDI exposure due to less use of protective equipment by smokers. We find it probable, however, that those workers who show an acute decrease in lung function over a week are more vulnerable than other workers, and that repeated exposures in these workers will result in a long term chronic decrease in their lung function.

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