Bronchial symptoms and respiratory function in workers exposed to methylmethacrylate

T Marez, J L Edmé, C Boulenguez, P Shirali, J M Haguenoer

Abstract

This study aimed to investigate the pulmonary effects of methylmethacrylate (MMA) in a group of occupationally exposed workers. In the exposed group 20% had chronic cough compared with 1% in controls. Spirometric values at the beginning of the workshift were similar in both groups, but a mild airways obstruction appeared during the workshift. The maximum expiratory flow when 50% of the forced vital capacity remained to be exhaled (MEF_{50}) and the ratio of MEF_{50} to maximal expiratory flow (MEF_{50}/MEF) decreased significantly during the workshift among exposed workers *v* controls ($p = 0.04$ and 0.01 respectively). Results remained unaffected after adjustment for smoking. Exposure to MMA seems to be responsible for a mild airways obstruction but further study on a larger population would be useful.

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Monomeric methylmethacrylate (MMA) has widespread use in the manufacture of acrylic resins. It is a component of paints and laquers. Polymers produced from MMA are widely used in various applications—for example, in the automobile, furniture, and construction industries and in orthopaedics and dentistry. Available data on the biological effects and toxicity of MMA have become voluminous and MMA has been generally regarded as an innocuous substance. Because of its great irritant power, however, exposure to MMA has resulted in respiratory disorders. Many experi-

mental studies have shown alterations of the respiratory system of animals exposed to MMA. Thus hypocapnia, hypercapnia, acidosis,¹ pulmonary oedema,² haemorrhage, congestion, and necrosis,^{3,4} and Cheyne Stokes dyspnoea,⁵ have been described. In humans, functional disorders such as cough, sore throat, respiratory irritation,⁶ and occupational asthma⁷ have been noted. A recent study has shown a twofold higher prevalence of respiratory obstruction among workers exposed to MMA and styrene than among controls.⁸ The aim of the present study was to assess the effects of MMA on the lung function of workers occupationally exposed exclusively to the monomer. For this purpose, we carried out a study including a questionnaire and a maximum expiratory flow volume curve (MEFV) among exposed workers and controls.

Materials and methods

The study included a questionnaire, spirometry, and an evaluation of the atmospheric concentration of MMA.

ATMOSPHERIC MONITORING

Atmospheric concentrations of MMA were evaluated by passive sampling on activated charcoal (badge 3M). After desorption in carbon disulphide MMA was analysed by direct injection into a gas chromatograph equipped with a flame ionisation detector. Atmospheric concentrations of MMA (ppm) were calculated from a formula given by the manufacturer. Monitoring was conducted in each workshop when production was running normally. The monitoring time was eight hours.

QUESTIONNAIRE

Smoking history and information on the presence of respiratory symptoms were gathered by a modified British Medical Research Council questionnaire.⁹ It included questions about present and past smoking habits. Non-smokers were persons who have never smoked. Smokers were persons who smoked cigarettes at the time of the interview. Ex-smokers were those who once smoked cigarettes

Laboratoire de toxicologie, Institut de Médecine du travail-Faculté de Médecine 1, place de Verdun-59045 Lille, Cédex, France

T Marez, P Shirali, J M Haguenoer

Laboratoire de Médecine du travail, Faculté de Médecine, Lille II, France

J L Edmé, C Boulenguez

but who had not smoked for at least two years. From current and ex-smokers, the number of cigarettes smoked daily was ascertained and the pack-years of cigarettes smoked (pack-year = number of cigarettes smoked per day $\times$ number of years smoked /20) were calculated. Chronic bronchitis was defined as cough and phlegm production on most days for at least three months a year for two consecutive years or more. Asthma was defined as a positive answer to the question "Have you ever had bronchial asthma?"

SPIROMETRY

Maximum expiratory flow volume (MEFV) curves were obtained by the same well trained operator with the same FUKUDA Spiroanalyzer ST-200. Each period of measurement was preceded and followed by calibration with a 3l syringe. After being instructed in the procedure for measurement of forced vital capacity (FVC), subjects performed the test in a standing position without a nose clip. To insure that emphasis was put on both the completeness and the speed of the manoeuvre criteria used to choose the best curve were stricter than recommended by the American Thoracic Society.^{10,11} To consider the test as valid, in less than six attempts, three acceptable expirations of which the sum of FVC + forced expiratory volume in one second (FEV₁) did not differ by more than 5% from each other had to be obtained. All variables were then recorded from the curve with the greatest sum of FVC + FEV₁, unless the corresponding maximal expiratory flow (MEF) was lower by more than 10% of the best one performed by the subject. In that case the MEFV curve was withdrawn from the survey. Standard lung function variables included FVC, FEV₁, FEV₁/FVC, MEF, and maximal expiratory flows at 75, 50, and 25% of FVC (MEF₇₅, MEF₅₀, MEF₂₅). The MEF₅₀/MEF ratio, which seems to be equivalent to the β of Kapp *et al.*,¹² was also calculated to obtain information about the morphology of the curve.

POPULATIONS ANALYSED

Questionnaires were offered to 108 workers exposed to MMA in four factories and 105 controls engaged in similar job categories but without exposure to MMA. The response rate was 81.48% and 87.61% respectively. After processing questionnaire data, it was noted that the two groups were not comparable with regard to occupational history. In particular, there were more ex-miners and other workers previously exposed to dust (particularly fertiliser dusts) in the control group than in the exposed group. As bronchial hyper-reactivity is more often found in coal miners,¹³ variations in spirographic variables across the shift may be more intensive than in other workers. Similarly, respira-

Table 1 Anthropometric data and smoking habits among exposed workers v controls

	Control group	Exposed group	Statistical significance
Age (y)	39 (6)	37 (7)	NS
Weight (kg)	78 (13)	75 (10)	NS
Height (cm)	174 (7)	173 (7)	NS
Tobacco (pack-years)	16 (11)	13 (11)	NS
Non-smokers	20 (44.5%)	13 (32.5%)	NS
Ex-smokers	7 (15.5%)	11 (27.5%)	NS
Smokers	18 (40%)	16 (40%)	NS

tory function disorders have been described in workers exposed to fertiliser dusts.¹⁴ Consequently, the following persons were excluded from the study: 81 workers whose occupational history included work in coal mines or exposure to fertiliser dust and 14 persons exposed to MMA for less than five years who worked in two factories where the mean concentration of MMA was very low (2.7, and 0.7 ppm). Thus the study population was composed of eight workers with more than five but less than 10 years exposure and 32 workers with more than 10 years exposure. They worked in two factories where the mean atmospheric concentrations of MMA were 18.5 and 21.6 ppm with ranges of 9–32 and 11.9 to 38.5 ppm. Table 1 shows the anthropometric data and smoking habits of 40 exposed workers and 45 controls.

PROTOCOL

Questionnaires were administered by the same trained interviewer, followed by a training session in spirometry, to avoid an eventual learning effect.¹⁵ One or two days later, two respiratory measurements were performed, one before the shift and the second in the last two hours of the eight hour shift. To avoid circadian variations,^{16–19} investigations were always done in afternoon workshifts.

STATISTICAL ANALYSIS

Data were coded and computer assisted analyses were performed. Spirometric values before the workshift were expressed as ratios of observed/predicted values. The predicted values were given by Knudson *et al.*^{20,21} Variations between the beginning and the end of the workshift were also expressed as ratios of after and before workshift values. As stated previously, our study was performed on 40 workers exposed exclusively to MMA for at least five years and on a comparable control group of workers never exposed to MMA or any other respiratory irritant. Analysis in this study employed the Student's *t* test for comparing two means and a χ^2 analysis of contingency tables for comparison of qualitative variables. When cells had numbers less than five, Fisher's exact test was used. To study the effects of tobacco, we used a two way variance

Table 2 Chest symptoms among exposed workers and controls

	Control group No (%)	Exposed group No (%)	Statistical significance
Morning cough	6 (13)	10 (25)	NS p = 0.04
Chronic cough	2 (<1)	8 (20)	
Morning sputum production	5 (11)	6 (15)	NS
Chronic sputum production	1	4 (10)	NS
Dyspnoea	8 (18)	15 (37)	NS
Wheezing	5 (11)	5 (12)	NS
Asthma	0	0	NS
Previous bronchitis	17 (38)	19 (48)	NS

analysis with the SAS general linear models procedure. The χ^2 test (Mantel-Haenszel) was also used for testing the influence of smoking on chronic cough.

Results

Table 1 shows anthropometric data and smoking habits. There was no significant difference in age, weight, and height between exposed and control workers. Cigarette smoking was also similar. There were no pipe or cigar smokers. Table 2 shows the chest symptoms. Functional signs were more frequent in the exposed group but the difference was significant only for chronic cough ($p = 0.04$). This difference remained significant after adjustment for smoking ($\chi^2 = 4.75$, $p = 0.03$). Table 3 shows the frequency distribution of chronic cough in respect of smoking and exposure to MMA. Thus tobacco consumption was not a confounding factor and cannot solely explain the difference between exposed and control workers.

Spirometric values before the shift did not differ between control and exposed groups. There was no significant difference shown in observed/predicted ratios (table 4). With regard to functional changes within the workshift, all variables (except MEF_{75}) decreased (table 5). This could be explained by circadian variations, but the decrease was higher in

Table 3 Frequency distribution of chronic cough in respect of smoking and exposure to MMA

	No cough No (%)	Cough No (%)
Non-smokers:		
Controls	19 (57.58)	1 (3.03)
Exposed	11 (33.33)	2 (6.06)
Ex-smokers:		
Controls	7 (38.89)	0 (0)
Exposed	9 (50)	2 (11.11)
Smokers:		
Controls	17 (50)	1 (2.94)
Exposed	12 (35.29)	4 (11.76)

the group of exposed workers than in controls. The difference for after shift/before shift ratios was significant for MEF_{50} and MEF_{50}/MEF ($p = 0.04$ and 0.01 respectively). Other ratios decreased but not significantly. The variance analysis with regard to the after shift/before shift ratios of MEF_{50} and MEF_{50}/MEF supports the hypothesis that MMA is exclusively responsible for the decrease in the variables considered (tables 6 and 7 respectively).

Discussion and conclusion

This study showed an increase in the prevalence of chronic cough in a group of workers exposed to MMA. In the same group, airway resistance increased during an eight hour workshift of workers exposed to MMA for at least five years. This obstruction was mild, and FEV_1 did not decrease during the workshift. As in France workers are medically examined at least once every year, however, and in case of health problems the occupational physician can recommend transfer to other job; it may be that without such a transfer the respiratory effects of MMA would have been more severe and widespread. From a methodological point of view, the after shift/before shift ratios of MEF_{50} and MEF_{50}/MEF seem to be useful on a group level, for the detection of mild airways obstruction caused by exposure to an irritant substance such as MMA. Our results support the

Table 4 Spirometric variables for exposed group and controls

	Control group (n = 45)	Exposed group (n = 40)	Statistical significance
FVC	1.01 (0.17)	1.02 (0.12)	NS
FEV_1	1.00 (0.17)	1.01 (0.15)	NS
FEV_1/FVC	0.98 (0.01)	0.98 (0.07)	NS
MEF	1.03 (0.18)	1.05 (0.2)	NS
MEF_{25-75}	0.95 (0.27)	0.98 (0.35)	NS
MEF_{75}	1.03 (0.23)	1.05 (0.22)	NS
MEF_{50}	1.06 (0.3)	1.08 (0.42)	NS
MEF_{25}	0.85 (0.33)	0.91 (0.38)	NS
MEF_{50}/MEF	0.56 (0.17)	0.55 (0.15)	NS

Figures are observed values before shift/predicted values (SD).

Table 5 Spirometric variables for exposed group and controls

	Control group (n = 45)	Exposed group (n = 40)	Statistical significance
FVC	0.99 (0.05)	0.99 (0.05)	NS
FEV_1	0.99 (0.05)	0.98 (0.05)	NS
FEV_1/FVC	0.99 (0.04)	0.99 (0.04)	NS
MEF	0.99 (0.09)	1.00 (0.08)	NS
MEF_{25-75}	0.98 (0.12)	0.95 (0.12)	NS
MEF_{75}	1.00 (0.11)	1.00 (0.09)	NS
MEF_{50}	1.00 (0.12)	0.94 (0.11)	p = 0.04
MEF_{25}	0.98 (0.17)	0.94 (0.19)	NS
MEF_{50}/MEF	1.01 (0.12)	0.94 (0.12)	p = 0.01

Figures are observed values after workshift/observed values before a workshift (SD).

Table 6 Analysis of variance concerning the MEF_{50} (after shift/before shift values)

	MEF_{50} ratio	
	Controls Mean (SD)	Exposed Mean (SD)
Non-smokers	1.00 (0.14) (n = 20)	0.97 (0.10) (n = 13)
Ex-Smokers	1.02 (0.10) (n = 7)	0.94 (0.13) (n = 11)
Smokers	1.00 (0.10) (n = 18)	0.95 (0.11) (n = 16)
F Value:		
MMA	4.16	p = 0.044
Tobacco	0.1	p = 0.908
MMA + Tobacco	0.29	p = 0.75

hypothesis that MMA can be responsible for pulmonary functional disorders⁶ and for airway obstruction⁸ among occupationally exposed workers. Differences between exposed and control groups remained after adjustment for smoking habits. There was no interaction between MMA and smoking ($p > 0.05$ for both variables). A further prospective survey on larger population samples would be of great interest because such a study could include those who move to other jobs because of respiratory disorders.

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Table 7 Analysis of variance concerning the MEF_{50}/MEF ratio (after shift/before shift values)

	MEF_{50}/MEF ratio	
	Controls Mean (SD)	Exposed Mean (SD)
Non-smokers	1.01 (0.11) (n = 20)	0.96 (0.08) (n = 13)
Ex-smokers	1.08 (0.16) (n = 7)	0.94 (0.15) (n = 11)
Smokers	0.99 (0.12) (n = 18)	0.94 (0.14) (n = 16)
F Value		
MMA	6.18	p = 0.015
Tobacco	0.57	p = 0.568
MMA + Tobacco	0.84	p = 0.437

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