SHORT REPORT

Changes in airway function and bronchial responsiveness after acute occupational exposure to chlorine leading to treatment in a first aid unit

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Abstract

Objectives—To describe the baseline characteristics and the time course of changes in lung function in workers accidentally inhaling high concentrations of chlorine in a prospective study.

Methods—Baseline spirometry and methacholine challenge test were performed in a cohort of 278 workers at risk of accidental inhalation of chlorine. Workers in whom accidental inhalation led to intervention in a first aid unit were reassessed five to 25 days after the accident and serially thereafter when there were notable changes.

Results—During a four year follow up period, 13 workers were seen at the first aid unit after a symptomatic accidental inhalation. Three of them experienced notable functional changes: one worker experienced a 10% fall in forced expiratory volume in one second (FEV₁), and the other two had a notable fall in the concentration of methacholine that caused a 20% fall in FEV₁ (PC₂₀). Two workers were smokers and one had a personal history of atopy. Baseline assessment was within the normal range in these three workers. Recovery was complete three months after the accidental inhalation.

Conclusion—Transient but notable decreases in airway function or increases in bronchial responsiveness can occur after an accidental inhalation of high concentrations of chlorine in workers at risk.

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Keywords: bronchial diseases; irritants; occupational exposure; reactive airways dysfunction syndrome

Reactive airways dysfunction syndrome (RADS) can be considered a type of occupational asthma, when it occurs at the workplace after an accidental inhalation exposure to high concentrations of an irritant agent.¹ Several cases of RADS have been documented after massive chlorine exposure.²⁻⁵ In workers at risk of acute overexposure to chlorine, epidemiological studies from visits to first aid departments have provided some evidence of long

term persistent symptoms, abnormalities in airway calibre, and bronchial hyperresponsiveness.⁴⁻⁶

The diagnosis of RADS is based on the history. Consequently, an assumption that a worker has been free of previous respiratory complaints may lead to a misdiagnosis.⁷ Moreover, functional assessment before the offending exposure is rarely available. The presence of bronchial hyperresponsiveness, which is mandatory for the diagnosis, is related to accidental massive exposure to an irritant agent. However, in some subjects, bronchial hyperresponsiveness might pre-exist as an underlying condition and might favour the onset of asthma-like symptoms when exposed to an offending agent. We previously performed a cross sectional study of respiratory symptoms, airway function, and bronchial responsiveness in a group of workers at risk of exposure to chlorine in a metal production plant.⁶ A slight but significant reduction in expiratory flow rates and an increase in bronchial responsiveness were documented in workers who had experienced repeated exposure to chlorine with mild symptoms compared with those who had reported asymptomatic exposure. A surveillance programme for workers who experienced accidental inhalation of chlorine was initiated in the same plant after the first survey. We describe here the time course of changes in lung function after accidental overexposure to chlorine in workers who were referred to the plant's first aid unit between 1992 and 1996 and for whom lung function variables had been previously measured.

Subjects and methods

EXPOSURE ASSESSMENT

The study took place in a metal production plant that started operations in 1989. Chlorine and HCl are used in the processes leading to purification of the metal. Workers can experience accidental inhalation exposure to chlorine in any area of the plant. Chlorine concentration is monitored on a continuous basis in the main areas with stationary sampling devices; if peak chlorine concentration reaches 1 ppm, workers are told to leave the upper floors of the

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Table 1 Baseline characteristics of the 13 workers who registered for first aid for an accidental chlorine inhalation over the four year study period, and the other workers

	Acute chlorine inhalation		p Value
	Yes (n = 13)	No (n = 265)	
n (%):			
Smoking habits:			
Smokers	4 (30.7)	66 (24.9)	0.84*
Ex-smokers	3 (23)	80 (30)	
Nonsmokers	6 (46.1)	119 (44.9)	
Chronic symptoms:			
Yes	1 (7.6)	10 (3.7)	0.41
No	12 (92.3)	255 (96.2)	
Atopy	6 (46.1)	76 (28.6)	0.21
Yes	7 (53.8)	189 (71.3)	
No			
Previous report for first aid:			
≥ 1	3 (23)	32 (12)	0.21
None	10 (76.9)	233 (87.9)	
FEV ₁ < 85 % predicted	4 (30.7)	21 (7.9)	0.02
FVC < 85 % predicted	2 (15.3)	12 (4.5)	
PC ₂₀ mg.ml ⁻¹ :	2 (15.4)	25 (9.4)	0.41†
≤ 16	1 (15.4)	13 (4.9)	
> 16–32	10 (69.2)	227 (85.6)	
> 32			
Mean (SD) % predicted:			
FEV ₁	90.2 (9.4)	99.6 (12)	0.006
FVC	95.1 (8.5)	101.5 (10.6)	0.03
FEV ₁ /FVC	94.4 (4.8)	97.9 (5.8)	0.03

* χ^2 analysis from a 2 row (non-smokers v others) 2 column analysis.† χ^2 analysis from a 2 row (PC₂₀ ≤ 16 v PC₂₀ > 16) 2 column analysis.

area, if chlorine peak concentration reaches 3 ppm, workers are requested to leave the contaminated area immediately. The portable apparatus currently in use, the Metrosonic PM7700, does not assess maximal peak chlorine concentrations. This instrument reads chlorine concentrations progressively over a three minute recording period. That is, the instrument's reading is accurate only when continuous exposure for three minutes has occurred. However, workers—especially those not wearing respiratory protective equipment—can sense the presence of chlorine gas and consequently leave the contaminated area before that time has elapsed. After two minutes the instrument's electrochemical cells can read about 90% of the actual concentration of chlorine gas.

BASILINE ASSESSMENT OF SYMPTOMS AND LUNG FUNCTION

Details on the initial assessment of this cohort of workers are provided elsewhere.⁶ Briefly, data were collected by a trained nurse and two medical technologists at the workplace during three months in the Autumn of 1992. A French adapted version of the International Union against Tuberculosis and Lung Diseases questionnaire⁸ was used to assess the presence

of chronic respiratory symptoms, smoking, and history of atopy (defined by at least one positive answer to "Have you ever suffered from hay fever", or "eczema", or "urticaria").

Spirometry was performed according to the American Thoracic Society standards.⁹ Reference values for forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) were obtained from Knudson *et al.*¹⁰ Bronchial responsiveness was assessed with methacholine to a maximum of 32 mg.ml⁻¹ with a Wright's nebuliser (output, 0.14 ml.min⁻¹) at tidal volume breathing for two minutes.¹¹ The concentration of methacholine causing a 20% fall in FEV₁ (PC₂₀) was derived from individual dose-response curves drawn on a semilogarithmic scale. A PC₂₀ ≤ 16 mg.ml⁻¹ implied bronchial hyperresponsiveness. All workers employed after the end of the cross sectional study (n = 39) were assessed in the same way when starting their jobs and were included in this study.

REPORTING OF ACCIDENTS AND MANAGEMENT OF WORKERS

The medical unit at the workplace is equipped to provide round the clock first aid care as needed for accidental exposure to high concentrations of chlorine, or occasionally, other irritant agents (HCl, ammonia, SF₆, H₂S, or S). From the time the plant started its operations to the 1992 baseline assessment, 42 workers reported at least one accidental inhalation to the first aid unit. After the baseline assessment the following procedures were set up: any worker who was accidentally exposed to high concentrations of chlorine or another irritant gas, and who immediately experienced severe respiratory symptoms, would report this accidental inhalation episode to the first aid unit. Also, workers present on a site where a peak overexposure was measured were given instructions to report to the first aid station even if they would not have done so on their own. The nurse or, during the night, another trained person would assess respiratory complaints, give bronchodilator medication, and monitor the worker as needed until recovery from the acute symptoms. Furthermore, both spirometry and a methacholine bronchial challenge test were performed within three weeks of the accidental inhalation. If notable changes from baseline occurred, monthly reassessment was done until recovery.

Table 2 Surveillance of accidental chlorine inhalation 1992–6: results of repeated functional assessments and methacholine challenge tests

Subject	Age (y)	Smoker status	Previous visits to first aid (n)	Duration of acute symptoms (h)	FEV ₁ , % predicted			FVC, % predicted			PC ₂₀ mg.ml ⁻¹		
					Baseline	Accident	Follow up	Baseline	Accident	Follow up	Baseline	Accident	Follow-up
1	31	Yes	0	12	90.4	90.2	89.4	94.9	94.7	93.9	>32	11.5	>32
2	36	Yes	2	1	94.1	87.3	91.7	104.3	100.5	104.1	>32	19.5	>32
3	24	No	0	72	102.5	97.1	100.5	101.6	97.7	98.8	17	5.2	13.2
4	36	No	0	1	102.0	102.2		99.6	98.3		>32	>32	
5	28	No	3	5	85.7	85.4	85.1	91.7	91.7	87.4	4	24	21
6	28	No	0	8	94.6	100.6		99.1	101.6		>32	>32	
7	37	Yes	0	5	76.0	74.6		90.3	86.3		>32	>32	
8	20	No	0	8	84.3	79.1		83.5	79.0		>32	>32	
9	32	No	1	1	97.4	101.4		106.1	106.1		>32	>32	
10	30	Yes	0	1	81.9	88.0		85.9	91.4		>32	18	
11	30	No	0	1	83.1	87.3		83.5	89.1		16	>32	
12	34	No	0	24	86.4	82.5		86.3	82.6		>32	>32	
13	35	No	0	48	102.9	104.8		107.5	112.5		>32	>32	

ANALYSIS

Definition of a notable functional change included: (a) a decline in $FEV_1 \geq 10\%$ (absolute values) from baseline (FEV_1 before the accident– FEV_1 after the accident)/ FEV_1 before the accident), (b) a $PC_{20} \leq 16$ mg/ml at follow up in subjects with normal baseline bronchial responsiveness, (c) a 3.2-fold decrease in PC_{20} (the 95% confidence interval (95% CI) for reproducibility) if baseline PC_{20} was <16 mg/ml.^{12,13} Unpaired Student's *t* tests, χ^2 analysis, and Fisher's exact tests were used, and a *p* value <0.05 was considered to be significant. The study protocol was approved by the Hôpital du Sacré-Coeur ethics committee and written consent was obtained from all participants.

Results

From 1 January 1993 to 1 November 1996, 13 workers were seen at the first aid unit for accidental inhalation of high concentrations of chlorine. All were men, and the mean (range) age was 31 (20–37) years. Table 1 shows the characteristics at the initial assessment for these 13 subjects, as well as for the remaining workers who were not seen at the first aid unit during that period. No significant differences were found between the two groups for smoking habits, frequency of either reported chronic symptoms or history of personal atopy, number of previous accidents reported to the first aid unit, or distribution into categories of abnormal bronchial responsiveness; the mean FEV_1 , FVC, and FEV_1/FVC ratio were significantly lower in the 13 workers seen at the first aid unit.

All 13 subjects reported an immediate onset of symptoms after accidental inhalation exposure. The main acute symptoms were throat irritation ($n=7$), cough ($n=10$), and shortness of breath ($n=10$). Mean (range) duration of acute symptoms was brief (14.4 (1–72) hours). Immediate treatment consisted of inhaled bronchodilators in 10 cases. No anti-inflammatory drugs were given.

Functional assessment and a methacholine challenge test were performed five to 25 days (mean 11.5 days) after the offending exposure (table 2). Two subjects showed a notable fall in PC_{20} , as defined above and one subject, a 9.5% fall in FEV_1 (4.2 v 3.8 litres). These three subjects had a baseline assessment of airway calibre and bronchial responsiveness within the normal range. Two of these subjects were smokers and one had a history of personal atopy. Subjects 1 and 3 showed bronchial hyperresponsiveness after the acute inhalation. However, PC_{20} returned to the baseline after three to four months of follow up. In subject 2, a transient decrease in FEV_1 , from 94.1% to 87.3% predicted, was found with recovery thereafter. Among the remaining 10 subjects, subject 5 had reported three previous accidental inhalation episodes to first aid, had a history of atopy, and had shown bronchial hyperresponsiveness at the baseline assessment. After the accidental inhalation, PC_{20} was above 16 $mg \cdot ml^{-1}$.

Discussion

This study shows that a transient but notable decrease in airway function or increase in bronchial responsiveness can occur after an accidental inhalation of high concentrations of chlorine in workers at risk. Three subjects among the 13 who consulted the first aid unit after an accidental inhalation experienced such changes. As no anti-inflammatory treatment was given, these changes might reflect the natural history of bronchial injury after accidental inhalation to high concentrations of an irritant agent. For the first time to our knowledge, data from baseline assessment before the occurrence of an accidental inhalation episode were available. From these data, it is evident that baseline characteristics of workers who experienced an accidental inhalation episode were not significantly different from those of other workers, except for FEV_1 , FVC, and FEV_1/FVC , which were lower. Whether subjects with lower spirometric values are more prone to experience symptoms after exposure remains to be elucidated. The three subjects who showed a notable change in airway function and responsiveness had normal values before the accidental exposure. On the other hand, a fourth subject with normal PC_{20} values after the accidental inhalation had increased bronchial responsiveness when first assessed. This subject reported a history of atopy, but had also experienced three previous episodes of accidental inhalation. These factors may account for the initial abnormal findings.

Our findings suggest that after an accidental inhalation exposure to high concentrations of chlorine, severe respiratory symptoms are no more likely to occur in subjects with pre-existing bronchial hyperresponsiveness than in other workers at risk. D'Alessandro *et al* studied airway response to chlorine at a concentration of 1 ppm, which is the recommended occupational 15 minute ceiling short term exposure limit, for 60 minutes in five subjects with and five subjects without airway hyperresponsiveness.¹⁴ Two subjects in the so called bronchial hyperresponsiveness group experienced symptoms after exposure. Although a notable fall in FEV_1 occurred in the groups both with and without bronchial hyperresponsiveness immediately after exposure, the fall was greater in the bronchial hyperresponsiveness group. This suggests that a susceptible subpopulation may respond acutely to the offending agent with a greater decrement in pulmonary function. Our results are not contradictory, but show that surveillance of workers at risk of chlorine exposure cannot be restricted to those subjects with pre-existing airway hyperresponsiveness.

It is difficult to compare the time course of abnormalities in function and airway responsiveness after massive exposure to an offending agent with other studies because of the lack of baseline assessment in previous reports. Blanc *et al* studied 10 subjects recovering from a single toxic inhalation exposure; none had abnormal airflow when assessed within two weeks of exposure, but eight showed airway hyperresponsiveness.¹⁵ By three months, airway

hyperresponsiveness had reversed in only one subject. Bhrer *et al* studied 51 construction workers at risk of developing RADS due to repeated exposure to chlorine gas during renovations to a pulpmill: functional assessment at 18–24 months after exposure showed that 16 (31%) had abnormal airflow, and 29 (56%) had airway hyperresponsiveness.¹⁶ When further assessed by Malo *et al* 30 to 36 months after exposure, 18 of these 29 subjects showed no notable change in FEV₁, but six of them had considerable improvement in PC₂₀ results.¹⁷ These findings, like those of the present study, suggest that less pronounced bronchial alterations induced by exposure to chlorine may be reversible.

Few workers, specifically 4.6% (13/278), visited the first aid unit after accidental inhalation episodes during this four year study period. It seems unlikely that workers experiencing severe symptoms after acute exposure to chlorine would not contact first aid, because all workers had been advised in advance to pay a visit to the first aid department if such an event occurred. Salisbury *et al* studied a group of 316 pulpmill workers, and reviewed first aid reports of incidents of acute chlorine inhalation over an eight year period.¹⁸ There was a greater decline in FEV₁/FVC ratio and midmaximal flow rate in the exposed group than in the non-exposed group. The authors suggested that first aid reports may be reliable predictors of abnormalities of lung function. In a study of 281 construction workers repeatedly exposed to chlorine, Courteau *et al* found that first aid referral was significantly associated with the presence of immediate respiratory symptoms.¹⁹ However, the proportion of workers who reported accidental inhalation but had never gone to the first aid unit was high (153/257). This could be attributed to the fact that these construction workers were not familiar with the occupational hazard of chlorine or the first aid facilities.

In summary, this is the first report that shows deterioration in airway function of subjects who experienced an accidental inhalation episode and in whom pre-exposure function measures were available. Changes were transient. Pre-existing bronchial hyperresponsiveness did not seem to be a predisposing factor, although the limited number of workers who experienced events and presented at the first aid unit precludes drawing any firm conclusions.

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