Bronchoconstriction in potroom workers

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ABSTRACT The effect on airway responsiveness of an oral dose of a β -adrenergic blocker (80 mg propranolol) given before work, was studied in 15 potroom workers who complained of dyspnoea, chest tightness and wheezing after they had started to work in potrooms. The same study was performed in a group of 10 potroom workers, selected at random, who had not complained of such symptoms. In addition, another group of 12 potroom workers with respiratory symptoms were given 1 mg atropine subcutaneously. Ventilatory function was assessed from forced expiratory curves (by means of a waterless spirometer) and from maximum expiratory flow-volume curves (by means of a digital pneumotachograph). Bronchoconstriction during the first few hours' work was significantly potentiated by propranolol in the group of potroom workers with respiratory complaints. Propranolol did not produce this effect in workers who had not complained of respiratory symptoms. Atropine sulphate abolished the fall in ventilatory volumes which occurred during the first few hours of work. These findings suggest that acute bronchoconstriction, particularly in small airways, and respiratory symptoms occurring in certain potroom workers may be based on an alteration in autonomic balance with vagal preponderance.

Our previous study of 207 workers employed in a plant for the electrolytic extraction of aluminium (Šarić *et al.*, 1979) showed that a considerable number of workers (10.2%) complained of dyspnoea and wheezing in the chest. Of 21 subjects with complaints, 19 claimed that the symptoms appeared after they had started to work in potrooms. Only two of them had previously suffered from similar symptoms. Pulmonary functions tests also showed bronchoconstrictive changes in these workers.

In view of the technological process used in the plant (the Alu-Swiss process) it is probable that the respiratory effect was caused by exposure to hydrogen fluoride (and particulate fluorides) and to sulphur dioxide. However, the mechanism of this effect, particularly from the point of view of an increased respiratory susceptibility in a number of exposed workers, at that time remained unexplained.

From the studies of Widdicombe *et al.* (1962), Bouhuys (1971) and Nadel (1973, 1974) it seems that the autonomic nervous system is important in

determining the lung's response to dust inhalation. The same authors demonstrated that alteration of the balance between vagal and sympathetic stimuli can markedly influence individual sensitivity to dust exposure. The reflex nature of bronchoconstriction seems to be involved in the bronchoconstrictive effect during the inhalation of sulphur dioxide (Nadel *et al.*, 1965).

In the studies of Žuškin *et al.* (1974) and Žuškin and Bouhuys (1975), propranolol, by blocking β -receptors, significantly increased bronchial sensitivity to cigarette smoke in regular smokers, and to hemp dust in byssinotic textile workers.

The purpose of the present study was to examine the impaired balance between vagal and sympathetic stimuli as a possible cause of increased susceptibility to exposure in the electrolytic extraction of aluminium.

Sample and method

From a group of 207 potroom workers examined in 1976, 21 workers who complained of dyspnoea, chest tightness and wheezing in the chest were selected for the experimental study with a β -adrenergic antagonist drug. Fifteen of these workers were actually included in the study: others were found to have left the industry in the meantime.

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Received for publication 28 March 1978
Accepted for publication 4 December 1978

Ventilatory capacity testing was first performed in the morning, before work (6 00 am). After these tests, workers were given two tablets of a β -adrenergic antagonist (80 mg propranolol). The ventilatory capacity measurements were repeated two hours later. The same experiment was conducted on the following day, in the same group of workers, with a placebo instead of the drug. During both experiments the pulse rate of each worker was recorded. The workers who smoked were instructed not to smoke for at least half an hour before testing.

Tests of ventilatory functions included recording of forced expiratory curves on a waterless spirometer (Pulmonor, Jones Medical Instrument Corp, USA) and of maximum expiratory flow-volume (MEFV) curves on a digital pneumotachograph (Vertek, VR 4000). At least three forced expiratory manoeuvres were recorded on each spirometer. Forced vital capacity (FVC) and the one-second forced expiratory volume (FEV_{1.0}) were calculated from two identical or similar curves. Peak expiratory flow (PEF) and the flow rates at 50% and 25% of the control vital capacity (MEF_{50%} and MEF_{25%}) were read from the best MEFV curves, assuming that total lung capacity (TLC) does not change materially during the experimental procedure (Žuškin *et al.*, 1974). Smoking habit and occupational histories were also recorded for each worker. Subsequently, the same study was performed in a group of 10 potroom workers without respiratory symptoms, selected at random.

In addition, a study with atropine sulphate was carried out in another group of 12 potroom workers, who also complained of acute respiratory symptoms similar to those already described (dyspnoea, chest tightness, wheezing). These subjects were selected from a group of 100 potroom workers employed in another plant in which the Alu-Swiss process was also used.

The same ventilatory tests used for the previous groups were first completed in the morning before work, then two hours later. After the second testing, workers were given 1 mg atropine sulphate subcutaneously. The ventilatory measurements were repeated about 1.5–2 hours later.

Individual samples were taken from the breathing zones of all subjects included in the studies described. Each worker wore two samplers, one of which served for the collection of particulate fluorides and hydrogen fluoride and the other for sulphur dioxide.

Sulphur dioxide was determined as sulphate ion by titration with barium perchlorate and thorin indicator. For the determination of fluorides a specific electrode was used.

Student's paired *t* test was used to evaluate the significance of volume changes.

Results

STUDY WITH PROPRANOLOL

Potroom workers with respiratory complaints (Group I)

The mean age in this group of workers was 31.7 (± 6.5) years and the mean height 176.9 (± 7.1) cm. Of 15 workers, six were current smokers, three were non-smokers and six were ex-smokers, who had stopped smoking mainly because of difficulty in breathing, which they attributed to their work.

In most cases, breathing difficulties, chest tightness and wheezing were reported by workers during the work shift (seven workers), but sometimes only after the end of the shift (two workers). Six workers complained both at work and subsequently after work. Symptoms usually started five or more months after the beginning of exposure and were still present at the time of examination. In only two workers were the symptoms less intense at the time of the study than they had been previously.

Table 1 shows comparative changes in ventilatory measurements after treatment with propranolol or placebo. After treatment with 80 mg of propranolol the ventilatory volumes showed a fall which was statistically significant for all volumes measured. When placebo was used instead of propranolol, FVC and FEV_{1.0} values showed a tendency to increase. However, PEF, MEF_{50%} and MEF_{25%} values were slightly decreased two hours after the administration of placebo, but the difference was not statistically significant.

The preshift values of ventilatory capacity were somewhat lower on the second day (when placebo was used) than on the first day of the experiment, with propranolol.

Table 2 shows the fluorine and sulphur dioxide concentrations to which workers were exposed during the shift. The results indicate that individual exposure to hydrogen fluoride and particulate fluorides, or to sulphur dioxide, was not high. The maximum allowable concentration (MAC) in Yugoslavia for hydrogen fluoride is 1.7 mg/m³, for fluorides (as F) 1 mg/m³ (weighted average), and for sulphur dioxide 10 mg/m³ (JUS.Z.BO.001, 1971).

Potroom workers without respiratory complaints

The mean age (31.0 $\pm$ 7.5 years) and mean height (177.6 $\pm$ 4.1 cm) of these workers were similar to those of the previous group. There was a higher proportion of smokers (6 out of 10) than in the group of workers with respiratory complaints.

Table 3 shows comparative changes in ventilatory volumes after treatment with propranolol or placebo. After treatment with propranolol the mean

Table 1 Comparison of ventilatory volumes after treatment with (1) propranolol and (2) placebo in potroom workers with respiratory symptoms

Ventilatory measurements	(1) Before work		Two hours after propranolol: mean difference (%) of initial values	(2) Before work		Two hours after placebo: mean difference (%) of initial values
	$\bar{X}$	SD		$\bar{X}$	SD	
FVC (litre)	5.34	0.94	- 3.6*	5.17	0.95	+ 2.0
FEV _{1.0} (litre)	4.12	0.77	- 8.0**	3.83	0.99	+ 3.2
PEF (litre s ⁻¹)	6.01	0.85	- 12.5**	5.59	0.97	- 3.6
MEF _{50%} (litre s ⁻¹)	4.47	1.34	- 20.0*	4.07	0.92	- 4.0
MEF _{25%} (litre s ⁻¹)	2.23	0.64	- 25.6*	2.19	0.59	- 0.5
Pulse rate	75.5 (56-88)		65.6 (50-80)	64.3 (52-76)		65.9 (52-76)

* $P < 0.05$ ** $P < 0.01$

Table 2 Exposure to fluorine and sulphur dioxide measured during the work shift for workers with respiratory symptoms

Exposure	Hydrogen fluoride	Particulate fluorides	Total fluorides	Sulphur dioxide
Mean (mg/m ³)	0.63	0.88	1.51	1.48
Range (mg/m ³)	0.28-1.09	0.46-2.15	0.77-3.24	0.56-2.54

ventilatory volumes tended to decrease, with the exception of FVC, but the mean changes, expressed as percentages of initial values, were not statistically significant. When placebo was used instead of propranolol the ventilatory volumes (with the exception of FVC) showed a slight but insignificant increase two hours later.

Table 4 shows fluorine and sulphur dioxide concentrations during the work shift for this group of workers without respiratory symptoms. The values were similar in range and mean to those found for the potroom workers with respiratory complaints (Table 2).

STUDY WITH ATROPINE IN POTROOM WORKERS WITH RESPIRATORY COMPLAINTS (GROUP II)

In this group of workers the mean age was 41.1 (± 11.4) years, and the mean height 174.4 (± 6.1)

cm. Five were current smokers, one an ex-smoker and six were non-smokers.

All ventilatory measurements tended to decrease in the first two hours of work, but all showed an increase after treatment with atropine (Table 5).

The levels of exposure to fluorine and sulphur dioxide in this group of potroom workers are shown in Table 6. The concentrations were slightly higher than those found for the groups described previously.

Discussion and conclusion

Treatment with propranolol in the group of workers who complained of dyspnoea, chest tightness and wheezing in connection with exposure at work was followed by a significant decrease in ventilatory indices, particularly in flow rates. The administration of a placebo to the same group of workers under the same conditions did not have such an effect.

In the group of potroom workers without respiratory complaints, treatment with propranolol also produced a decrease in ventilatory volumes (with the exception of FVC) but the changes were slight and not statistically significant.

The results of the two studies performed with propranolol show that, in the group of potroom workers who complained of respiratory symptoms,

Table 3 Comparison of ventilatory volumes after treatment with (1) propranolol and (2) placebo in potroom workers without respiratory symptoms

Ventilatory measurements	(1) Before work		Two hours after propranolol: mean difference (%) of initial values	(2) Before work		Two hours after placebo: mean difference (%) of initial values
	$\bar{X}$	SD		$\bar{X}$	SD	
FVC (litre)	5.32	0.73	+ 0.2	5.44	0.77	- 0.9
FEV _{1.0} (litre)	4.54	0.75	- 0.6	4.56	0.76	+ 0.7
PEF (litre s ⁻¹)	9.80	1.34	- 4.1	9.65	1.77	+ 4.2
MEF _{50%} (litre s ⁻¹)	6.85	1.60	- 7.3	6.55	1.14	+ 1.7
MEF _{25%} (litre s ⁻¹)	3.36	0.64	- 10.1	3.18	0.59	+ 0.7
Pulse rate	85.4 (68-96)		66.4 (52-72)	73.4 (68-80)		75.2 (68-80)

Table 4 Exposure to fluorine and sulphur dioxide measured during the work shift for workers without respiratory symptoms

Exposure	Hydrogen fluoride	Particulate fluorides	Total fluorides	Sulphur dioxide
Mean (mg/m ³)	0.85	0.36	1.21	1.08
Range (mg/m ³)	0.24–3.21	0.08–1.91	0.36–5.12	0.74–2.00

Table 5 Comparison of ventilatory volumes after treatment with atropine sulphate in potroom workers with respiratory symptoms (Group II)

Ventilatory measurements	Before work		Mean difference (%) of preceding values	
	$\bar{X}$	SD	Two hours later (before atropine was given)	1.5–2 hours after treatment with atropine
FVC (litre)	4.18	1.51	–6.3	+7.3
FEV _{1.0} (litre)	3.29	1.27	–5.8	+5.8
PEF (litre s ^{–1})	7.91	2.83	–6.2	+4.9
MEF _{25%} (litre s ^{–1})	5.23	2.38	–0.6	+8.5
MEF _{75%} (litre s ^{–1})	2.82	1.33	–2.5	+7.3

Table 6 Exposure to fluorine and sulphur dioxide measured during the work shift for workers with respiratory symptoms (atropine study)

Exposure	Hydrogen fluoride	Particulate fluorides	Total fluorides	Sulphur dioxide
Mean (mg/m ³)	1.46	0.51	1.97	1.93
Range (mg/m ³)	0.75–2.30	0.30–0.97	1.09–3.01	0.97–3.06

the initial values of measured flow volumes were much lower than the initial values of the same indices in workers without respiratory symptoms, in spite of the fact that the mean FVC and FEV_{1.0} were similar in both groups. However, the decrease in the flow rates after treatment with propranolol was significant in the first but not in the second group of potroom workers.

Measurements of fluorine and sulphur dioxide in the work environment were similar for both groups, and these workers were also of similar ages. The percentage of smokers was higher in workers without respiratory complaints.

The bronchoconstrictive effect of propranolol in subjects with asthma is undisputed, although there are pronounced individual variations in reaction (McNeill, 1964; Zaid and Beall, 1966; Jones, 1972; Gayrard *et al.*, 1975) which overlap those of normal subjects (McDonald *et al.*, 1967).

In normal non-asthmatic subjects, β -adrenergic blockade with propranolol has been reported not to produce any effect (Richardson and Sterling, 1969;

Tattersfield *et al.*, 1973), or a small decrease in ventilatory volumes, or even significant bronchoconstriction, with marked individual differences (McNeill and Ingram, 1966; Stone *et al.*, 1973). A study of β -adrenergic function in airways of healthy and asthmatic subjects (Gayrard *et al.*, 1975) indicated that normal subjects have a weak and a variable bronchodilator β -adrenergic activity. In most asthmatics, β -adrenergic tone appeared to be more pronounced. Asthmatic patients differ quantitatively rather than qualitatively from healthy subjects with respect to β -adrenergic receptor function.

Jones (1972) studied the effect of β -blockers on ventilatory function in normal and asthmatic subjects and found that 15% of the normal subjects showed a certain degree of lability after propranolol. Individual differences in reaction to propranolol could be explained by individual differences in vagal activity (Simonsson *et al.*, 1967). This proportion of normal subjects is potentially more labile than the remainder of the population.

Our potroom workers with respiratory complaints, including those from the atropine study, comprised 10–12% of the workers potentially exposed to fumes in plants where studies were performed. None of them gave a history of bronchial asthma or atopy. Thus, these subjects could be regarded as normal. However, our investigations show that the response of these workers to β -blockers was intense, and much more pronounced than that in workers without respiratory complaints. From the data obtained we deduce that the workers who showed such a susceptibility to exposure had a response which was associated mainly with small airway constriction.

The study with atropine demonstrated that, in subjects with respiratory complaints, subcutaneous injection of atropine sulphate abolished the fall in respiratory volumes and flow-rates which occurred in the first two hours of work.

All these findings indicate that a functional imbalance between vagal and sympathetic effects on airway smooth muscle may be involved in the increased sensitivity of certain individuals to influences at work. A drug which blocks β -adrenergic receptors (propranolol) changes the vagal-sympathetic balance in the direction of vagal dominance. Under these circumstances, small airway constriction during exposure to respiratory irritants is potentiated (Bouhuys, 1971). Atropine sulphate abolished bronchoconstriction, probably by inhibition of the efferent cholinergic arc of the bronchoconstriction reflex (Simonsson *et al.*, 1967).

The studies described here, therefore, indicate that the acute respiratory symptoms and changes of lung function registered in certain workers employed

in the electrolytic extraction of aluminium may be based on functional imbalance of their autonomic nervous systems, with increased vagal activity resulting in increased sensitivity to potroom fumes and dusts.

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