Pharmacological prevention of acute ventilatory capacity reduction in flax dust exposure

F. VALIĆ and EUGENIJA ŽUŠKIN

Andrija Štampar School of Public Health, Zagreb University, Zagreb, Yugoslavia

Valić, F., and Žuškin, E. (1973). *British Journal of Industrial Medicine*, 30, 381-384. **Pharmacological prevention of acute ventilatory capacity reduction in flax dust exposure.** The protective effect of the preshift application of a bronchodilator (orciprenaline), an antihistamine drug (diadril), and ascorbic acid on flax-induced acute bronchoconstriction was studied in 13 byssinotic and 7 non-byssinotic female workers exposed to airborne fibres of biologically retted flax. Orciprenaline was applied by inhalation, while diadril and ascorbic acid were given orally. All the three drugs exerted a significant preventive effect, diminishing the acute fall of ventilatory capacity during the shift. The fall in forced expiratory volume ($FEV_{1.0}$) was reduced by 50% and the fall in maximal flow rate at 50% vital capacity ($\dot{V}_{max}$ 50% VC) by over 65%.

In our previous studies (Žuškin and Valić, 1966; Valić and Žuškin, 1971, 1972a) we showed that a bronchodilator applied before a work shift significantly diminished the acute forced expiratory volume ($FEV_{1.0}$) reduction over the shift in cotton, hemp, jute, and sisal workers. Bouhuys and van de Woestijne (1970) have shown in four hemp workers that the oral administration of 10 mg orciprenaline before hemp dust exposure considerably diminished the acute decrease of $FEV_{1.0}$ and vital capacity (VC). Bouhuys, van Duyn, and van Lennep (1961) administered an antihistamine to three flax dressers on Monday before work and did not find much less change in the lung volume than after dust exposure without treatment. Later, however, Bouhuys (1963) succeeded in preventing the acute $FEV_{0.75}$ fall in 13 byssinotic cotton weavers by administering the antihistamine, methdilazine. Our study in hemp workers (Valić and Žuškin, 1972b) demonstrated the preventive action of an antihistamine and of ascorbic acid (vitamin C) on the bronchoconstricting effect of hemp dust. Some studies in vitro (Dawson and West, 1965; Dawson, Hemsworth, and Stockham, 1967) and in vivo (Žuškin, Lewis, and

Bouhuys, 1973) indicated that ascorbic acid antagonized histamine and also 5-hydroxytryptamine.

In a previous study (Žuškin and Valić, 1973) we found significant acute falls of ventilatory capacity over the work shift in a group of non-smoking female flax workers. In the present study an attempt was made to evaluate the application of a bronchodilator, an antihistamine, and ascorbic acid with a view to preventing acute reductions of ventilatory capacity in workers exposed to airborne flax dust.

Subjects and methods

Subjects

Twenty female flax workers took part in the study (13 with and 7 without symptoms of byssinosis). Byssinosis was diagnosed according to Schilling *et al.* (1964). All were volunteers. Their mean age was 35 years, and the mean duration of employment in the flax industry was 10 years. They were exposed to a mean total flax dust concentration of 16.9 mg/m³ (respirable fraction 3.4 mg/m³).

Ventilatory function tests

The one-second forced expiratory volume ($FEV_{1.0}$) traced with a Bernstein type spirometer was measured and the

maximum expiratory flow-volume curve was recorded on a flow-volume spirometer (Peters, Mead, and van Ganse, 1969). The $FEV_{1.0}$ data were corrected to BTPS. From the maximum flow-volume curve the maximum flow rate at 50% of the control vital capacity ($\dot{V}_{max}$ 50% VC) was calculated. Three maximally rapid expirations were performed on each spirometer, and the mean of the two highest values was used as the result of the respective test. The ventilatory function was recorded before and at the end of the work shift.

To evaluate the comparative effect of different drugs on preventing the acute ventilatory function change over the work shift, the study was conducted on four consecutive Mondays. In the first week the ventilatory capacity measurements were performed without any drug treatment. On the following Monday orciprenaline¹ was administered by inhalation before the shift. Three doses of orciprenaline (750 µg each) were applied by a pocket nebulizer. On the third Monday the subjects were given a tablet of an antihistamine (diadril²) orally before the shift. On the fourth Monday one tablet of a placebo was given before the shift, and then, starting from the following Tuesday, 500 mg daily of ascorbic acid was given through the remaining days of the week including the following Monday before the shift.

Statistical analysis

Data on ventilatory function tests before and after the shift were tested for difference by using the *t* test for paired variables. To compare ventilatory capacity between the different groups, the *t* test for unpaired variables was used. The results were considered significant when the probability of obtaining the results by chance alone was less than 0.05.

Results

The mean acute changes in $FEV_{1.0}$ and $\dot{V}_{max}$ 50% VC in 13 byssinotics on the first working day without

¹Alupent: 1-(3,5-dihydroxyphenyl)-2-isopropylamino-aethanol sulphate

²Diadril: one tablet contains 25 mg 1-p-chlorbenzhydriol-4-(m-methyl-benzyl)-piperazine hydrochloride.

drug treatment and with the drugs administered before the shift are presented in Table 1.

In both $FEV_{1.0}$ and $\dot{V}_{max}$ 50% VC a statistically significant decrease was recorded over the shift ($P < 0.01$). By comparing the mean acute changes in $FEV_{1.0}$ and $\dot{V}_{max}$ 50% VC measured on the Monday when no drug was administered, significantly larger relative mean acute reductions were observed in the latter (18.3%) than in the former (9.9%) parameter.

Significantly smaller acute reductions in $FEV_{1.0}$ and $\dot{V}_{max}$ 50% VC ($P < 0.05$) occurred after the preshift administration of orciprenaline, diadril and ascorbic acid compared with the mean acute reductions in ventilatory capacity on Monday without drug treatment. The preventive effect of all these drugs was found to be more pronounced in the reduction of $\dot{V}_{max}$ 50% VC than in the reduction of $FEV_{1.0}$. In spite of a pronounced preventive effect of the drugs administered before the work shift, making the falls of ventilatory capacity become much smaller, the acute reductions over the work shift on Monday still remained statistically significant, except for $\dot{V}_{max}$ 50% VC after the antihistamine administration.

The mean changes of $FEV_{1.0}$ and $\dot{V}_{max}$ 50% VC in seven non-byssinotic subjects without and with drug treatment before the first working shift in the week are presented in Table 2. The preventive effect in workers without byssinosis was slightly less pronounced than in those with byssinosis. Because of a small number of subjects, the data were not statistically evaluated.

Analysing the workers' comments on their subjective feeling, it was found that 12 byssinotic workers claimed to have felt much better during the dust exposure following the administration of ascorbic acid tablets. After the antihistamine or bronchodilator drug eight byssinotic subjects said

TABLE 1
MEAN CHANGES IN $FEV_{1.0}$ AND $\dot{V}_{max}$ 50% VC IN 13 BYSSINOTIC FLAX WORKERS
WITHOUT AND WITH DRUG TREATMENT BEFORE THE WORK SHIFT

	$FEV_{1.0}$ (ml)				$\dot{V}_{max}$ 50% VC (l/sec)			
	Before shift	Mean reductions over shift			Before shift	Mean reductions over shift		
		ml	%	P		l/sec	%	P
Without treatment	2 598	257	9.9	< 0.01	3.72	0.68	18.3	< 0.01
Placebo	2 590	237	9.2	< 0.01	3.70	0.61	16.5	< 0.01
Bronchodilator	2 578	119	4.6	< 0.01	3.79	0.18	4.7	< 0.05
Antihistamine	2 605	103	3.9	< 0.01	3.70	0.16	4.3	NS
Ascorbic acid	2 583	127	4.9	< 0.01	3.77	0.29	7.7	< 0.05

NS = difference statistically not significant ($P > 0.05$)

TABLE 2
MEAN CHANGES IN $FEV_{1.0}$ AND $\dot{V}_{max}$ 50% VC IN 7 NONBYSSINOTIC FLAX WORKERS
WITHOUT AND WITH DRUG TREATMENT BEFORE THE WORK SHIFT

	$FEV_{1.0}$ (ml)			$\dot{V}_{max}$ 50% VC (l/sec)		
	Before shift	Mean reductions over shift		Before shift	Mean reductions over shift	
		ml	%		l/sec	%
Without treatment	2 724	178	6.5	4.18	0.36	8.6
Placebo	2 720	186	6.8	4.14	0.39	9.4
Bronchodilator	2 724	64	2.3	4.00	0.10	2.5
Antihistamine	2 728	86	3.2	3.98	0.14	3.5
Ascorbic acid	2 744	86	3.1	4.22	0.20	4.7

they felt less dyspnoea or chest tightness during the following dust exposure. Two byssinotic workers mentioned a somewhat weakened effect of dust after placebo application. Out of seven workers without byssinosis four felt better after ascorbic acid or bronchodilator, three after antihistamine, and none after placebo.

Discussion

The preshift oral dose of the antihistamine, the inhalation of the bronchodilator, as well as the preventive administration of ascorbic acid diminished the mean acute reduction of ventilatory capacity over the shift on Monday in 13 byssinotic and 7 non-byssinotic subjects exposed to flax dust. The $\dot{V}_{max}$ 50% VC appeared to be a more sensitive test in detecting the protective effect of these drugs than the $FEV_{1.0}$. The mean acute reduction in $\dot{V}_{max}$ 50% VC on the days with drug treatment was about 33% of that measured on the first working day with no treatment, while the mean acute reduction of $FEV_{1.0}$ was about 50% of the reduction when no treatment was applied. The fall of ventilatory capacity over the shift, although considerably diminished, still remained statistically significant ($P < 0.05$).

The mechanism of the preventive effect of ascorbic acid is not quite clear. Previous studies in textile workers indicated that the reduction of ventilatory capacity during dust exposure resulted from the bronchoconstricting action of histamine and/or some other active substances. However, other factors such as oedema of the mucous membrane or other changes narrowing the respiratory airways may play an additional role (Bouhuys, 1966).

It has been reported that ascorbic acid decreases the permeability of the vessels (Goodman and Gilman, 1970). It is possible that ascorbic acid, by

decreasing capillary permeability (which is known to be increased by histamine), prevents oedema formation and, consequently, narrowing of the bronchial tubes—a phenomenon partially responsible for reduction in ventilatory capacity. The experiments of Dawson and West (1965) have shown that ascorbic acid exerted a protective effect on histamine, 5-hydroxytryptamine, and bradykinine bronchospasms in anaesthetized guinea-pigs. A recent study (Žuškin *et al.*, 1973) has confirmed this assumption, showing an antagonistic action of ascorbic acid (administered orally) against the effect of histamine on the human airway smooth muscle.

A further investigation is necessary to clarify the mechanism of this—interesting for practical application—preventive effect of ascorbic acid in textile workers exposed to biologically active dust.

References

- Bouhuys, A. (1963). Prevention of Monday dyspnea in byssinosis: A controlled trial with an antihistamine drug. *Clinical Pharmacology and Therapeutics*, **4**, 311-314.
- (1966). Byssinosis in textile workers. *Transactions of the New York Academy of Sciences*, series 2, **28**, 480-490.
- , van Duyn, J., and van Lennep, H. J. (1961). Byssinosis in flax workers. *Archives of Environmental Health*, **3**, 499-509.
- , and van de Woestijne, K. P. (1970). Respiratory mechanics and dust exposure in byssinosis. *Journal of Clinical Investigation*, **49**, 106-118.
- Dawson, W., Hemsworth, B. A., and Stockham, M. A. (1967). Action of sodium ascorbate on smooth muscle. *British Journal of Pharmacology and Chemotherapy*, **31**, 269-275.
- , and West, G. B. (1965). The nature of the antagonism of bronchospasm in the guinea-pig by ascorbic acid. *Journal of Pharmacy and Pharmacology*, **17**, 595-596.
- Goodman, L. S., and Gilman, A. (Editors) (1970). *The Pharmacological Basis of Therapeutics*, 4th ed., p. 1665. Macmillan, London and Toronto.
- Peters, J. M., Mead, J., and van Ganse, W. F. (1969). A simple flow-volume device for measuring ventilatory function in the field. *American Review of Respiratory Diseases*, **99**, 617-622.

- Schilling, R. S. F., Vigliani, E. C., Lammers, B., Valić, F., and Gilson, J. C. (1964). A report on a conference on byssinosis. *Proceedings of the XIVth International Congress on Occupational Health, Madrid, 1963*, vol. 2, pp. 137-145. Excerpta Medica Foundation, Amsterdam.
- lić, F., and Žuškin, E. (1971). Effects of hemp dust exposure on nonsmoking female textile workers. *Archives of Environmental Health*, 23, 359-364.
- , and — (1972a). Effects of different vegetable dust exposures. *British Journal of Industrial Medicine*, 29, 293-297.
- , and — (1972b). Prevention of acute ventilatory capacity reduction in hemp workers by antihistamine, bronchodilator and vitamin C. *XVII International Congress on Occupational Health, Buenos Aires, 1972*. Abstracts, pp. 108-109.
- Žuškin, E., Lewis, A. J., and Bouhuys, A. (1973). Inhibition of histamine-induced airway constriction by ascorbic acid. *Journal of Allergy and Clinical Immunology*, 51, 218-226.
- , and Valić, F. (1966). Acute effects of hemp dust on ventilatory capacity. *Proceedings of the XVth International Congress on Occupational Health, Vienna, 1966*, vol. 3, pp. 291-294.
- , and — (1973). Respiratory changes in two groups of flax workers with different exposure pattern. *Thorax*, 28, 579-583.

Received for publication January 29, 1973.

The July (1973) Issue

Role of dust in the working environment in development of chronic bronchitis in British coal miners

J. M. ROGAN, M. D. ATTFIELD, M. JACOBSEN, S. RAE, D. D. WALKER, AND W. H. WALTON

A radiographic survey of monumental masonry workers in Aberdeen

T. A. LLOYD DAVIES, A. T. DOIG, A. J. FOX, AND M. GREENBERG

Comparison of effects of glass fibre and glass powder on guinea-pig lungs

SUSAN K. BOTHAM AND P. F. HOLT

Preprocessing cotton to prevent byssinosis

J. A. MERCHANT, J. C. LUMSDEN, K. H. KILBURN, V. H. GERMINO, J. D. HAMILTON, W. S. LYNN, H. BYRD, AND D. BAUCOM

Histochemical study of asbestos fibre coating in experimental carrageenin granulomas

M. GOVERNA AND C. ROSANDA VADALA

A review of agricultural pesticide incidents in man in England and Wales, 1952-71

C. E. D. HEARN

Chest symptoms and farmer's lung: a community survey

D. C. MORGAN, J. T. SMYTH, R. W. LISTER, AND R. J. PETHYBRIDGE

John Thomas Arlidge (1822-99) and the Potteries

E. POSNER

Subject variability in short-term audiometric recording

B. P. R. HARTLEY, R. W. HOWELL, A. SINCLAIR, AND D. A. D. SLATTERY

Chloracne from the accidental production of tetrachlorodibenzodioxin

G. MAY

Changes in zinc and serum proteins due to carbon disulphide exposure

R. EL-GAZZAR, Y. M. EL-SADIK, AND M. HUSSEIN

Lower fiducial limit of urinary metabolite level as an index of excessive exposure to industrial chemicals

T. IMAMURA AND M. IKEDA

Measurement of urinary mercury excretion by atomic absorption in health and disease

A. TAYLOR AND V. MARKS

Notes and miscellanea

Occupational health and safety in Great Britain in 1971 W. R. LEE

A note on the sensitivity of a method used to detect lead in the eighteenth century H. A. WALDRON

Book reviews

Information section

A number of copies are still available and may be obtained from the Publishing Manager, British Medical Association, Tavistock Square, London WC1H 9JR, price £1.25 (£1.50 in countries overseas; U.S.A. \$3.60).