Pharmacological prevention of acute ventilatory capacity reduction in flax dust exposure

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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 (FEV₁₀) was reduced by 50% and the fall in maximal flow rate at 50% vital capacity (Vmax 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 (FEV₁₀) 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 FEV₁₀ 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 FEV₁₀ 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 (FEV₁₀) 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 FEV₁₀ data were corrected to BTPS. From the maximum flow-volume curve the maximum flow rate at 50% of the control vital capacity (Vₘₐₓ 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 FEV₁₀ and Vₘₐₓ 50% VC in 13 byssinotics on the first working day without

¹Alupent: 1-(3,5-dihydroxyphenyl)-2-isopropylamino-ethanol sulphate
²Diadril: one tablet contains 25 mg 1-p-chlorbenzhydril-4-(m-methyl-benzyl)-pipermane hydrochloride.

| TABLE 1 |
|-----------------|------------------|
| **Mean Changes in FEV₁₀ and Vₘₐₓ 50% VC in 13 Byssinotic Flax Workers without and with Drug Treatment before the Work Shift** |

<table>
<thead>
<tr>
<th>Drug Treatment</th>
<th>FEV₁₀ (ml) Mean reductions over shift</th>
<th>Vₘₐₓ 50% VC (l/sec) Mean reductions over shift</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before shift</td>
<td>ml</td>
<td>%</td>
</tr>
<tr>
<td>Without treatment</td>
<td>2598</td>
<td>257</td>
</tr>
<tr>
<td>Placebo</td>
<td>2593</td>
<td>237</td>
</tr>
<tr>
<td>Bronchodilator</td>
<td>2578</td>
<td>119</td>
</tr>
<tr>
<td>Antihistamine</td>
<td>2605</td>
<td>103</td>
</tr>
<tr>
<td>Ascorbic acid</td>
<td>2583</td>
<td>127</td>
</tr>
</tbody>
</table>

NS = difference statistically not significant (P > 0.05)
TABLE 2
MEAN CHANGES IN FEV<sub>1.0</sub> AND V<sub>max 50% VC</sub> IN 7 NONBYSSINOTIC FLAX WORKERS WITHOUT AND WITH DRUG TREATMENT BEFORE THE WORK SHIFT

<table>
<thead>
<tr>
<th></th>
<th>FEV&lt;sub&gt;1.0&lt;/sub&gt; (ml)</th>
<th>V&lt;sub&gt;max 50% VC&lt;/sub&gt; (l/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before shift</td>
<td>Mean reductions over shift</td>
</tr>
<tr>
<td></td>
<td>ml</td>
<td>%</td>
</tr>
<tr>
<td>Without treatment</td>
<td>2724</td>
<td>178</td>
</tr>
<tr>
<td>Placebo</td>
<td>2720</td>
<td>186</td>
</tr>
<tr>
<td>Bronchodilator</td>
<td>2724</td>
<td>64</td>
</tr>
<tr>
<td>Antihistamine</td>
<td>2728</td>
<td>86</td>
</tr>
<tr>
<td>Ascorbic acid</td>
<td>2744</td>
<td>86</td>
</tr>
</tbody>
</table>

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 nonbyssinotic subjects exposed to flax dust. The V<sub>max 50% VC</sub> appeared to be a more sensitive test in detecting the protective effect of these drugs than the FEV<sub>1.0</sub>. The mean acute reduction in V<sub>max 50% VC</sub> 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<sub>1.0</sub> 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 (Zuskin 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.

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