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CIRCULATING HISTAMINE LEVELS AND LUNG FUNCTION TEST IN COTTON MILL WORKERS

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Circulating histamine level and forced expiratory volume in one second (FEV_1) were measured by conventional methods in 39 selected workers (24 exposed and 15 controls) employed in a local cotton mill. There were 12 workers with byssinosis, who complained of breathlessness and tightness in the chest, showed elevated histamine concentrations in blood and a diminished percentage of predicted FEV_1 values. Non-byssinotic subjects who were exposed to cotton dust had lower blood histamine concentrations and a higher percentage of predicted FEV_1 values. Both exposed groups exhibited enhanced histamine levels and a lower percentage of predicted FEV_1 values than unexposed subjects. The circulating histamine concentrations were negatively correlated with FEV_1 among exposed workers.

Among Indian cotton mill workers the presence of byssinosis is well recognized (1, 2). The disease manifests itself in many ways. The most important symptoms are tightness in the chest, shortness of breath and cough (3, 4). These reflect bronchoconstriction which is probably a result of release of biogenic amines (5–8), chemotoxins (9) and endotoxins (10). In developing countries such as India, in accordance with the recommendations of the *World Health Organization* (11) attention is currently focussed on identification and prevention of this occupational disorder. Screening over a thousand cotton mill workers in a local mill we identified and selected for this study only 12 byssinotics (12). The fact that antihistamines provide considerable relief (13, 14) prompted the measurement of circulating histamine concentrations among these workers as well as among non-byssinotics exposed to cotton dust and unexposed subjects. Taking that histamine might be involved in the effector mechanism of byssinosis, histamine levels were compared with the results of measurement of one-second forced expiratory volume (FEV_1).

METHODS

Thirty-nine workers from a local cotton mill, were selected and classified into three groups: 12 byssinotics, 12 non-byssinotics exposed to cotton dust and 15 unexposed workers. The criterion for identification of byssinosis was based on clinical signs and symptoms following the WHO guidelines (11). The duration of exposure to cotton dust, age, medical and occupational histories etc. were recorded in a pre-designed clinical questionnaire. The respirable dust concentrations at the breathing zone level were measured and reported elsewhere (15). Biological estimation of blood histamine was done in two stages (16 – 18). Blood was collected from the antecubital vein after a weekend in the post-shift work period. The samples were transferred to heparinized tubes and processed for extraction by trichloroacetic acid. They were further washed and dried by evaporation on a water bath. The residue was then extracted three times in distilled water and neutralized with bromothymol to make up the same volume as that of blood. During the second stage biological assay was done on guinea pig ileum in a thermostatic aerated (95% O_2 + 5% CO_2) isolated organ bath using the method of *Woodruff and Oniwinde* (19). The guinea pig ileum was sensitized to histamine and against interfering substances by means of drugs, agonists and antagonists of substances other than histamine. The samples rich in histamine were acidified and then neutralized to a medium pH and the negative response of such samples was confirmed. The rest of the samples were boiled and alkalinized and histamine absence was ascertained at a neutral pH using the procedures reported earlier (20 – 24). The blood histamine was expressed as μg/ml. Pulmonary function testing was performed by means of a vitalograph spirometer in all subjects on a Monday after the shift work period. The best recording out of three of forced vital capacity in a worker was taken for one-second forced expiratory volume, and expressed at body temperature at saturated pressure level. The percentage of predicted FEV_1 value was computed from the regression equation of *Jain and Ramaiah* (25). The mean percentage of predicted values and standard deviation were calculated for byssinotic and non-byssinotic workers.

RESULTS

Table 1 shows physical characteristics and the incubation period for exposed and unexposed workers. Byssinosis was found among subjects with over 15 years of exposure to cotton dust. All the byssinotics in the study were aged 33 – 47 years with the mean duration of exposure of 19 years. The exposed workers, particularly byssinotics, exhibited higher histamine levels along with lower percentages of predicted FEV_1. The inverse relationship of the two parameters was directly related to the intensity of the disease as shown in Table 2. The grade II and grade III byssinotics showed elevated histamine levels and diminished ventilatory function, concurrently with increased severity of symptoms. The histamine release among subjects exposed to cotton dust shows a relationship with the dusty environment of the cotton processing

Table 1

Physical parameters in textile mill workers (means ±S.D.)

Parameters	Unexposed (control) n = 15	Exposed	
		Non-byssinotics n=12	Byssinotics n=12
Age (yr)	26.3 ± 2.7	38.8 ± 10.7	40.3 ± 7.4^{ns}
Weight (kg)	53.6 ± 8.5	47.7 ± 9.0	55.7 ± 7.5*
Duration of exposure to cotton dust (yr)	nil	16.7 ± 7.7	19.6 ± 13.2^{ns}

* Difference in mean valucs significant at P < 0.05 level in comparison to non-byssinotics
ns = not significant

Table 2

Circulating histamine levels (μg/ml) and FEV_1 in byssinotics according to clinical grades and symptoms (means ±S.D.)

Byssinotics grade	Clinical symptoms of byssinosis*	Blood histamine levels ± S.D. (μg/ml)	$FEV_{1.0}$ (L) (% of predicted value)
0	No symptoms	–	–
1/2	Occasional chest tightness or cough on the first day of the working week	–	–
1 (n=3)	Chest tightness and/or shortness of breath on every first day of the working week	8.42 ± 2.53	76.8 ± 27.2
2 (n=7)	Chest tightness and/or shortness of breath on the first and other days of the working week	10.52 ± 1.58	68.2 ± 31.4
3 (n=2)	Grade 2 symptoms accompanied by evidence of permanent loss of lung function	12.03 ± 2.51	37.2 ± 10.1

* Adopted from WHO Technical Report

departments (blow, frame and carding sections) as shown in Table 3. Enhanced circulating histamine concentrations were determined among workers from the carding section as compared to those from the blow and frame section, although there were no byssinotics among them. In both sections, the percentages of predicted FEV_1 values were significantly reduced. Table 4 shows the percentages of predicted FEV_1 values in non-byssinotics and byssinotics from the blow room and frame room and also in cardroom workers. In non-byssinotics, the histamine level was higher than in control subjects and FEV_1 values were significantly reduced. The severe reduction in the percentage of predicted FEV_1 in byssinotics from both rooms is associated with greatly elevated blood histamine levels. The correlation between histamine level and FEV_1 was found to be -0.537 ($p<0.001$) and the corresponding regression $FEV_1 = 2.852 -$

Table 3

Respirable dust concentrations and circulating histamine levels (µg/ml) in workers exposed to cotton dust from different cotton mill departments

Department	Respirable dust concentration (mg/m^3)*	Blood histamine (means ± S. D.)	$FEV_{1.0/L}$ (% of predicted value)
Control (n = 15)	–	0.55 ± 0.43	88.4 ± 16.5
Blow room and Frame room (n = 15)	0.48	4.43 ± 4.86	70.9 ± 19.7**
Card room (n = 11)	0.81	7.83 ± 4.26	74.5 ± 24.5**

n = number of workers
* Adopted from *Bhagia and co-workers* (15)
** significant at 1% level compared to controls ($P < 0.01$)

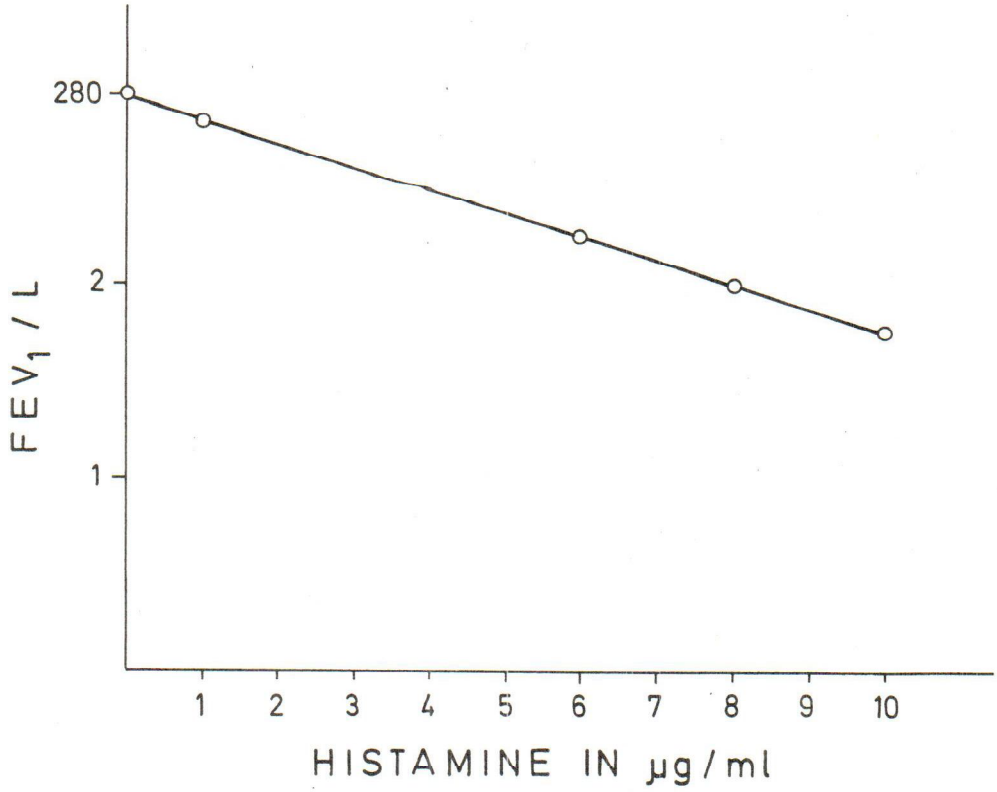

Figure 1 *Regression line of FEV_1 and blood histamine concentration in cotton mill workers*

(0.112) histamine level. Thus on the average, a one-unit increase in the histamine level is expected to bring down FEV_1 by 0.112 units per subject (Figure 1).

DISCUSSION

This study is a follow-up of an epidemiologic screening carried out by *Parikh and co-workers* (3) in a large number of textile workers from a local factory. Knowing that in Indian workers working in tropical climate and indoors, histamine is released in blood *Parikh and co-workers* (4) determined plasma histamine levels in clinically identified byssinotics and non-byssinotics exposed to cotton dust. According to *Malvanker and co-workers* (26) liberation of histamine in the blood of the diseased is associated with the peak expiratory flow rate. The present study aims at establishing the effect of circulating histamine on lung function (FEV_1) among these workers. The equation of *Jain and Ramaiah* (25) developed for Indian healthy subjects was used in our data analysis as ideal for calculating predicted FEV_1 values. Over the past two decades several investigations have been reported in other countries among workers consistently exposed to cotton dust and bracts with resultant liberation of biogenic amines (5, 11, 27). In this study, the liberation of histamine in blood and the intensity of bronchoconstriction were compared to the percentage of predicted forced expiratory volume in 24 exposed and in 15 unexposed workers in the cotton mill. Byssinosis is a disease resulting from exposure to fibres or vegetable dust such as cotton (28), flax (20), and sisal (21). The liberation of endotoxins, which increase histamine in circulation by disruption of mast cells, has been associated with bronchoconstriction (11, 31). The enhanced histamine could also have been produced from the basophils.

Bhagia and co-workers (15) reported variable dust concentration in different sections in the same mill. In a pilot study, we noted elevated levels of blood histamine in both byssinotic and non-byssinotic Indian workers exposed to cotton dust under Indian conditions and our data are in accordance with an earlier report (5). Therefore blood histamine levels in subjects working in the dust area were compared and found to have bearing to inhalation. Also, FEV_1 showed a mild effect commensurate with the blood histamine level. The increased histamine level on the first working day is also in agreement with the occurrence of Monday morning sickness among byssinotics. Histamine levels determined in the blood samples taken from persons suffering from byssinosis were high. The reason could have been partly psychogenic or due to oversensitization (disruption of pulmonary mast cells) resulting in the fractional response of the *in vitro* assaying system. Although our method of measuring histamine was pharmacological and different from that of *Nowier* (5), we observed a similar pattern in workers exposed to cotton dust. While measuring histamine, precision and caution against interfering agents and their effects were blocked by addition of atropine sulphate (as antagonist of the muscarinic effect of acetylcholine) (32), bromolysergic acid diethylamide (as potent antagonist of 5-hydroxytryptamine) (33) and mepyramine maleate (a selective antagonist of histamine) (34). We could have used another method of histamine assay e.g. the enzymatic assay of plasma histamine by the double isotope

Table 4

Blood histamine and FEV_1 levels in textile mill workers

Workers	Group	Department	Histamine (μg/ml)	$FEV_{1(L)}$ % of predicted value
Unexposed to cotton dust	Control n = 15	–	0.55 ± 0.43	88.4 ± 16.5
Exposed to cotton dust (I)	Non-byssinotics n = 15	Blow room and Frame room n = 10	1.47 ± 1.24	78.3 ± 18.4*
		Card room n = 5	1.63 ± 0.39	79.6 ± 15.3^{ns}
Exposed to cotton dust (II)	Byssinotics n = 12	Blow room and Frame room n = 5	10.22 ± 2.87	57.9 ± 20.4**
		Card room n = 7	10.26 ± 1.73	70.4 ± 28.6**

n = number of workers
* significant at 5% level compared to controls ($P < 0.05$)
** significant at 1% level compared to controls ($P < 0.01$)

technique (35), but the trend in histamine release was similar to the one observed earlier (36).

Hence the present data for Indian workers relate blood histamine and FEV_1. Other influencing factors or mediators are the products of mast cells, eosinophils or even neutrophils, particularly arachidonic acid metabolites (thromboxane A_2) (31). Therefore blood or urine levels of these mediators or breakdown products can be of further interest to explain the mechanism of what takes place in bronchial airways and alveolar surfaces (36). The measurement of these mediators in the lung epithelial fluid or in lung cells obtained by lavage (37, 38) may also be interesting.

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Sažetak

RAZINE CIRKULIRAJUĆEG HISTAMINA I TESTOVI PLUĆNE FUNKCIJE U RADNIKA IZ PREDIONICE PAMUKA

U skupini od 15 neizloženih i 24 izložena radnika predionice pamuka, mjeren je standardnim metodama histamin i forsirani ekspiratorni volumen (FEV_1) nakon radne smjene.

U 12 radnika s bisinozom koji su se tužili na pomanjkanje daha i stezanje u prsima, nađene su povišene razine histamina u krvi i smanjeni ekspiratorni volumen. U preostalih radnika izloženih prašini pamuka nađene su niže razine histamina u krvi i povećani ekspiratorni volumen. U obje ove skupine vrijednosti histamina u krvi bile su više, a ekspiratorni volumen FEV_1 niži negoli u neizloženih radnika.

Među izloženim radnicima koncentracija cirkulirajućeg histamina u krvi bila je u negativnoj korelaciji s vrijednostima FEV_1.

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