

The Importance of Ventilation in Exercise-Induced Asthma

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The degree of post treadmill-running decrease in pulmonary function (Exercise-Induced Asthma) in 11 adult asthmatics was compared with the decrease in pulmonary function followed by resting isocapnic hyperventilation. It was checked that ventilation during the hyperventilation was kept identical to the ventilation during treadmill-running by continuous recording of respiratory frequency, minute ventilation, tidal volume and accumulated ventilation. The temperature of the inspired air was identical in the two situations and the relative humidity was 40 % during treadmill-running and 15 % during hyperventilation. The average accumulated ventilation during treadmill-running and hyperventilation was 411 l/6 min in both events. The decrease in peak expiratory flow after treadmill-running was 25 % and after isocapnic hyperventilation 24 %. It is concluded that the ventilation is of more importance for the decrease in pulmonary function after exercise, than the work load.

Key words: EIA, hyperventilation.

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CLINICAL ASPECTS

The finding in this article that ventilation is of more importance for the decrease in pulmonary function after exercise than is the work load implies that future research concerning the pathogenesis of exercise-induced asthma must be concentrated to the bronchial tree and the epithelium and mucosa of the upper part of respiratory system.

Muscular exercise causes decrease in pulmonary function in most asthmatics (Exercise-Induced Asthma) (EIA)) (1). It is also a clinical feature that some asthmatics can provoke acute asthma by simple hyperventilation (2, 3, 4, 5, 12, 13, 16) even though some studies have failed to demonstrate this effect of hyperventilation (8, 9, 15). Standardization of ventilation, the ambient temperature and relative humidity of the inhaled air are crucial points when comparing the decrease in pulmonary function after exercise (7). The aim of this study was to assess whether ventilation *per se* more than the muscular exercise itself is the main factor in provoking EIA.

METHODS AND PATIENTS

Three females and eight males with perennial asthma and reproducible exercise-induced asthma (EIA) gave informed consent to the study. The reproducible EIA was documented by a post-exercise fall in PEF > 15 % from base-line value. Average age was 34 years (range 19–48 years). Five had had asthma since childhood and six had their first attack after 20 years of age. All presented a decrease in peak expiratory flow (PEF) greater than 20 % after inhalation of less than 500 µg histamine. One patient received steroids orally, none of the

others had used steroids or disodium cromoglycate for at least 4 weeks before entering the study. All refrained from taking any medication for 8 h before the provocation. None were smokers. Treadmill-running was performed on the first day and 3 days later the hyperventilation test was done. All patients were familiar with treadmill-running. The patients ran 6 min with speeds between 6 and 10 km/h, 7% uphill resulting in a pulse rate over 160 beats/min. Hyperventilation was done with the patient sitting in a chair, inhaling air during 6 min from a Douglas bag containing 20% O₂, 6% CO₂ and 74% N₂ with temperature 23°C and relative humidity 15%. The exercise and the hyperventilation test were performed in a climate chamber with a temperature of 23°C and a relative humidity of 40%. The relative humidity in the Douglas bag was controlled by a control-hygrometer (Electronic type novo isna MIK 5317) and the relative humidity in the climate chamber was controlled by a thermohygrograph (Haenni, No. 508). The ventilation was measured with a Fleisch No. 4 pneumotachograph (flow range 0–10 l/sec) with a Godart (No. 17212) pressure transducer transforming the signals into minute volume, accumulated volume, respiratory frequency and flow. The pressure transducer was connected to a 4-pen recorder (Rikadenki) which continuously wrote out the above mentioned parameters. The pneumotachograph was calibrated at three different flow levels, 25, 50 and 100 l/min with a constant gas flow. The gas flow was led through the pneumotachograph to a balanced Collins spirometer and the collected volume and the collection time were measured, making it possible to calculate $\dot{V}_E$ and V_{tot} . At the same time the $\dot{V}_E$ and V_{tot} signals were recorded on the 4-pen recorder and it was thus possible to compare the actual $\dot{V}_E$ and V_{tot} with the amplitudes from the recorder. At all three levels of $\dot{V}_E$ there was a linear relationship to the amplitude so the pneumotachograph could be used at all levels of minute ventilation relevant to this study.

Comparing the respiration when the patient performed the hyperventilation with recordings obtained from the treadmill-running made it possible to adjust the hyperventilation in a way

which made the ventilation on the 2 days identical.

Pulmonary function was assessed by peak expiratory flow (PEF), measured as the best of three readings with a Wright's peak flow meter. PEF was measured immediately before provocation, immediately after provocation and 1, 3, 5, 10 and 15 min after provocation.

Post-exercise decrease in pulmonary function was described as per cent fall in PEF, comparing the differences between the lowest post-exercise value and the highest of the two PEF-values obtained immediately before or immediately after exercise with the highest PEF. For example, if PEF immediately before the provocation was 400 l/min, immediately after the provocation 450 l/min and the lowest value after provocation 350 l/min, the result would be: $(450 - 350)/450 = 22\%$.

Statistical analysis. Paired t-test was used to compare the decrease in pulmonary function after the two different provocations.

RESULTS

The average decrease in PEF after treadmill running was $25\% \pm 5\%$ (mean $\pm$ SEM). After hyperventilation a decrease in PEF of $24\% \pm 4\%$ was seen. Statistical analysis gave $P = 0.42$, confirming that no difference between the two provocations was obtained. The total ventilation for the 6 min provocation averages 411 l equal to 68 l/min for both the treadmill-running and the hyperventilation. Individual figures for decrease in PEF after the two provocations are shown in Table 1 and Fig. 1.

The course of the average PEF can be seen in Fig. 2. The pre-exercise values are very close to each other. During treadmill-running an increase in PEF is seen. No such increase is seen after the hyperventilation. The decreases in PEF are identical after the two provocations, and 15 min after provocation the pulmonary function is returning to pre-exercise values.

Table 1
Individual figures for 11 patients

Patient No.	Hyperventilation			Treadmill-running		
	EIA %	V _{tot} (l)	$\dot{V}_E$ (l/min)	EIA %	V _{tot} (l)	$\dot{V}_E$ (l/min)
1	25	370	75	9	420	85
2	13	720	130	51	620	120
3	42	610	110	42	490	105
4	27	240	80	40	220	85
5	36	230	85	11	435	85
6	32	460	75	14	385	72
7	20	410	80	12	460	100
8	18	150	60	16	140	60
9	0	540	90	23	450	100
10	32	655	120	22	740	130
11	22	135	65	40	160	90
$\bar{x}$	24	411	88	25	411	94

EIA % = decrease in lung function after provocation.
V_{tot} = accumulated ventilation during the 6 min of provocation.
 $\dot{V}_E$ = minute ventilation in the last minute of provocation.
Note: Patient Nos. 4, 8 and 11 were tested during 3 min.

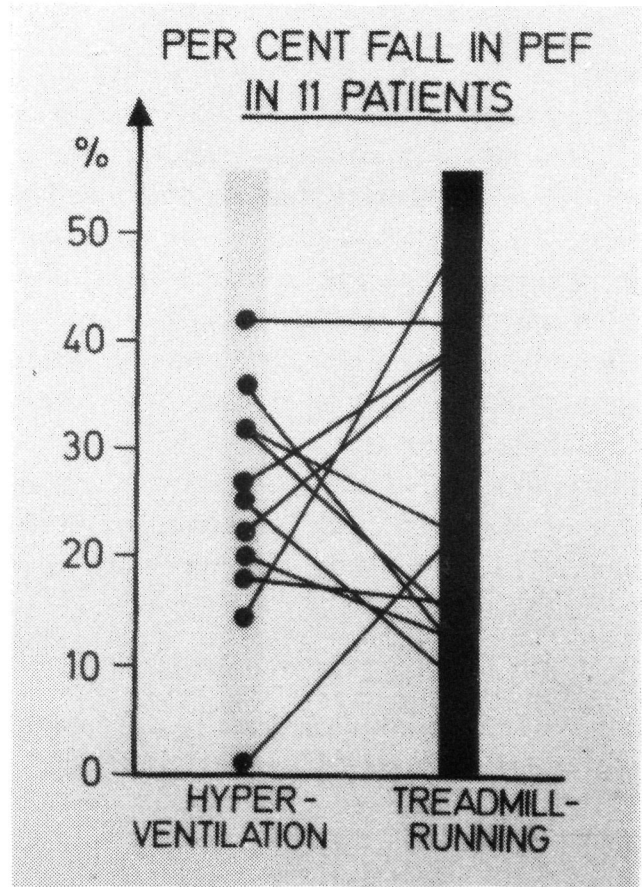


Fig. 1. The individual decreases in PEF after 6 min treadmill-running and 6 min hyperventilation.

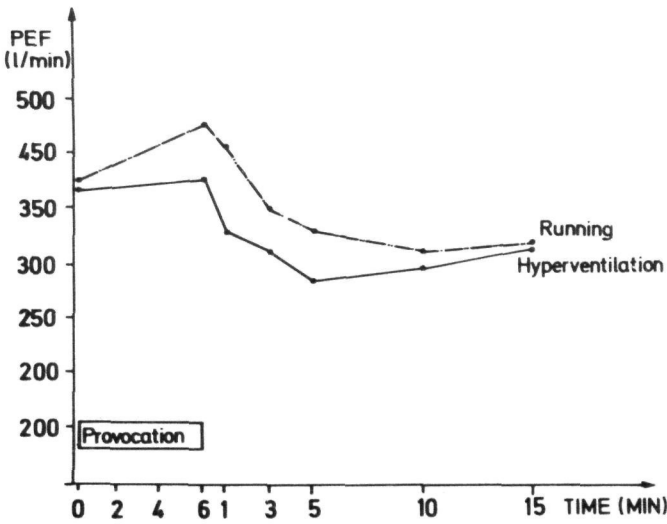


Fig. 2. The average of PEF after 6 min treadmill-running and 6 min hyperventilation ($n = 11$).

DISCUSSION

This study demonstrates that the ventilation is an important factor in EIA, as the same degree of bronchoconstriction was obtained by exercise and by hyperventilation when the $\dot{V}_E$ during the two provocations was identical. This is in accordance with Chan-Yeung (2) who 9 years ago concluded that EIA could be caused by hyperventilation. The hyperventilation, however, represents an increase in work load due to the use of ventilatory muscles, expressed as an increase in $\dot{V}_{O_2}$. However, the increase in $\dot{V}_{O_2}$ caused by the ventilatory muscles will only reach about 10% of the $\dot{V}_{O_{2max}}$ during maximal ventilation (17). The mean $\dot{V}_E$ in the present study obtained by treadmill-running represents a $\dot{V}_{O_2}$ of about 60–70% of $\dot{V}_{O_{2max}}$. The difference in $\dot{V}_{O_{2max}}$ between treadmill-running and sitting hyperventilation in this study therefore was about 60% of $\dot{V}_{O_2}$. The ventilation, however, was the same during the two provocations and the bronchoconstriction in this study therefore seems to be caused by the ventilation more than by the muscular exercise.

It is clinical observation that hyperventilations or coughing may initiate an asthmatic attack (14). The mechanisms behind this kind of asthma is probably different from the mechanism behind exercise-induced asthma, because 1 or 2 min exercise usually will improve pulmonary function (1).

The humidity in the climate chamber was continuously 40% during and after exercise. The temperature was held at a constant 23°C. The same temperature was obtained when the hyperventilation was performed, whereas the relative humidity in the inspired air during hyperventilation was only 15%. The difference in relative humidity on the 2 test days was due to technical problems regarding humidification of the air in the Douglas bag from which the patients inspired during hyperventilation. The water content in the air at 23°C and 40% relative humidity is 7 g/kg dry air, while the water content at 23°C and 15% relative humidity is 3 g/kg dry air. In another study (Bundgaard et al., submitted for publication) no difference was found in post-exercise decrease in pulmonary

function whether the patient exercised in a climate chamber with ambient air containing 3 g water/kg dry air or the exercise was performed in ambient air containing 8 g water/kg dry air. Therefore the difference between inhaling air containing 3 or 7 g water/kg dry air as in this study is of little or no importance.

Some studies have failed to demonstrate that hyperventilation is of importance in EIA (8, 9, 15). The reason for this could be that the ventilation was not high enough or that the inspired air contained too much water from partial re-breathing. Some studies have documented that hyperventilation is an important feature of EIA (2, 3, 5). Ciliae, bronchial muscle and oedema of the bronchial mucous layer could be of importance in EIA. Complete cessation of mucous velocity in the trachea occurs when dogs breathe dry air for 3 h (6). This cessation of mucous velocity might cause increased obstruction in the bronchial tree due to accumulation of secretion. During the increased ventilation where water from the airways is lost, a cessation of the ciliary movements in the human respiratory system might result in an obstruction.

As inhalation of air with a high water content prevents EIA, it is possible that the water content of the bronchial mucous layer is of importance as a pathogenetic factor in EIA. The present study confirms that the loss of water from the airways may be an important feature of EIA. O'Cain et al. found a decrease in lung function even in normal subjects after hyperventilation of cold air (11). This cold air contains very little water, whereas the water-content of the expired air is high, due to heating and water saturation.

The conclusion of this study is that the magnitude of the ventilation is a more important feature of EIA, than is the muscular exercise.

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