Hyperventilation or exercise to induce asthma?

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ABSTRACT Bronchoconstriction was induced in asthmatic patients by means of isocapnic hyperventilation with dry air. Responses both within a day and between days did not differ significantly and corresponded closely with those observed after exercise. The mean fall in forced expiratory volume in one second (FEV₁) observed with both techniques was equivalent to 36%. Isocapnic hyperventilation with dry air, as used in this study, was a potent stimulus and provoked a reproducible response. The method was physically less demanding than exercise and was more acceptable to patients.

As early as the seventeenth century, it was recognised that asthma could be provoked by exercise, and it was stated that "Those exercises that move the arms, exercise the lungs most".¹ Thus, Anderson *et al*² found that jogging on a treadmill produced a greater fall in peak expiratory flow rate in asthmatics than exercise on a bicycle ergometer. However, others³ found that provided rates of oxygen uptake were matched in the two forms of exercise, they were equipotent in effect. More recent research^{4,5} has shown that the triggering stimulus for exercise-induced asthma (EIA) may be cooling of the airways. During inspiration, air is warmed and humidified by heat and water loss from the mucosa. This loss is caused by convection and evaporation and therefore the degree of mucosal cooling depends on the temperature and humidity of inspired air, and minute ventilation. Isocapnic hyperventilation has been proposed as a practical alternative to exercise for inducing bronchoconstriction.^{6,7} It has also been suggested that the effect of hyperventilation can be maximised by cooling the inspired air.⁸ We have studied isocapnic hyperventilation with dry air to determine magnitude and reproducibility of response in a group of asthmatic patients.

Methods

Ten patients were studied, six male and four female, aged between 13 and 37 years. Seven were atopic. All gave a clinical history suggestive of exercise-induced asthma. None had previously performed

controlled laboratory tests. Informed consent was given by the patients or parents of patient where appropriate. Each was requested to stop all medication for 24 hours before the laboratory visits.

Patients attended for tests on two separate afternoons within a two-week period. On day 1, two isocapnic hyperventilation tests with dry air were performed (tests A and B), separated by a three-hour interval. On day 2, another hyperventilation test (test C) and an exercise test were performed, again three hours apart. The order of test C and exercise was allocated randomly.

Isocapnic hyperventilation was carried out using an open circuit (figure) with the expiratory side based on the method of Deal *et al*.⁷ Patients initially breathed, at rest, to and from room air, and end-tidal carbon dioxide concentration was recorded. The circuit was then adjusted so that the patient breathed in dry air from the cylinder via the inspiratory reservoir (6 l) and out to the expiratory bag (6 l). The expiratory bag was connected to a vacuum cleaner (Electrolux) fitted with a variable transformer and the vacuum was set at the target ventilation rate. The patient was instructed to breathe fast enough to maintain inflation of the expiratory bag. Inspired ventilation was recorded using a dry gas meter (Parkinson-Cowan) and ink recorder (Mingograf 81). Hyperventilation was maintained for six minutes. End-tidal carbon dioxide was measured by infrared analysis (Capnograph) and monitored throughout the hyperventilation period. Carbon dioxide was added as necessary to the inspired air to maintain end-tidal carbon dioxide at resting level (on average 0.25-2 l/min). The target hyperventilation rate was set for each individual at

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Figure Diagram of isocapnic hyperventilation circuit.

the four-minute maximum voluntary ventilation (predicted from FEV_1) by the formula of Clark *et al.*⁹

The exercise test on day 2 took the form of six minutes jogging or walking on a treadmill (cardio-exercise treadmill, Quinton Instruments). The slope was set at 10%, and speed adjusted to achieve the desired minute ventilation. Cylinder air was breathed throughout the exercise.

FEV_1 and forced vital capacity (FVC) were measured at 1, 5, 10, and 15 minutes after each hyperventilation and exercise period. Statistical analysis was by paired *t* test using both actual FEV_1 values and logarithms of the values.

Results

FEV_1 recordings before, and the lowest recorded

Table Recordings of FEV_1 (i) before and (ii) after isocapnic hyperventilation (tests A, B, and C) and exercise

Patient number	Age (yr)	Atopy	Day 1						Day 2					
			Test A			Test B			Test C			Exercise		
			FEV_1			FEV_1			FEV_1			FEV_1		
			i	ii	V_E	i	ii	V_E	i	ii	V_E	i	ii	V_E
1	21	—	2.7	1.7	43	2.5	1.6	41	2.6*	1.3	45	2.6	1.8	40
2	13	+	1.5	0.9	33	1.8	1.1	32	1.6*	1.1	30	1.7	0.8	31
3	20	—	3.7	1.0	60	3.6	2.2	58	—	—	—	3.6*	1.4	53
4	35	+	2.7	1.9	45	2.8	2.1	53	2.8	1.9	51	2.7*	1.5	57
5	15	+	1.9	1.9	41	2.4	2.4	45	2.4*	1.3	41	2.6	1.6	40
6	17	+	2.6	1.7	47	2.4	1.4	47	2.1	1.5	43	2.4*	1.4	48
7	37	+	3.2	2.0	55	3.7	2.4	54	2.8	2.0	54	2.9*	1.6	58
8	36	—	2.4	1.0	44	2.6	1.1	43	2.7	1.7	42	2.3*	1.2	46
9	34	+	3.2	2.3	58	2.9	2.2	56	2.9*	1.9	56	3.0	1.5	64
10	24	+	3.6	2.3	54	3.0	1.5	49	3.6*	2.2	54	3.6	2.1	58
Mean			2.7	1.7	48	2.8	1.8	48	2.6	1.6	46	2.7	1.5	49
Standard deviation			0.7	0.5	8	0.6	0.5	8	0.6	0.4	8	0.6	0.3	10

FEV_1 = litres BTPS
 V_E = mean minute ventilation
 * = test performed first on day 2

value after each stimulus, are shown in the table, together with ventilation rates. Any difference in pre-test FEV_1 within or between days was taken into account in calculating target ventilation rate. All patients showed a fall in FEV_1 after each stimulus with the exception of patient 5 on day 1. Patients were allowed to recover spontaneously after each test. Mean falls in FEV_1 (BTPS) for the group in tests A and B were 1.00 l (SD 0.26) and 1.09 (SD 0.34) respectively. Mean falls in test C and exercise were 0.96 l (SD 0.28) and 1.16 l (SD 0.27) respectively. These figures represent a fall in FEV_1 of approximately 36%.

Responses to hyperventilation were insignificantly different both within a day (tests A and B) and between days (where test C was performed first on day 2, comparison was made with test A, and where second, with test B). This was true whether actual

FEV₁ values or logarithms of values were used. Response to exercise was insignificantly different from that to hyperventilation on the same day, or the matched test on day 1.

Temperature in the laboratory on test days varied from 19°C to 23.5°C but for any patient, variation was never greater than 0.5°C within a day, or 1.5°C between days. The cylinder air used has for practical purposes zero humidity.

Discussion

With the recent suggestion that respiratory heat exchange is the triggering stimulus for exercise-induced bronchoconstriction,⁵ any provocation test must take into account temperature and humidity of inspired gas and minute ventilation.

Since our laboratory temperatures were fairly constant, no attempt was made to alter inspired air temperature. The use of cylinder gases ensured that the humidity of inspired air was constant and near zero. The small amount of rebreathing permitted by the Otis-McKerrow valve (dead space 115 ml) was assumed to have a constant effect on humidity for each patient. The continuous monitoring of inspired and expired gas flow during hyperventilation allowed relevant instructions to be given to the patients regarding respiratory rate and depth to maintain their minute ventilation at target level. During treadmill exercise, ventilation control was found to be more difficult. It was impossible to predict the effect of alteration of treadmill speed on minute ventilation in these untrained subjects.

No previous training was necessary for patients to carry out hyperventilation satisfactorily. All patients preferred hyperventilation to exercise as the former required less physical exertion and was not associated with dyspnoea on completion of the six-minute period.

The magnitude of change in FEV₁ shown by the patients was greater than expected when compared at similar temperature, humidity, and ventilation rate with the data of Deal *et al.*⁷ However, our method required each subject to achieve maximum sustained voluntary ventilation rate. This not only provided a stronger provocation to the airways but also made provocation equivalent in each patient. In the later study by Deal *et al.*⁸ where hyperventilation with cold air was used and patients breathed at two-thirds indirect maximum breathing capacity, response was very similar to that found in the present study.

Hyperventilation challenge was similar to exercise in its effect on airways. This has been shown by other authors.^{6,7} Anderson *et al.* calculated the coefficient of variation for pairs of treadmill exercise

tests carried out two hours apart, and found it to be 25%. The coefficient of variation for our nine patients who responded to hyperventilation tests on all three occasions was 18% (patient 5 could not be included in analysis since failure to respond on two out of three tests invalidates calculation of standard deviation). This is in agreement with the results of Anderson and the variation in bronchial lability of 20% found by Jones.¹¹ Our patient 5 did not show an asthmatic response on day 1 but had a "normal" asthmatic response on day 2 after both hyperventilation and exercise. This suggests that the lack of response on day 1 was not caused by inadequacy of the hyperventilation challenge, but may have been a reflection of altered reactivity of the patient's airways which cannot be explained in terms of differing pre-test FEV₁ values. This variability must be borne in mind both in screening for exercise-induced asthma and in clinical research.

Our findings suggest that isocapnic hyperventilation with dry air is a reliable method of inducing bronchoconstriction, and has practical advantages over exercise testing in untrained subjects. It can also be performed with less complicated equipment than that required for isocapnic hyperventilation with cold air.

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