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Short communication

Combining a β_2-agonist with a face mask to prevent exercise-induced bronchoconstriction

Background: In this study, we aimed to test the effect of combining a β_2-agonist with a heat- and moisture-exchanging cellulose face mask in patients with bronchoconstriction induced by exercise in cold air.
Methods: Nine allergic, asthmatic patients with a history of adverse reaction to exercise were tested on an ergometric bicycle at a temperature of approximately -10°C. They were in turn given no treatment, given premedication with a β_2-agonist, allowed to breathe through a heat- and moisture-exchanging cellulose face mask, and given both premedication and the face mask. After each treatment regimen, they were subjected to provocation with exercise and cold air.
Results: The decrease in FEV_1 was greatest with no therapy (mean maximal change: 27%), and this diminished when the face mask was used (mean maximal change: 12%) or premedication with a β_2-agonist was given (mean maximal change: 7%); no decrease in FEV_1 occurred with the combination of agonist and face mask.
Conclusions: The results suggest that different mechanisms are involved in the pathophysiology of exercise-induced bronchoconstriction (EIB). This finding may be of importance for asthmatic athletes who train and compete in a cold climate and are affected by small changes in their lung function.

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Key words: exercise-induced bronchoconstriction (EIB); face mask; long-acting β_2-agonist.

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It has been known for many years that exercise and/or inspiration of cold air may cause bronchoconstriction in patients with asthma (1–6). Exercise-induced bronchoconstriction (EIB) is thought to be induced mainly by loss of heat and moisture from the airways (1–3) or a change in the osmolarity of the bronchial mucosa as a result of dehydration (4, 5), but also by other mechanisms including various reflexes (6). In athletes, the high prevalence of asthmatic symptoms is supposedly related to inhalation of large amounts of cold air (7), although a cold climate *per se* may be a risk factor for developing asthma (8, 9). Inhalation of fully saturated air that is at body temperature may prevent EIB in asthmatics (1); even pretreatment with warm, humid air significantly reduces EIB (10). The use of premedication, such as a β_2-agonist, disodium cromoglycate, or an antileukotriene, attenuates EIB (11–13), as do various heat- and moisture-exchanging breathing devices (14–16). However, no premedication or breathing device has been shown to protect asthmatic patients from EIB completely (11–16).

The aim of the present study was to test whether a combination of medical and physical methods would be more effective in preventing EIB in cold air than either method used on its own.

Material and methods

Nine patients, six women and three men (22–38 years, mean age 29), with a history of asthma caused by exercise, took part in the study. All of them had a history of allergy and in a skin prick test had a positive reaction to more than two allergens. All had previously shown an increase of at least 20% in forced expiratory volume during 1 s (FEV_1) after the inhalation of a β_2-agonist. Their FEV_1 value (% of the predicted value) varied between 70% and 109%. Mean baseline FEV_1 was 3.1 $l \pm 0.48$ SD.

The patients were also sensitive to methacholine, with PC_{20} less than 4 mg/ml (17). On most days, they had no asthmatic symptoms. Eight patients required regular treatment with inhaled corticosteroids, and all intermittently inhaled a β_2-agonist. Five patients regularly inhaled a long-acting β_2-agonist and two used topical nasal corticosteroids. One patient was a regular smoker.

The patients were asked to take no medication for a minimum of 4 h before any test. Long-acting bronchodilators were withheld for at least 48 h. The patients were subjected to stress loads on an ergometric bicycle (RE 820, Rodby Elektronik, Sweden) in three load increments of 6 min each; that is, 30, 70, and 100 W for

women, and 50, 100, and 150 W for men. The ergometric bicycle was placed in a cold storage room with a temperature of approximately -10°C. A nasal clip was used in all tests to prevent nasal warming of the inspired air.

Each patient performed the test exercise on four separate occasions. On the first occasion, the exercise was performed without any premedication or face mask. Only patients with a drop in FEV_1 of at least 15% entered the next stage of the study and were thereafter provoked with one of the following methods, which were applied in random order:

1) premedication with formoterol 12 μg (Foradil, Novartis), inhaled 30 min before exercise.
2) a face mask (Tenoterm, AB Pulmoterm, Norrköping, Sweden) which covered the mouth and nose, and consisted of a porous cellulose fabric with heat- and moisture-exchanging properties. The cellulose fabric of the mask was the same kind used in a respirator (Servo-Humidifier-150, Siemens-Elema, Sweden) worn mainly to humidify the inspired gas (18). Resistance to airflow by the face mask reached 0.1 and 0.15 kPa/l per s at flow rates of 0.4 l/s, and 3 l/s, respectively.
3) formoterol *and* the face mask.

The tests were performed at intervals of about 1 week and with identical load increments. The FEV_1 values were determined by a spirometer (Vitalograph, UK) at normal room temperature. The highest FEV_1 value of three satisfactory expirations was used in the subsequent analyses. FEV_1 was determined prior to premedication; immediately before each test; and at 0, 3, 6, and 9 min after completion of the test.

The protective effect of the premedication and/or face mask was calculated by the following formula:

(ΔFEV_1 with no therapy – ΔFEV_1 with premedication and/or a face mask) $\times 100/\Delta FEV_1$ with no therapy

where ΔFEV_1 corresponds to the mean reduction in percentage of the initial value.

The effects of the provocations were analyzed by calculating the areas under the curves and by analysis of variance (ANOVA). The local ethics committee approved the study.

Results

The averages for the four tests are shown in Fig. 1. After provocation with exercise and cold air, the greatest decrease in FEV_1 occurred when patients were given no therapy. With the face mask, or with premedication with a β_2-agonist, the drop in FEV_1 was less significant. No decrease in FEV_1 occurred when the latter two methods were combined. Analysis of FEV_1 with repeated measurements of variance (ANOVA) showed that the recordings after exercise with no therapy differed significantly ($P<0.01$) from the other three test series. Recordings after exercise when using either premedication with a β_2-agonist or a face mask differed significantly ($P<0.05$) from those seen after combining the β_2-agonist with a face mask. However, FEV_1 values were similar when either a β_2-agonist or a face mask was used. The maximum exercise-induced drop in FEV_1 for each patient is shown in Fig. 2.

The average protective effects of the face mask, the β_2-agonist, and the agonist-mask combination were 64%, 70%, and 107%, respectively.

Because of breathing problems after the initial provocation test with no therapy, two women could not continue after 4 min and 1 min of exercise, respectively, at 100 W, and two men after 3 min and 4 min of exercise, respectively, at 150 W. Three of the women inhaled a short-acting β_2-agonist (salbutamol $2\times$ 0.4 mg) 3 min after the first provocation because of respiratory difficulties and low FEV_1 values. In all of these patients, the exercise and postexercise recordings were stopped at the same times in the three subsequent tests.

The average initial FEV_1 values for the four tests ranged from 88% to 91% of the predicted value and did not differ significantly. In the two tests in which premedication with formoterol alone, and with a face mask, was used, the average FEV_1 values after 30 min increased by $10\% \pm 2.7$ SE and $11\% \pm 4$ SE, respectively.

Discussion

This study shows that the combination of a β_2-agonist

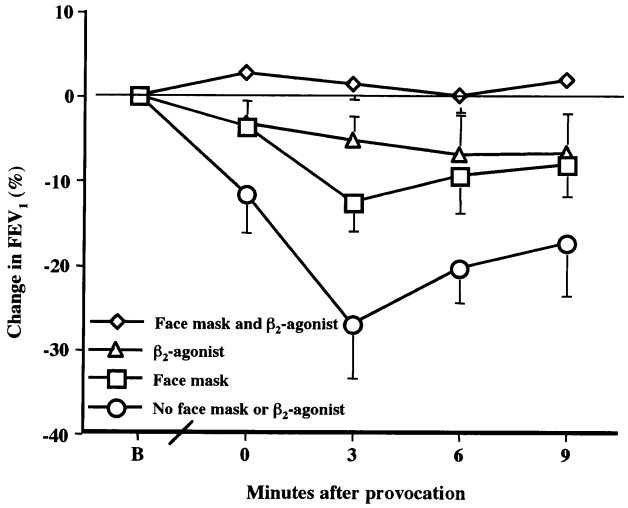

Figure 1. Changes in FEV_1 in nine asthmatic patients after exercise at temperature of about -10°C. Results were obtained after patients performed test either with no therapy, or with premedication with β_2-agonist, or with heat- and moisture-exchanging filter alone or in combination with β_2-agonist. Mean values (expressed in percentage of pre-exercise value) are shown. "B" denotes "before" exercise; bars represent standard error.

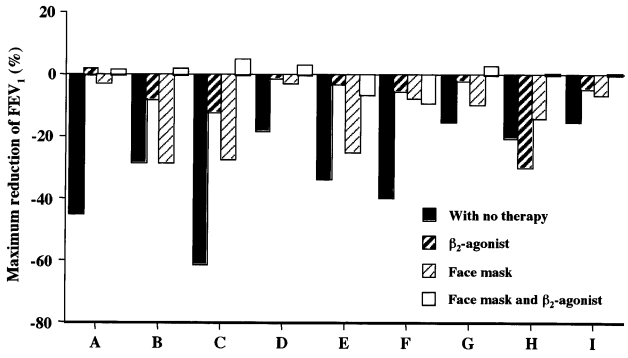

Figure 2. Maximum reduction from pre-exercise FEV_1 in each patient after exercise on ergometric bicycle at temperature of about $-10°C$. Results were obtained after patients performed test with no therapy, were given β_2-agonist, or used heat- and moisture-exchanging filter alone or in combination with β_2-agonist. Reduction is expressed in percentage of pre-exercise value.

with a heat- and moisture-exchanging face mask prevented any reduction in FEV_1 in this group of asthmatic patients. To our knowledge, no other study on medication or breathing devices in EIB has shown similar results. The challenge tests were not performed double-blindly, with a placebo and/or a "dummy mask". Four more exercise tests for each patient would have been trying, and it seems unlikely that the patients would voluntarily have influenced the recordings. Furthermore, the results after using either a heat- and moisture-exchanging face mask or premedication with a β_2-agonist are in accordance with the results of other studies (11, 12, 15, 16).

Since a nose clip was used in this study, no warming of the inhaled air could have occurred in the nose. Therefore, the cold air had a direct influence on the lungs. Some authors have shown that bronchoconstriction caused by cold air may be reduced by having the patients breathe through their noses (19). The reduction has, however, been shown to be moderate, and it is also known that when ventilation increases during exercise, people start to breathe through the mouth instead of the nose (20, 21).

This investigation seems to indicate that there may be various mechanisms underlying EIB, and that a combination of edema and bronchoconstriction may cause a fall in FEV_1. Premedication with a β_2-agonist cannot prevent possible edema, although a face mask probably can. On the other hand, since the exchange of heat and moisture alone is not enough to prevent EIB entirely, it seems likely that the exercise itself induces a certain amount of bronchoconstriction, probably via mediators. It would be of interest to analyze different inflammatory markers during the same circumstances.

Five of the patients in this study could not complete the test owing to breathing problems. A standardized provocation based on heart rate or maximal voluntary ventilation would probably have given more complete information.

Asthma in athletes has been the subject of great interest in recent years (22, 23). A high prevalence of asthma has been observed among skiers who train and compete in a cold climate. An explanation may be that great amounts of cold air (during hard training, several hundred litres per minute) dry out and injure the mucosa, inducing asthma or asthma-like bronchitis. Use of a β_2-agonist makes it possible for more cold, dry air to reach the lower airways, and the relief of symptoms in the training asthma patient may in the end cause more damage to the mucosa.

Today, many asthmatics are advised to use a β_2-agonist before any training if they are prone to developing exercise-induced symptoms. In many cases, physicians encourage patients to continue training with the help of premedication. Exercise on a regular basis is important to the patients' well-being, and the aim of management is to ensure that exercise be not avoided. Competing athletes, however, must not only be free of symptoms but must also have small variation in lung function because the winner's margin is often so small. An improvement of 5–10% in FEV_1 could be important.

Asthmatic patients who exercise in cold air, and particularly athletes who train and compete in a cold climate, should therefore consider the value of protecting their airways with a breathing device. This study shows an improvement in lung function when an ordinary premedication is combined with a face mask. Resistance to air in the cellulose fabric has been reported to be low (15), and the patients in this study had no complaints about high resistance.

In conclusion, the results suggest that different mechanisms are involved in the pathophysiology of EIB, which may be of importance to asthmatic patients who train and compete in a cold climate, and who are affected by small changes in their lung function.

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