Efficacy of a Heat Exchanger Mask in Cold Exercise-Induced Asthma*

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Study objectives: To determine the efficacy of a novel mask device in limiting cold air exercise-induced decline in lung function in subjects with a history of exercise-induced asthma (EIA).

Setting: In spite of appropriate medical therapy, many asthma patients are limited in cold weather activities.

Design: In study 1, 13 asthmatic subjects performed two randomized, single-blind treadmill exercise tests while breathing cold air (−25 to −15°C) through a placebo or active heat exchanger mask. In study 2, five subjects with EIA performed three treadmill exercise tests while breathing cold air: one test using the heat exchanger mask, one test without the mask but with albuterol pretreatment, and one test with neither the mask nor albuterol pretreatment (unprotected exercise). For all studies, spirometry was performed before and at 5, 15, and 30 min after exercise challenge.

Patients: For both studies, a total of 15 subjects with a history of asthma symptoms during cold air exercise were recruited.

Results: In study 1, the mean decrease (± SE) in FEV₁ was 19 ± 4.9% with placebo, and 4.3 ± 1.6% with the active device (p = 0.0002). The mean decrease in maximum mid-expiratory flow (FEF₂₅₋₇₅) was 31 ± 5.7% with placebo and 4.7 ± 1.7% with the active device (p = 0.0002). In study 2, the mean decrease in FEV₁ was 6.3 ± 3.9%, 11 ± 3.7%, and 28 ± 10% for the heat exchanger mask, albuterol pretreatment, and unprotected exercises, respectively (p = 0.4375 for mask vs albuterol, p = 0.0625 for mask vs unprotected exercise). The mean decrease in FEF₂₅₋₇₅ was 10 ± 4.8%, 23 ± 6.0%, and 36 ± 11%, respectively (p = 0.0625 for mask vs albuterol, p = 0.0625 for mask vs unprotected exercise).

Conclusions: This heat exchanger mask blocks cold exercise-induced decline in lung function at least as effectively as albuterol pretreatment.

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Key words: exercise-induced asthma; masks; protective devices; respiratory function tests

Abbreviations: EIA = exercise-induced asthma; FEF₂₅₋₇₅ = maximum mid-expiratory flow; PRHE = personal respiratory heat exchanger

Exercise-induced asthma (EIA) is present in up to 90% of all patients with asthma, and exercise is one of the most common precipitants of acute asthma.1,2 While pre-exercise inhalation therapy aimed at reducing EIA may help significantly, many patients are left with limitations in their ability to exercise, particularly in cold weather, and some patients prefer minimizing pharmacologic approaches to treatment. Even in mild asthma, multiple medications may be needed to control EIA, and with high levels of exercise patients may still have incomplete symptom control.1,2 The mechanism of EIA has been well studied but is still incompletely understood.1,3–9 The magnitude of temperature difference and increase in minute ventilation in asthmatics is related to the degree of bronchospasm in a dose-dependent fashion.3 Increases in ventilation that occur with exercise cause airway cooling as well as increased water loss from...
Inhaled corticosteroids were allowed as long as subjects continued to demonstrate EIA on this regimen. After an initial history and physical examination, the subjects completed three cold air exercise tests separated by at least 3 days. For the first test, the PRHE mask was worn with exercise in cold air, exactly as in the initial study (mask exercise). For the second test, subjects were pretreated with two puffs of albuterol, and exercised in cold air without the mask (albuterol exercise). For the third test, subjects exercised in cold air without albuterol pretreatment or the mask (unprotected exercise). Spirometry was performed at 5, 15, and 30 min after exercise, and subjects were rescued with albuterol if they demonstrated a >40% decline in FEV₁ at any time.

The primary outcome for both studies was the maximum postexercise percentage decline in FEV₁. Secondary outcomes included the percentage decline in maximum mid-expiratory flow (FEF₂₅₋₇₅), FEF₂₅₋₇₅/FVC ratio, and for study 1, the presence or absence of EIA as defined by a decline in FEV₁ > 10%. The maximal percentage decrease in lung function was expressed as a mean ± SE. Data from two exercise visits within a study were compared by applying the Wilcoxon signed-rank test to the percentage of maximal decline in lung function. In study 1, the McNemar test was used to compare placebo and active device exercises with respect to the presence of EIA.

RESULTS

Study 1 enrolled 13 subjects, and study 2 enrolled 5 subjects. All subjects met inclusion and exclusion criteria, and no subjects dropped out. Of the 15 people who participated in one or both studies, 9 were women, and the average age of participants was 29 years (Table 1). Mean baseline FEV₁ was 3.24 ± 0.17 L (88 ± 4.0% of predicted).

Study 1 subjects demonstrated improved lung function after exercise with the active device, compared to placebo (Fig 2). The mean fall in FEV₁ was 19 ± 4.9% with placebo and 4.3 ± 1.6% with the active device (p = 0.0002). The mean fall in
FEF$_{25-75}$ was 31 ± 5.7% with placebo and 4.7 ± 1.7% with the active device (p = 0.0002).

Since exhaled flow rates can vary significantly with lung volume, particularly the FEF$_{25-75}$, we calculated the decrease in the ratio FEF$_{25-75}$/FVC with exercise. For study 1, the mean percentage decrease in the FEF$_{25-75}$/FVC ratio was 21 ± 4.3% with placebo exercise and 0.4 ± 1.7% with the PRHE mask exercise (p = 0.0002). Thus, the difference in the decline in FEF$_{25-75}$ when normalized to lung volume was still highly significant.

During the placebo device exercise, 6 of 13 subjects demonstrated EIA by a fall in FEV$_1$ > 10% from baseline. Of those six subjects, two had a > 40% fall in FEV$_1$, necessitating early rescue with albuterol. However, during exercise with the active device, only one of these six subject demonstrated EIA (p = 0.0253) and no subjects required albuterol rescue.

Because some subjects met criteria for EIA with placebo exercise (“responders”) and some did not (“nonresponders”), we analyzed the data separately to see if the mask improved lung function in the seven nonresponders. For responders, the mean declines in FEV$_1$ during placebo and active device exercise were 34% and 8%, respectively (p = 0.02). For nonresponders, the mean declines in FEV$_1$ for placebo and active device exercise were 6.8% and 1.5%, respectively (p = 0.006). Therefore, this subgroup analysis shows that the mask device significantly improves lung function whether or not subjects have EIA with placebo exercise.

In study 2, five subjects with documented EIA participated in three cold air exercise tests. Again, there were indications that the heat exchanger mask prevented a decline in lung function, although results did not quite achieve statistical significance. The mean fall in FEV$_1$ was 28 ± 10% with placebo and 6.3 ± 3.9% with the active device (p = 0.0625, Fig 3). The mean fall in FEF$_{25-75}$ was 36 ± 11% with placebo and 10 ± 4.8% with the active device (p = 0.0625). With albuterol, the mean fall in FEV$_1$ and FEF$_{25-75}$ was 11 ± 3.7% and 23 ± 6.0%, respectively. While there was no difference in the change in FEV$_1$ between the mask and albuterol exercises (p = 0.4375), the mask performed better than albuterol with respect to the decline in FEF$_{25-75}$ (p = 0.0625). Correcting for lung volume, the FEF$_{25-75}$/FVC fell only 6.2 ± 3.0% with the

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*PC$_{20}$ = provocative concentration causing a 20% fall in FEV$_1$.
†Subjects 1 to 13 participated in study 1; subjects 2, 9, 11, 14, and 15 participated in study 2.

Figure 2. Individual changes in FEV$_1$ with cold air exercise in study 1. Solid bars represent the placebo exercise; striped bars represent the active device exercise. The active heat exchanger mask is highly effective, particularly in subjects demonstrating a > 10% decline in FEV$_1$ with placebo exercise.
mask, compared to 19 ± 5.9% with albuterol pretreatment, a finding that also approached statistical significance (p = 0.125). As in the first study, two of the five subjects required early albuterol rescue after the placebo exercise due to a marked decline in FEV₁. This did not occur with the mask or albuterol pretreatment exercises.

**DISCUSSION**

This heat exchanger mask is highly effective at blocking cold air exercise-induced decline in lung function. The mean decrease in FEV₁ was 19 ± 4.9% with placebo, and 4.3 ± 1.6% with the active device (p = 0.0002). While all subjects had better lung function after exercise with the active device compared to placebo, those individuals who demonstrated a > 10% decline in FEV₁ with placebo exercise had the most dramatic improvement with the active device mask (Fig 2). For example, subject 1 had a 54% drop in FEV₁ with placebo, compared to a 4.9% drop with the active device. The drop in FEF₂₅₋₇₅ was similarly attenuated in this subject: 70.7% with placebo vs 10.4% with the active device.

The treatment of patients with predominantly EIA symptoms usually involves pretreatment with an inhaled short-acting bronchodilator. This approach is highly effective and is associated with minimal cost and adverse effects, so the benefit of any new device or treatment for EIA should be at least as effective as albuterol pretreatment. We intended to address this question after our initial investigation established the efficacy of this PRHE mask, by taking a small sample of subjects with known EIA and comparing the mask to albuterol pretreatment. While the sample size is small, the cold air exercise-induced declines in FEV₁ with the mask and albuterol pretreatment exercises were similar (6.3% and 11%, respectively, p = 0.4375), and the decline in FEF₂₅₋₇₅ suggested that the mask may be superior to albuterol (10% and 23%, respectively, p = 0.0625). While study 2 demonstrates that the heat exchanger mask is effective at limiting the decline in lung function with cold air exercise, it also suggests that the mask is at least as effective as albuterol pretreatment. While this implies that some patients could try to use this mask in place of albuterol for winter activities, this mask will likely be used in combination with albuterol pretreatment to achieve two goals: to improve symptoms that occur despite appropriate albuterol dosing and to reduce the frequency of albuterol redosing for extended activities in cold dry air.

One of the limitations of this study is the small sample size. While larger studies may be necessary, study 1 results are highly significant. This suggests that the trends toward significance in study 2 probably reflect the limitations of a small sample size, and less likely reflect spurious findings due to chance.

Outliers did not drive these results. In the first study, there were three subjects who demonstrated a > 30% fall in FEV₁ during the placebo exercise, who later showed near complete absence of EIA with the active device visit. We believe these data demonstrate the remarkable efficacy of this device. However, even when these three subjects were removed from the analysis, the results were still significant: the mean fall in FEV₁ would be 11 ± 2.4% with placebo and 3.8 ± 2.4% with the active device (p < 0.01). The mean fall in FEF₂₅₋₇₅ would be 22 ± 3.3% with placebo and 3.6 ± 2.0% with the active device (p < 0.01). In fact, the efficacy of this mask may have been underestimated in both studies with the inclusion of data from the subjects needing early albuterol rescue after placebo exercise. Their maximal decline in FEV₁ may have been much greater in that visit, had we not prevented further decline in lung function with albuterol administration.

While all subjects stated that they experienced symptoms of asthma in cold air prior to enrollment and had positive methacholine challenge results, more than half of the study 1 subjects had a decrement in FEV₁ with placebo exercise that was < 10%. Nevertheless, the heat exchanger device prevented lung function decline in this population, as well as in those with more significant lung function decline. This gives the device broad applicability to the general asthma population, and may suggest that there is a disconnect between EIA symptoms and change in FEV₁.

The use of a mask that heats inspired air to
ameliorate symptoms related to cold weather is not new. Several PRHEs already exist, and some have been studied in cold air.\textsuperscript{12-15} The Qxtec PRHE device is a plastic heat exchanger module embedded within a mesh pocket overlying the mouth opening of a fleece facemask. The module is composed of multiple folds of desiccant-coated plastic that provides a large surface area for rapid heat and moisture transfer, and requires no power source. As the user exhales, heat and moisture are trapped within the device; as the user inhales, cold air is warmed and humidified as it travels across the material. As the imbedded desiccant traps exhaled water vapor, it is warmed further by the exothermic transition from gas to liquid. According to the unpublished data from the manufacturer (L. Bagby, MBA; DMCE Engineering; Arvada, CO; September 2003), at steady-state exercise in cold air, inspired air at –40°C can be warmed to as high as 15°C, and exhaled air temperature drops from 37°C to –23°C–40°C can be warmed to as high as 15°C, and steady-state exercise in cold air, inspired air at –40°C can be warmed to as high as 15°C, and exhaled air temperature drops from 37°C to –23°C as it leaves the device. Humidification data were not supplied by the device manufacturer, and the authors did not have the ability to measure inhaled air humidity in front of and behind the device during exercise.

What is unique to this device is its light weight, ease of use, and lack of external power source. The proposed mechanism of action of this device also addresses both temperature and humidity, both of which are believed to play a role in exercise-induced bronchoconstriction.\textsuperscript{1,3-7,10} It may be a promising adjunctive therapy for asthmatics that want to work, exercise, or spend time in the cold, particularly for those individuals who still experience symptoms of EIA after pretreatment with albuterol.

One potential explanation for improved exercise lung function with the device is the expiratory resistance afforded by the system. If back pressure increases, one could argue that the improvement in lung function is due to the known beneficial effect of positive end-expiratory pressure on obstructive lung disease.\textsuperscript{16} The manufacturer of the device reports unpublished studies demonstrating a pressure drop across the mask during tidal breathing of only 0.5 cm of water (L. Bagby, MBA; September 2003). This pressure difference should increase with an increase in minute ventilation during exercise, but no subjects complained of feeling an increase in breathing resistance during these studies.

We chose an inhaled temperature range of –25 to –15°C, which is colder than previous studies of mask devices to prevent EIA. We wanted to significantly challenge the device, and it is common to experience these very cold and dry conditions during winter recreation. Further studies might look at two or three different inhaled air temperatures and humidities to ascertain the optimal performance characteristics of this device with respect to symptoms and lung function in asthma.

Exhaled flow rates can vary significantly with lung volume, particularly the FEF\textsubscript{25-75}. One way to correct for this is by using the ratio of FEF\textsubscript{25-75} to FVC. For both studies, this ratio yielded similar results to the FEF\textsubscript{25-75} data. The difference in the decline in FEF\textsubscript{25-75} when normalized to lung volume was still highly significant in study 1, and suggested a trend toward significance in study 2. This analysis, while not a replacement for lung volume measurement, supports the validity of the FEF\textsubscript{25-75} data.

This novel heat exchanger mask is highly effective in blocking cold exercise-induced bronchospasm in a broad population of asthmatics, as demonstrated by changes in FEV\textsubscript{1} and FEF\textsubscript{25-75}. Compared to pretreatment with albuterol, the magnitude of its effect is similar for FEV\textsubscript{1} and greater for FEF\textsubscript{25-75}. This mask promises to be a useful adjunctive therapy for asthmatic patients who work, live, or exercise in cold environments.

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