Exercise capacity and exercise-induced bronchoconstriction (EIB) in a cold environment

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Summary

Introduction: Exercise in a cold environment has been reported to increase exercise-induced bronchoconstriction (EIB). However, the effect of a cold environment upon exercise capacity in subjects with EIB has, to our knowledge, not been previously reported.

Purpose: Primary: To examine the influence of changing environmental temperature upon exercise capacity measured by peak oxygen uptake ($VO_{2}$peak), peak ventilation ($VE_{\text{peak}}$) and peak running speed in subjects with diagnosed EIB.

Secondary: To assess the influence of changing environmental temperature upon EIB.

Methods: Twenty subjects (10–45 years old, male/female: 13/7) with EIB underwent exercise testing by running on a treadmill in a climate chamber under standardised, regular conditions, 20.2°C (±1.1) and 40.0% (±3.3) relative humidity [mean (±SD)], and in a standardised cold environment, −18.0°C (±1.4) and 39.2% (±3.8) relative humidity in random order on separate days. Oxygen uptake ($VO_{2}$), minute ventilation ($VE_{\text{peak}}$), respiratory exchange ratio (RER), heart rate (HR) and running speed were measured during exercise.

EIB (forced expiratory volume in 1 s (FEV$_{1}$) ($\Delta FEV_{1}$) increased significantly from 24% (19,29) to 31% (24,38), respectively ($p = 0.04$) after exercise in the cold environment. No correlation was found between reduction in $VO_{2}$peak and the increased maximum fall in FEV$_{1}$ in the cold environment.
Introduction

Inspiring cold, dry air during exercise is reported to increase exercise-induced bronchoconstriction (EIB) in asthmatic subjects compared with regular, indoor environment and humid environment.1–3

Most of the previous reports concern the effect of inspiring cold air through a mouthpiece, while the subjects are exposed to regular, laboratory environmental temperature. Only very few studies have investigated the effect of the whole body exposure to cold air upon exercise capacity and/or lung function in asthmatic subjects.4–8

As far as we know, only three studies have investigated the influence of cold air upon oxygen uptake (VO2) in asthmatic subjects6–8 and only one of them has reported on maximum oxygen uptake (VO2 max).6 Kallings et al.7 did not find any differences in VO2 or other physiological parameters in asthmatic subjects during exercise under room tempered conditions when inhaling cold, dry air as compared with inhaling warm, humid air. Also Sandsund et al.6 concluded with no differences in VO2 at submaximal workloads, in VO2 max or in lung function in seven mild asthmatic subjects between inhaling cold air and warm air in a cold environment during exercise. Eschenbacher et al.8 found that the workload in watts performed per L min–1 of oxygen consumed was significantly greater during the cold and dry conditions than during hot and humid conditions in eight male asthmatic subjects.

The effect of cold air on physiological parameters in healthy subjects is reported to vary depending on different factors such as type, intensity and duration of exercise, amount of fatty tissue, wind, ambient temperature, clothing, fluctuations in body temperature and energy reserves.9 Quirion et al.9 found significantly decreased VO2 max, maximum workload and time to exhaustion, whereas minute ventilation (VE) did not change during a short exhaustive exercise at –20 and 0 °C as compared with 20 °C in eight healthy males. Sandsund et al.10 reported increased VE and VO2 at submaximal workloads in an environment of –15 °C as compared with 23 °C whereas no difference was found for VO2 max. They suggested that exercise stress increased in a cold environment, probably as a response to increased metabolic demand. Their findings in healthy subjects are supported by Claremont et al.11

As EIB influences daily life activities and sports activities in children and adolescents, an accurate assessment of EIB is important to enable optimal choice of treatment. EIB is best assessed by a standardised exercise test, commonly used is running on a treadmill for 6–8 min at a submaximal work load.12,13 Lately it has been maintained that an exercise load corresponding to 95% of maximum heart rate (HR max) is preferable to obtain a high sensitivity.14 EIB consists of bronchoconstriction occurring immediately or soon after physical exercise triggered by increased ventilation during exercise.12,14–16 Two main hypotheses have been proposed to explain the relationship between exercise and EIB. Gilbert and McFadden17 suggested that airway cooling is probably the cause of EIB. Anderson18 suggested that respiratory water loss due to increased ventilation is the main stimulus to provoke EIB.

Although it has been generally accepted that cold air inhalation increases EIB, this has recently been challenged by Evans et al.19 They concluded that cold air inhalation had no additive effect upon the severity of EIB after exercise or decrease in lung function after eucapecnic voluntary hyper-ventilation.

However, it is not known if cold environment may influence exercise capacity or if there is a relationship between the magnitude of EIB and exercise capacity in subjects with EIB. Such knowledge is needed for giving optimal advice and treatment to asthmatic children and adolescents competing in different sports, especially endurance winter sports. It is also needed in relationship to regular physical training of asthmatic children and adolescents especially in the Scandinavian countries and in other countries with temperature to subartic climate where the winter season can be quite cold.

The aims of the present study were primarily to assess any possible change in exercise capacity measured by peak oxygen uptake (VO2 peak), peak ventilation (VE peak) and peak running speed during exercise in a cold environment as compared to regular indoor environmental conditions and secondarily to assess the influence of cold environment upon EIB in subjects with diagnosed EIB.

Material and methods

Design

The present study has an open randomised, cross-over design with one exercise test performed under standard, regular indoor conditions, temperature of 20 °C and 40.0% relative humidity, and another test in a standardised cold environment, –18 °C and 40% relative humidity on two different days. An interval of at least 48 h was required between the two tests. There were three study days in total. On day one, all subjects underwent an EIB-test to assess if they satisfied the inclusion criterion, reduction in forced expiratory volume in 1 s (FEV1) ≥ 10% from before to after exercise. If satisfying inclusion criterion the subjects were randomised consecutively to one of the two climate blocks in random order generated by a computer programme. The study could not be blinded because the subjects could immediately feel which climate they went into. The present study was part of a larger study aiming to assess the effect of different environments, altitude20 and humidity21 upon exercise capacity and upon EIB in subjects suffering from EIB.

Conclusion: Exercise capacity (VO2 peak and peak running speed) was markedly reduced during exercise in a cold environment whereas EIB increased in subjects suffering from EIB.

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The study was performed according to the principles stated in the Declaration of Helsinki. The Regional Medical Ethics committee approved the study and all subjects signed an informed written consent before inclusion.

Ambient conditions

On study days 2 and 3, the subjects performed exercise testing according to identical test procedures. The exercise tests were performed in a conditioned climate chamber (Norwegian Sub diving Techniques A/S, Haugesund, Norway) with relative humidity of 40.0% (+ 3.3) and temperature 20.2 °C (+ 1.1) [mean(+SD)] on one of the study days and −18 °C (+ 1.4) and relative humidity of 39.2% (+ 3.8) on the other study day. The barometric pressure during the exercise tests were 98.7 kPa (+ 1.1) or 740 mmHg (+ 8).

Subjects

Twenty subjects between 10 and 45 years of age with diagnosed EIB were included in the study. EIB was defined by a reduction in FEV1, of 10% or more from before to after a standardised EIB-test performed under standard, regular conditions. Exclusion criteria consisted of any other diseases or use of any regular medication that might influence test results and any respiratory tract infection during the last 3 weeks before study inclusion. The subjects were also excluded if the baseline FEV1 measurement varied more than 5% between the two test days.

Antihistamic medication was withheld according to ERS guidelines. Inhaled short-acting β2-agonists and sodium cromoglycate were withheld for 8 h prior to testing, inhaled long-acting β2-agonists, theophylline and leukotriene antagonists for the last 72 h, anti-histaminic for the last 7 days and orally administered glucocorticosteroids for the last 7 weeks before study inclusion. The subjects were also included if the baseline FEV1 measurement varied more than 5% between the two test days.

Seventeen of the 20 subjects were atopic as defined by positive skin prick test (SPT). Seven subjects used regular inhaled steroids and ten subjects used regular daily long-acting inhaled β2-agonists. Seventeen subjects used short-acting β2-agonists on demand, one subject used oral theophylline and two subjects used a leukotriene antagonist daily. Four subjects used antihistamines, whereas nine subjects were without any regular asthma medication. Five subjects participated in competitive sports, 14 participated in regular physical activity in school or leisure time, and one subject rarely or never participated in physical activity.

Lung function

Lung function was measured by maximally forced expiratory flow loops (Mastertab, Erich Jaeger®️, Germany). FEV1, forced vital capacity (FVC) and forced expiratory flow at 50% of FVC (FEF50) were measured before exercise and 1, 3, 6, 10 and 15 min after exercise and 15 min after inhaled salbutamol (5 mg mL⁻¹; 0.05 mg kg⁻¹). All lung function measurements were performed in a regular, indoor environment outside the climate chamber. All manoeuvres complied with the general acceptability criteria of The European Respiratory Society (ERS). Predicted lung function values, when used, were according to Zapletal et al. and Quanjer et al.

Exercise test

EIB was determined by running on a motor-driven treadmill (“Bodygaurd” 2313, Sweden) for 8 min at a submaximal work load. The inclination of the treadmill was 5.3%. The running speed was adjusted during the first 4 min to achieve a work load corresponding to the maximum speed the subjects were able to maintain the last 4 min, about 95% of estimated HRmax (220 beats min⁻¹-age). If the subjects indicated that higher speed was necessary to achieve exhaustion after 8 min the running speed was also adjusted after 5 and 6 min. The estimated HRmax is elaborated from epidemiological studies, and it is a circumstantial estimation for individual subjects. The standard deviation for maximum heart rate during exercise is ± 10 beats min⁻¹. Therefore, the exercise workload was standardised by a combination of 95% of estimated HRmax and the test leader’s evaluation of exhaustion after 8 min.

VO2, VE, breathing frequency (BF) and respiratory exchange ratio (RER) were measured 5, 6 and 7 min after starting exercise test. The EIB protocol used in our study is different from a standard, incremental protocol for assessing VO2 peak, but has been evaluated in a previous study. A comparison of the EIB protocol and a stepwise protocol showed no difference in VO2 peak or VE peak. Douglas bags were used for collecting gas samples of the expired gas. The variations reported for the Douglas bag method used with cycle ergometry are 2.3–2.5% for daily variations and 3.3–5.1% for between days variations. The Douglas bag system was chosen because the measurements with the automatic equipment were unstable and not reproducible in the cold environment.

The subjects, wearing a nose clip, breathed through a Hans Rudolph mouthpiece (2700 Series; Hans Rudolph Inc, USA). Expiratory gas samples were taken for at least 30 s and analysed for the oxygen and carbon dioxide content (Oxygen analyser model S-3A/1 and Carbon dioxide analyzer model CD-3A; Ametek Inc, USA). The volume, temperature and pressure of the expired gas were measured at the time the air was analysed (“Ventilation measuring system”, model S-430, KL-Engineering, Northridge, California, USA). The heart rate (HR) was recorded electronically and registered every minute (Polar Sports tester PE 3000®, Polar Electro OY, Kempele, Finland).

Maximum percentage reduction in FEV1 after exercise test was calculated by (pre-exercise FEV1-minimum post-exercise FEV1)/(pre-exercise FEV1) × 100%. Minimum post-exercise FEV1 was the lowest recorded value at 1, 3, 6, 10 or 15 min after exercise test. Similar calculations were performed for FEF50 and FVC. The highest recorded HR, VO2, VE, BF, RER and running speed during exercise tests were determined as HRpeak, VO2 peak, VE peak, BFpeak, RER peak and peak running speed.

Assuming that the inhaled air during exercise is fully saturated with vapour and reaches the temperature of 37°C, the respiratory water loss during the last 3 min of exercise was calculated by using a web-based online calculator designed by the Department of Physics and Astronomy Georgia State University Atlanta, based on...
empirical fit for density data (http://hyperphysics.phyastr.gsu.edu/hbase/kinetic/relhum.html 2004).

**Skin prick test**

The skin prick test was performed according to the Nordic guidelines with the following prevalent ambient allergens: moulds (Cladosporium herbarum), house dust mites (Derma-tophagoideus pteronyssimus), dog dander, cat dander, birch pollen, grass pollen (timothy), mug worth pollen, milk, shrimp and egg (Soluprick, ALK, Copenhagen, Denmark). To be considered allergic to an allergen, a positive skin prick test of at least ++ (1/2 of the reaction to histamine 10mg/mL) was required. The size was recorded by measuring (maximum+minimum diameter (mm)) x 2⁻¹.

**Statistical analysis**

Demographics are given as mean values and standard deviation (SD) and results as means with 95% confidence intervals (CI). Differences between the two tests were analysed by Student’s paired t-tests when satisfying normal distribution. Correlation was calculated by Pearson’s correlation coefficient. The bronchoconstrictor response following exercise was measured as the maximum per cent fall in FEV₁ and FEF5₀ after exercise and the area under the curve (AUC) per cent fall of the pre-exercise value in FEV₁ time⁻¹, up to 15-min post-exercise, using the trapezoid rule. Identical analysis was made for FEF5₀. If FEV₁ or FEF5₀ increased from baseline after exercise, the corresponding area was subtracted from the AUC measurements. All tests were two-tailed with a significance level of 5%

Statistical analyses were performed with Statistical Package for Social Sciences (SPSS) version 11.0.

**Results**

Demographic data and baseline lung function are given in Table 1. Baseline lung function (FEV₁, FEF5₀ and FVC) did not differ significantly on the two test days. VO₂ peak decreased significantly, 6.5%, from 47.9 ml kg⁻¹ min⁻¹ (45.0, 51.8) [mean (95% confidence intervals)] to 44.8 ml kg⁻¹ min⁻¹ (41.2, 48.4), respectively (p = 0.004) during exercise under regular conditions as compared with exercise in the cold environment (Table 2). Four subjects reduced VO₂ peak more than 10%, nine subjects had a reduction between 5 and 10% and six subjects reduced VO₂ peak less than 5% in the cold environment. One subject increased VO₂ peak 5% in the cold environment. Peak running speed was also significantly lower in the cold environment: 10.2 km h⁻¹ (9.5, 11.0) vs. 9.7 km h⁻¹ (8.9, 10.5), respectively (p = 0.02) (Table 3).

There were no differences in VE peak, RE peak, HR peak or BF peak during exercise between the two climatic conditions (Table 2). VO₂ was significantly reduced after 5, 6 and 7 min run in the cold environment (p = 0.01) (Fig. 1). The running speed was also significantly lower in the cold environment after 5 and 7 min (p = 0.01 and p = 0.03, respectively) (Fig. 1). No significant differences were found for VE, RER,
BF or HR after 5, 6 and 7 min run between the two climatic conditions.

Maximum reduction in FEV\(_1\) and AUC for FEV\(_1\) increased significantly after exercise in the cold environment as compared with regular, indoor conditions. Maximum reduction in FEV\(_1\) as per cent of baseline lung function after exercise in the cold environment was 31% (24, 38) vs. 24% (19, 29), respectively, after exercise under regular conditions (p = 0.04) (Table 3). AUC for FEV\(_1\) was higher after exercise in the cold air, 358 (261, 455) vs. exercise under regular conditions, 250 (182, 317), respectively (p = 0.01) (Table 3). Increased maximum reduction in FEF\(_{50}\) after exercise in the cold environment was also found; 47% (38, 55) vs. 38% (30, 46), but on the border of significance (p = 0.06).

Maximum reduction in FVC as per cent of baseline lung function or AUC for FEF\(_{50}\) did not differ significantly between the climatic conditions (Table 3). Reduction in FEF\(_{50}\) was significantly higher 1 and 6 min after exercise in the cold environment (Fig. 2).

Calculated respiratory water loss during the last 3 min of exercise in the cold environment was 12.5 g (10.8, 14.3) vs. 10.8 g (9.7, 12.0) under regular indoor conditions (p = 0.03).

No significant correlation was found between reduction in lung function after exercise and water loss during the last 3 min of exercise. Nor was there any significant correlation between increased maximum fall in lung function (measured by FEV\(_1\) and FEF\(_{50}\)) or increased AUC after exercise and reduced VO\(_2\) peak in the cold environment.

### Discussion

The present study demonstrated that exercise capacity measured by VO\(_2\) peak and peak running speed decreased significantly during exercise in a cold environment as compared with regular environmental conditions, whereas VE\(_{\text{peak}}\), RER\(_{\text{peak}}\) and BF\(_{\text{peak}}\) did not differ in subjects suffering from EIB (Table 2).

Maximum reduction in FEV\(_1\) after exercise and AUC for FEV\(_1\) increased significantly in the cold environment as compared with exercise under standard, regular conditions. Maximum reduction in FEF\(_{50}\) did not reach statistically significant difference. The increased reduction in FEF\(_{50}\) reached statistical significance only at 1 and 6 min after exercise in the cold environment whereas AUC for FEF\(_{50}\) did not change (Fig. 2 and Table 3). Mean FEF\(_{50}\) at baseline was only 74% and 76% of that predicted (Table 1). This demonstrates the presence of airway obstruction in the peripheral airways in this group of asthmatics. Only seven out of 20 subjects used anti-inflammatory treatment (inhaled steroids).

According to the present study, the differences in VO\(_2\) and running speed occur when the subjects were close to their maximal aerobic capacity, the last 3 min of the EIB-test (Table 2 and Fig. 1). No correlation was found between maximum reduction in lung function (FEV\(_1\) or FEF\(_{50}\)) after exercise or water loss during exercise and the reduced VO\(_2\) peak in the cold compared to the regular environment. The lack of correlation is possibly due to the number of subjects included. The power is probably too weak to detect any association. Nor can the reduction in VO\(_2\) be explained by reduction in VE. No significant difference was found in VE during the last minutes of the tests or in VE\(_{\text{peak}}\) (Fig. 1 and Table 2) between the two climatic conditions.

All except three subjects reported spontaneously that breathing during exercise in the cold environment was much more difficult as compared with that in regular conditions. These statements support that the subjects ran slower during the last 4 min of the test with decreased VO\(_2\) peak in the cold environment. Studies aiming to imitate "real climatic conditions", like the present study, cannot be blinded and psychological factors might influence the results. To minimise these effects, objective measurements and well-standardised test procedures are necessary. In the present study the standardisation of the exercise load was based upon the screening test of the individual subjects aiming a submaximal to maximal exercise load as assessed by HR. The speed of the treadmill thus becomes a measure of performance during the two different climatic conditions.

The measurement of VO\(_2\) in the cold environment was challenging because the instruments used for direct and continuously VO\(_2\) measurements during exercise did not work in −18 °C. The Douglas Bag System used in the present study is a precise and well-documented instrument, and it is in fact recognised as a "gold standard". The disadvantage using the Douglas Bag system was that the VO\(_2\) measurements during the entire exercise period and the feasibility to measure tidal breathing flow volume loops during exercise were missed.

The causes of reduced VO\(_2\) peak and peak-running speed in the cold environment are unknown. Possibly, an increased

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**Table 3** Difference (Δ) in maximum reduction in FEV\(_1\), FEF\(_{50}\) and FVC (% of baseline) and area under curves (AUC) for FEV\(_1\) and FEF\(_{50}\) after exercise test in a standardised regular environment, 20.2°C (+1.1) and 40.0% (+3.3) relative humidity [mean (+SD)] and in a standardised cold environment, −18°C (+1.4) and 39.2% (+3.8) relative humidity (n = 20).

<table>
<thead>
<tr>
<th>Variables</th>
<th>20°C</th>
<th>−18°C</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔFEV(_1)%</td>
<td>24 (19,29)</td>
<td>31 (24,38)</td>
<td>0.04</td>
</tr>
<tr>
<td>ΔFEF(_{50})%</td>
<td>38 (30,46)</td>
<td>47 (38,55)</td>
<td>ns</td>
</tr>
<tr>
<td>ΔFVC%</td>
<td>15 (11,19)</td>
<td>20 (14,27)</td>
<td>ns</td>
</tr>
<tr>
<td>AUC (FEV(_1))</td>
<td>250 (182,317)</td>
<td>358 (261,455)</td>
<td>0.01</td>
</tr>
<tr>
<td>AUC (FEF(_{50}))</td>
<td>386 (276,495)</td>
<td>485 (364,606)</td>
<td>ns</td>
</tr>
</tbody>
</table>

Values are given as mean with 95% confidence intervals in parentheses. ns = not significant.
strain level, especially for asthmatics starting exercise on a high intensity in a cold environment without warming-up, might reduce the performance. Neither HRpeak nor RERpeak differed during the two tests and indicate that the subjects achieved equal level of exhaustion even though the running speed was reduced in the cold environment. The subjects were only exposed to the cold environment for 10 min and no freezing or shivering were observed or reported. As they wore warm clothes suited for the cold environment, the decrease in $V_{\text{O}_2}$ peak had probably a direct relation to reduced running speed during exercise. An EIB-test with pre-medication of inhaled $\beta_2$-agonists in the cold environment or a control group of EIB-negative subjects might explain if the airway calibre is a possible reason. Our findings are supported by the study from Quirion et al. on healthy subjects. They demonstrated that $V_{\text{O}_2}$ max significantly decreased and the $V_E$ did not change in -20 and 0°C as compared with that in 20°C, and their subjects reported that submaximal exercise intensities were more tiring in a cold environment as compared with those in a warm environment. They suggested that the net efficiency of exercise at low temperatures is lower than under normal conditions. On the other hand, Sandsund et al. reported
increased VO₂ in eight healthy male athletes at submaximal exercise intensities in a cold environment compared with those in standard, indoor conditions, but there was no difference in VO₂ max. Time to exhaustion was shorter in the cold environment. They suggested that exercise stress is higher at submaximal exercise intensities in a cold environment in agreement with the reduced running speed during exercise in the present study. Claremont et al. 11 tried to explain the same observation by a catecholamine calorigenic effect.

In the studies of asthmatics from Kallings et al., 7 Sandsund et al. 6 and Eschenbacher et al., 8 only six, seven and eight subjects, respectively, were included, and their results only serve as pilot studies indicating the need for further investigations. The workload differed markedly between these studies and also from the present study. The workload, ventilation and the demand for oxygen is too low in the study from Kallings et al. and Eschenbacher et al. in order to be able to discover any difference in VO₂ peak as compared with the exercise load at which the difference occurred in the present study.

Sandsund et al. 6 found no differences in VO₂ max, VE max, HR peak or blood lactic acid when inhaling cold or warm air during exercise. However, in their study the temperature of the environmental air was –15 °C, the breathing mouth-piece acted as a heat exchanger and increased the inspired cold air to 2 °C. This is most probably not cold enough to observe any differences in lung function or in the physiological variables. Their exercise protocol was in fact not an exercise test for provoking EIB but a stepwise protocol for measuring anaerobic threshold and VO₂ max with a 20 min warming-up period.

The present study confirms previous reports that inhalation of cold air increases EIB in asthmatic subjects. 1,2 On the other hand, neither Evans et al. 19 nor Sandsund et al. 6 could find any additive effect of cold air inhalation upon EIB. The temperature of the inhaled air in their studies was actually –1 and 2 °C, respectively, and probably not cold enough to discover any difference. Evans et al. 19 mentioned that lack of exposure to ambient cold air during inhalation may explain the lack of an additive effect.

However, cold environmental conditions seem to aggravate the effect on EIB, and the respiratory water loss significantly increased in the cold environment as compared with that in the regular, indoor conditions. Air of 37 °C fully saturated with vapour contains 44 g H₂O/m³. Air of temperature 20 °C with 40% relative humidity contains 6.9 g H₂O/m³ and air of –18 °C with 40% relative humidity contains 0.01 g H₂O/m³. When the ventilation rates increase during exercise, the water loss increases. These findings indicate that the worsening effect on EIB in asthmatics is partly due to increased water loss and partly due to heat loss and support earlier reports on EIB.

In conclusion, exercising in a cold environment decreases exercise capacity as measured by VO₂ peak and peak running speed, and increases EIB in subjects suffering from EIB. This has important implications for training procedures in a cold environment for patients and athletes with EIB. Although similar effect of a cold environment upon exercise capacity in healthy subjects cannot be excluded.

Acknowledgment

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