Responses of asthmatic and non-asthmatic athletes to prolonged treadmill running

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Metabolic and cardio-respiratory responses of four asthmatic and four non-asthmatic athletes to two hours of treadmill running at 70 percent of maximal oxygen uptake are compared. The asthmatic group had pre-exercise airflow obstruction, as indicated by the lower forced expiratory volume in one second (FEV₁) even after medication (2.90 ± 0.66 l) compared to the non-asthmatic group (4.09 ± 1.33 l). Changes in blood lactate, glucose and catecholamine concentrations as a result of the two hour run were similar for the two groups. However, the pattern of breathing was different. The asthmatics had a slower breathing frequency but a similar tidal volume to the non-asthmatics. Both groups had an increase in the ventilation rate over the two hour run. For the non-asthmatic group, this increase in ventilation was achieved by an increase in the breathing frequency (p<0.01), whereas tidal volume was reduced (p<0.05). The increase in the ventilation rate over the two hour run for the asthmatic group was brought about by a small increase in breathing frequency (p<0.05), whereas tidal volume was not changed. This maintenance of the tidal volume by the asthmatic athletes during endurance running may compensate for the airflow obstruction, and so allow successful participation in endurance running.

Keywords: Asthma, running, exercise-induced asthma

Asthmatics are now encouraged to participate in a wide variety of sports1, including those which are likely to provoke exercise-induced asthma (EIA) such as endurance running. Indeed, endurance running training has been shown to improve the fitness of asthmatic children2 and adults3 without adversely affecting their asthma, thus supporting running as an additional recreational activity for the asthmatic. Despite respiratory impairment, a number of asthmatics engage in endurance running at a competitive level, racing in long distance events such as the half-marathon and marathon.

How do asthmatic athletes who compete in endurance events compensate for their airflow obstruction? Primarily, asthma does not prevent the normal adaptations to endurance running training. This allows asthmatic athletes to sustain a high percentage of their maximal oxygen uptake (VO₂ max) during endurance races such as the half-marathon4. Furthermore, there is evidence that trained asthmatics achieve and maintain an enhanced expiratory airflow during progressive maximal exercise, whilst untrained asthmatics are unable to do so5. Although these factors may help to explain why some asthmatics with impaired pulmonary function can compete in sports with high aerobic demands, it would be preferable to evaluate the physiological responses of asthmatic athletes actually engaged in endurance running.

We have previously shown that the cardio-respiratory and metabolic responses to a simulated half-marathon 'race' on a treadmill were similar for asthmatic and non-asthmatic athletes6. However, since the athletes were asked to race the half-marathon, they were able to change their running speed and so the exercise was not of constant intensity and represented different relative exercise intensities between athletes. Therefore it was not possible to determine whether the asthmatic athlete had an altered physiological response to endurance running compensating for their airflow obstruction.

The aim of the present study was therefore to describe and compare the physiological responses of asthmatic and non-asthmatic athletes to two hours of constant speed treadmill running at the same relative exercise intensity (70 percent VO₂ max), with a view to identifying any physiological adaptations which enable asthmatic athletes to overcome their condition and so compete in endurance sports.

Method

Four male endurance trained runners with asthma who were taking daily medication volunteered for the study. Their responses were compared with those of four non-asthmatic athletes of a similar age and running background, but who had no history of respiratory problems.

Each subject performed two preliminary tests. The first was an uphill treadmill test to determine the VO₂ max7. The second test involved horizontal treadmill running for four minutes at each of four submaximal running speeds selected to span the range of each athlete's VO₂ max (60, 70, 80, 90 percent VO₂ max). The regression equation between running speed and oxygen uptake was obtained for each subject, from which the running speeds required to elicit 60 percent VO₂ max (five minute warm-up) and 70 percent VO₂ max (two hours) were calculated.
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For the two hour run, the athletes came to the laboratory in the morning after an overnight fast. The asthmatic athletes had withheld their medication for six hours (B2 agonists) and 24 hours (disodium cromoglycate). Lung function was measured at rest using a dry-spirometer (Vitalograph Ltd) to obtain the forced expiratory volume in one second (FEV1) and the forced vital capacity (FVC). The asthmatic athletes then took their usual pre-exercise medication and measurements of FEV1 and FVC were repeated after 10 minutes. The pre-exercise FEV1 and FVC were expressed as a percentage of predicted normal values based on age, sex and height. A capillary blood sample from the thumb and a venous blood sample were also taken at rest for measurements described below.

Each subject then underwent a five minute warm-up on the treadmill at an exercise intensity equivalent to 60 percent Vo2 max and then completed two hours of treadmill running at a constant speed selected to elicit 70 percent Vo2 max. Details of the time elapsed and distance covered were displayed on the screen of a microcomputer interfaced to the treadmill. Water and a sponge were available throughout the run for fluid replacement and temperature regulation. The volume of water drunk, the humidity and temperature were recorded.

The FEV1 was also measured every 15 minutes throughout the two hour run without stopping the treadmill and then at five minute intervals for 20 minutes during recovery. The FEV1 was expressed as a percentage change from resting values. The asthmatics were allowed to take further medication during exercise.

One minute collections of expired air were made at 15 minute intervals during the two hour run. Subjects breathed room air through a two-way low resistance respiratory valve and exhaled into a 150 litre Douglas bag. The expired air samples were analysed for the percentages of oxygen and carbon dioxide using a paramagnetic oxygen analyser (Servomex-Taylor Ltd, Model 370A) and an infra-red carbon dioxide analyser (Mines Safety Equipment Ltd, Lira Model 303). The volume of expired air was determined by evaporating the contents of the Douglas bag through a dry gas meter (Parkinson-Cowen Ltd), Oxygen uptake (Vo2), carbon dioxide production (VCO2) and ventilation rate (Ve) were calculated. The respiratory exchange ratio (R) (VCO2/Vo2) and the ventilatory equivalent for oxygen (Ve/vo2) were derived. A temperature probe was inserted and sealed into the two-way respiratory valve. The increase in temperature on expiration was amplified and the output linked to a chart recorder, allowing the measurement of breathing frequency (Bf) and the subsequent calculation of tidal volume (Vt) (Ve/Bf). Heart-rate and ECG profiles were monitored throughout the two hour run using three chest electrodes and an oscilloscope (Rigel Ltd). The oxygen pulse (HR/Vo2) was also calculated.

Duplicate 25μl capillary blood samples were obtained from the thumb at 15 minute intervals throughout the two hour run for later analysis of blood lactate and glucose concentrations. Venous blood samples (10ml) from an ante-cubital vein were obtained at rest and immediately after exercise. The plasma was analysed for adrenaline and noradrenaline by high performance liquid chromatography (HPLC) with electrochemical detection. The pre-and post-exercise haemoglobin and haematocrit values were determined from the venous blood samples and used to estimate the changes in plasma volume.

Statistical comparisons of the physiological responses of the two groups were limited to a description of the means and standard deviations because of the small number of subjects. A Page trend test was used to examine the changes in the physiological responses over time for each group separately.

Results

The physical characteristics and maximum exercise performance, along with the running speed and the actual percent Vo2 max sustained during the two hour run are shown for each athlete in Table 1. Although the asthmatic group had a lower Vo2 max and therefore a slower running speed for the two hour run, the exercise intensity did demand approximately 70 percent Vo2 max for both groups.

Temperature and humidity in the laboratory during the study period ranged from 18.6 to 22.0°C and 55 to 78 percent, respectively. The fluid intake was modest for both the asthmatic (254 ± 113ml) and non-asthmatic (158 ± 128ml) groups. Both groups lost an average of 2kg or three percent of body weight during the two hour run and the change in plasma volume was −7.8 ± 4.5 percent and −5.9 ± 2.9 percent for the asthmatic and non-asthmatic groups, respectively.

The four asthmatic athletes took their usual pre-exercise medication before the two hour run which increased the FEV1 slightly in two asthmatics (A and C) and markedly in the other two asthmatics (B and D) as shown in Table 2. After medication, the FEV1 was however still below the predicted normal values, the FVC was normal (4.82 ± 0.39I, 102 ± 6 percent predicted) and consequently the FEV1/FVC ratio was low (60 ± 9 percent). The pre-exercise spirometric values for the non-asthmatic group were all within normal limits, with an FEV1 of 4.09 ± 1.33I (102 ± 17 percent predicted), an FVC of 4.98 ± 1.24I (104 ± 13 percent predicted) and an FEV1/FVC ratio of 81 ± 8 percent. However, one of the non-asthmatics (E) had both a reduced FEV1 and FVC (84 percent and 85 percent of predicted values, respectively), accounting for the large standard deviations for the group. The FEV1 remained higher for the non-asthmatics compared to the asthmatics during and after exercise.

Figure 1 shows the FEV1 during and after exercise for the four asthmatic athletes. Asthmatic A did not experience a significant reduction in FEV1 (>15 percent) either during or after exercise. Asthmatic B had a 17 percent fall in FEV1, from resting values after 15 minutes of exercise. He took inhaled salbutamol at 16, 32 and 88 minutes into the two hour run, after which the FEV1 increased slightly but fell by 30
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Table 1. The physical characteristics, maximal exercise performance and 2 hour running speed for the asthmatic and non-asthmatic athletes

<table>
<thead>
<tr>
<th></th>
<th>Age (yr)</th>
<th>Height (m)</th>
<th>Weight (kg)</th>
<th>VO2 max ml.kg.⁻¹.min⁻¹</th>
<th>VE max l.min⁻¹</th>
<th>HR max b.min⁻¹</th>
<th>2 hour run m.s⁻¹</th>
<th>%VO2 max</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asthmatics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>44</td>
<td>1.84</td>
<td>66.1</td>
<td>61.5</td>
<td>132.5</td>
<td>184</td>
<td>3.78</td>
<td>71.0</td>
</tr>
<tr>
<td>B</td>
<td>44</td>
<td>1.77</td>
<td>65.3</td>
<td>57.6</td>
<td>121.3</td>
<td>172</td>
<td>3.47</td>
<td>72.6</td>
</tr>
<tr>
<td>C</td>
<td>43</td>
<td>1.76</td>
<td>69.4</td>
<td>52.8</td>
<td>131.0</td>
<td>176</td>
<td>3.36</td>
<td>69.7</td>
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<tr>
<td>D</td>
<td>41</td>
<td>1.72</td>
<td>59.7</td>
<td>51.1</td>
<td>86.0</td>
<td>174</td>
<td>3.40</td>
<td>69.9</td>
</tr>
<tr>
<td><strong>Mean ± SD</strong></td>
<td>43 ± 1</td>
<td>1.77 ± 0.05</td>
<td>65.1 ± 4.0</td>
<td>55.8</td>
<td>117.6</td>
<td>177</td>
<td>3.50 ± 0.19</td>
<td>70.8 ± 1.3</td>
</tr>
<tr>
<td><strong>Non-asthmatics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>36</td>
<td>1.69</td>
<td>60.4</td>
<td>61.2</td>
<td>134.5</td>
<td>187</td>
<td>3.48</td>
<td>69.9</td>
</tr>
<tr>
<td>F</td>
<td>30</td>
<td>1.90</td>
<td>72.4</td>
<td>70.5</td>
<td>149.2</td>
<td>181</td>
<td>4.29</td>
<td>66.7</td>
</tr>
<tr>
<td>G</td>
<td>46</td>
<td>1.65</td>
<td>53.6</td>
<td>61.8</td>
<td>120.7</td>
<td>183</td>
<td>4.20</td>
<td>73.2</td>
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<tr>
<td>H</td>
<td>43</td>
<td>1.80</td>
<td>76.8</td>
<td>60.1</td>
<td>163.8</td>
<td>185</td>
<td>3.61</td>
<td>72.0</td>
</tr>
<tr>
<td><strong>Mean ± SD</strong></td>
<td>39 ± 7</td>
<td>1.76 ± 0.11</td>
<td>65.8 ± 10.7</td>
<td>63.4</td>
<td>142.1</td>
<td>184</td>
<td>3.90 ± 0.41</td>
<td>70.4 ± 2.8</td>
</tr>
</tbody>
</table>

percent after exercise. Asthmatic C had a 15 percent reduction in FEV₁ during exercise, although this resolved immediately with the cessation of exercise. Asthmatic D had a 39 percent reduction in FEV₁ after exercise. The two asthmatics who experienced marked post-exercise bronchoconstriction (B and D) had the poorest pre-exercise FEV₁ (Table 2). The non-asthmatic with the lowest baseline spirometry (E) had a 20 percent fall in FEV₁ during exercise, although the FEV₁ returned to pre-exercise levels after exercise. No other non-asthmatic athlete experienced a significant (>15 percent) fall in FEV₁ either during or after exercise (Figure 2).

Figure 3 shows the mean and standard deviation and statistical significance of the trend over time of the VO₂, HR, oxygen pulse, VE, Vt and Bf for both groups during the two hour run. The HR and VE were lower for the asthmatic group, but the mean values during exercise were similar when expressed as a percentage of maximum HR (asthmatic 85.3 ± 3.3 vs non-asthmatic 86.6 ± 3.5 percent) or maximum VE (asthmatic 62.3 ± 4.7 vs non-asthmatic 59.7 ± 5.8 percent). The pattern of breathing was different, however, with Bf approximately 10 breaths.min⁻¹ lower for the asthmatic group compared with the non-asthmatic group. The Vt was slightly higher for the asthmatic group, and represented higher percentages of the baseline FEV₁ (asthmatic 79 ± 20 vs non-asthmatic 50 ± 7 percent) and FVC (asthmatic 46 ± 5 vs non-asthmatic 40 ± 4 percent). There was no difference in the mean ventilatory equivalent for oxygen for the two groups (asthmatic 23.4 ± 0.91 vs non-asthmatic 24.1 ± 2.11).

The VO₂, HR and VE showed significant increases over the two hour run for both groups (Figure 3). A correspondingly larger increase in HR resulted in a reduction in the oxygen pulse for both groups, whereas the ventilatory equivalent showed no significant change over time for either group. For the non-asthmatic group, the increase in the ventilation rate over time, as Vt decreased significantly, was brought about by an increase in Bf. For the asthmatic group, the increase in the ventilation rate was accompanied by a slight increase in Bf whereas Vt was maintained over the two hour run. However, asthmatic D, who developed bronchoconstriction towards the end of the two hours, had a reduction in Vt (~16.2 percent) with a corresponding increase in Bf (20.8 percent).
Table 2. The baseline FEV₁ (before and after medication) expressed in litres and as a percentage of predicted values, daily medication and pre-exercise* medication taken before the two hour run, for the asthmatic group.

<table>
<thead>
<tr>
<th></th>
<th>Pre-Med. Litres (% predicted)</th>
<th>Post-Med. Litres (% predicted)</th>
<th>Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>3.25 (78.7)</td>
<td>3.48 (84.3)</td>
<td>7.1</td>
</tr>
<tr>
<td>B</td>
<td>1.98 (51.7)</td>
<td>2.85 (74.4)</td>
<td>43.9</td>
</tr>
<tr>
<td>C</td>
<td>3.06 (80.1)</td>
<td>3.26 (85.3)</td>
<td>6.5</td>
</tr>
<tr>
<td>D</td>
<td>1.08 (29.2)</td>
<td>1.99 (51.0)</td>
<td>84.3</td>
</tr>
<tr>
<td>Mean</td>
<td>2.34 (59.9)</td>
<td>2.90 (73.8)</td>
<td>35.5</td>
</tr>
<tr>
<td>± SD</td>
<td>1.01 (24.3)</td>
<td>0.66 (15.9)</td>
<td>37.0</td>
</tr>
</tbody>
</table>

Blood lactate and glucose concentrations and the respiratory exchange ratio during the two hour run were similar for the asthmatic and non-asthmatic groups (Figure 4). Page’s trend analysis revealed no significant changes with time in these quantities. At the end of the two hour run, blood glucose concentrations were always above 2.5 mmol.L⁻¹, and therefore by definition no one developed hypoglycaemia. The increase in the plasma catecholamines, adrenaline and noradrenaline with the two hour run were significant with adrenaline and noradrenaline concentrations were increased in the asthmatic group (Figure 4). Page’s trend analysis revealed no significant changes with time in these quantities. At the end of the two hour run, blood glucose concentrations were always above 2.5 mmol.L⁻¹, and therefore by definition no one developed hypoglycaemia. The increase in the plasma catecholamines, adrenaline and noradrenaline with the two hour run were similar for the asthmatic and non-asthmatic groups (Table 3).

Discussion

This study has described and compared the physiological responses of four asthmatic and four non-asthmatic athletes who all completed the two hours of constant speed treadmill running at approximately 70 percent VO₂ max. Due to the nature of the study, only a small number of subjects were involved, and therefore the statistical analysis of the data is limited. Although the oxygen uptake, heart-rate and ventilation rate were lower for the asthmatic group compared with the non-asthmatic group due to their slower running speed, the groups exercised at the same relative exercise intensity (70 percent VO₂ max). During the two hour run, the asthmatic athletes had a lower breathing frequency although they had a similar tidal volume compared with the non-asthmatics. The tidal volume represented a higher percentage of the resting FEV₁ and FVC for the asthmatic athletes compared with the non-asthmatic athletes. This altered pattern of breathing resulted in a similar ventilatory equivalent for oxygen and therefore was as efficient for gas exchange as that adopted by the non-asthmatic athletes.

Over the two hour run, both groups showed a significant upward trend in the oxygen uptake, heart-rate and ventilation, supporting other observations in non-asthmatics when exercise is prolonged. The increase in oxygen uptake over the two hour run was not accompanied by a reduction in the respiratory exchange ratio and therefore is not associated with higher oxygen demands of an increase in fat utilization. However, this apparent decrease in mechanical efficiency may be due to the recruitment of less efficient muscle fibres with fatigue. Alternatively, since the upward drift of the oxygen uptake was slightly greater for the asthmatic group, this may be associated with increased energy demands of the respiratory muscles as exercise continued.
The cardiovascular drift, as indicated by the increase in heart-rate for both groups, is associated with thermoregulatory control. During the two hour run, water intake fell short of the recommendations to replace fluid loss of one litre per hour, so that body fluids and hence plasma volume were reduced. Venous return, stroke volume and cardiac output would be reduced as a consequence of the reduced plasma volume, and this, combined with the shunting of blood to the peripheral subcutaneous vessels for thermoregulation, leads to a rise in heart-rate needed to maintain cardiac output.

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Both groups showed a significant upward drift in the ventilation rate over the two hour run, which may be a direct consequence of the increased oxygen uptake, although others disagree with this suggested explanation. The response in the breathing pattern over time was however different for the two groups. In the non-asthmatic group, the increase in ventilation rate with time was brought about by a significant increase in breathing frequency, whilst tidal volume was significantly reduced, confirming previous observations.

However, in the asthmatic group, the smaller
increase in ventilation rate was associated with a slight but significant increase in breathing frequency, whilst tidal volume was preserved. One asthmatic who experienced further bronchoconstriction during exercise did however have a reduction in tidal volume and an increase in breathing frequency over the two hour run. The maintenance of tidal volume throughout exercise by the asthmatics, if free from EIA, represents an important difference between the groups. This finding is consistent with the observations of Haas et al., who have shown that trained asthmatics increase and maintain their expiratory airflow throughout a progressive exercise test, allowing the end expiratory pattern to be maintained at or below resting lung volumes thus minimizing the work of breathing. Such observations may help to explain why some asthmatics can compete successfully in endurance running despite impaired pre-exercise pulmonary function.

The metabolic responses to short term exercise has previously been shown to be similar in untrained asthmatic and non-asthmatic subjects. In the present study, both the asthmatic and non-asthmatic athletes demonstrated low levels of blood lactate (approximately 2 mmol.l⁻¹) during the two hour run, compatible with exercise at 70 percent VO₂ max in trained subjects. The blood glucose concentrations during the two hour treadmill run were also comparable for the two groups, and no subject developed hypoglycaemia. The similar respiratory exchange ratios for the asthmatic and non-asthmatic groups suggested that the proportion of carbohydrate and fat metabolised during exercise was the same for both groups.

Furthermore, the similar rise of the catecholamines, adrenaline and noradrenaline, during the two hour run for the two groups is consistent with our previous findings from a treadmill half-marathon. In untrained asthmatics and non-asthmatics, the rise in the adrenaline levels with short term exercise have been shown to be reduced in the asthmatic group whereas others have demonstrated no difference. Our study would therefore support this latter study, and suggest that the adrenergic responses to endurance exercise of highly trained asthmatic athletes are not impaired.

Each of the asthmatic athletes took pre-exercise medication before the two hour run. One asthmatic and one non-asthmatic experienced a reduction in FEV₁ during exercise from resting values which resolved once exercise stopped. It is unlikely that the reduced FEV₁ experienced during exercise by these two subjects was associated with bronchoconstriction per se, but reflected respiratory muscle fatigue or difficulties performing an FEV₁ whilst exercising. However, the two asthmatics with the worst pre-exercise lung function, experienced a reduction in FEV₁ during exercise which was further reduced after the two hour run. The failure of conventional pre-exercise medication to prevent EIA in these two asthmatics is similar to our earlier findings with a half-marathon treadmill time trial.

It is also of note that the pre-exercise medication used by three of the asthmatics would not be allowed for use in international competition. Two asthmatics were taking a combination of disodium cromoglycate and isoprenaline sulphate (Intal Compound); isoprenaline is a stimulant and so substances containing it are banned by the International Olympic Committee. Furthermore, one asthmatic was taking pirbuterol hydrochloride (Exirel) which is not one of the five permissible B₂ agonists. Although these asthmatics were not international athletes, this highlights the need for athletes and physicians to be aware of the drugs banned in high level sports participation.

In conclusion, asthmatic athletes with airway obstruction have an altered pattern of breathing.
when engaged in endurance running which may help to explain why they can compete successfully against non-asthmatics. Furthermore, pre-exercise medication is not always effective in preventing EIA which questions the safety of endurance running for athletes with severe asthma.

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