The effects of carbon dioxide on exercise-induced asthma: an unlikely explanation for the effects of Buteyko breathing training

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THE INCREASING USE of alternative therapy in First World countries has led to suggestions that the relationships between healthcare professionals and society need to be reviewed. There is also a need to investigate the efficacy and therapeutic mechanisms of alternative treatments; once a treatment has been rigorously tested and shown to be effective, the distinction between alternative and conventional therapy becomes irrelevant.

One alternative treatment for the management of asthma, Buteyko breathing training (BBT), has been widely publicised in Australia and New Zealand and, more recently, in the United Kingdom. This technique of intermittent, regular, controlled, shallow breathing and breath holding was developed by Buteyko in the 1960s, and evolved from the meditative Eastern traditions such as tai chi, which emphasise the importance of conscious breathing control for physical and mental well-being. Buteyko suggests that hyperventilation and the associated hypocarbia in asthma tend to lead to reduced tissue oxygenation, which leads in turn to bronchial and arterial spasm and inflammation. According to the Buteyko hypothesis, restoring "normal" ventilation by voluntary hypoventilation training will alleviate asthma by increasing the level of carbon dioxide and reversing this process. Hypoventilation is used both regularly and at the onset of an asthma attack.

Exercise is a common trigger of acute bronchoconstriction in people with asthma, and a previous study has suggested that air enriched with 6% CO₂ could reverse exercise-induced asthma (EIA). Given that an increase in CO₂ is suggested as a mechanism for the improvement in asthma following BBT, we wished to examine whether breathing air enriched with CO₂ during and after exercise could prevent or reduce EIA.

Participants

People with a history of EIA were recruited by advertisement in the local community and through hospital-based respiratory clinics. Subjects with a history of cardiovascular disease or exercise-induced anaphylaxis were excluded. Volunteers who had had a severe exacerbation or hospital admission within the previous three months were also excluded. Before each study, short-acting β-agonists were withheld for at least six hours, and in one individual oral salbutamol was withheld for 24 hours. None of the participants were taking long-acting inhaled β-agonists. The number of participants needed...
Intervention studies of EIA usually measure maximum decline in FEV₁ as a percentage of the baseline value, and area under the FEV₁ response–time curve, which provides an assessment of the duration as well as the degree of post-exercise airway obstruction. We measured both these parameters. Differences in mean values were compared using paired t tests for normally distributed data and the Wilcoxon signed rank test for non-normally distributed data.

Ethics approval

The study was approved by the Wellington Regional Ethics Committee.

RESULTS

Twenty-two subjects with a history of EIA were recruited (Box 1). Eight subjects did not meet our criteria for EIA, and two were unable to complete the exercise test. A further two subjects were excluded because they experienced severe bronchoconstriction (a decrease in FEV₁ > 50% from baseline) immediately after exercise, and required immediate treatment with a bronchodilator. Ten subjects (six male) aged 18–46 years completed the study. All subjects were using inhaled β-agonists as required, seven were taking regular inhaled corticosteroids, and all but one subject had had asthma since childhood.

Box 2 shows mean percentage fall in FEV₁, following exercise, breathing air or air enriched with 3% CO₂. The mean maximum percent fall in FEV₁ after exercise was 19.9% (95% CI, 14.4%–25.1%) for air and 27.4% (95% CI, 19.7%–34.1%) for CO₂ (P=0.12) (Box 3). The mean AUC for the total 30-minute post-exercise period was 355 (95% CI, 216–493) for air and 520 (95% CI, 399–642) for CO₂ (P=0.07).

Ten minutes after exercise the mouthpiece was removed and subjects breathed room air. This had no effect on FEV₁ when the subjects were already breathing air, but when they changed from 3% CO₂ to room air there was a significant further fall in FEV₁ (Box 2). The mean AUC for the period 10–30 minutes after exercise was significantly greater after breathing CO₂ than after breathing air.
2: Mean decrease in forced expiratory volume in one second (FEV₁) for 30 minutes after exercise breathing air (*) or 3% CO₂ (●)

At 10 minutes after exercise subjects removed their mouthpieces and breathed room air for a further 20 minutes. Error bars indicate standard error of the mean.

3: Maximum percentage fall in FEV₁ following exercise for each subject while breathing air and 3% CO₂

<table>
<thead>
<tr>
<th>Subject</th>
<th>Air (%)</th>
<th>3% CO₂ (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>16.7%</td>
<td>16.3%</td>
</tr>
<tr>
<td>2</td>
<td>27.9%</td>
<td>15.4%</td>
</tr>
<tr>
<td>3</td>
<td>6.8%</td>
<td>21.1%</td>
</tr>
<tr>
<td>4</td>
<td>19.2%</td>
<td>19.3%</td>
</tr>
<tr>
<td>5</td>
<td>33.6%</td>
<td>27.5%</td>
</tr>
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<td>6</td>
<td>19.6%</td>
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<td>18.4%</td>
<td>19.2%</td>
</tr>
<tr>
<td>8</td>
<td>23.5%</td>
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</tr>
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<td>9</td>
<td>25.8%</td>
<td>43.6%</td>
</tr>
<tr>
<td>10</td>
<td>7.7%</td>
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</tr>
<tr>
<td>Mean</td>
<td>19.0%</td>
<td>27.4%</td>
</tr>
<tr>
<td>95% CI</td>
<td>14.4%–25.1%</td>
<td>19.7%–34.1%</td>
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4: Effects of increasing inspired CO₂ concentration on exercise-induced asthma (EIA)

Breathing CO₂-enriched air during and after exercise did not prevent EIA. However, the unexpected observation that the post-exercise FEV₁ decreased significantly when CO₂ was discontinued, 10 minutes after the cessation of exercise, suggests that an increased airway CO₂ level does have an effect on the airway. This observation requires explanation.

EIA is thought to be caused by release of mediators from mast cells triggered by airway drying, and this stimulus will be stronger with increased ventilation driven by a high CO₂ level. However, a high CO₂ level will oppose this effect by a direct relaxant action on airway smooth muscle. Our results are consistent with these opposing effects (Box 4). Despite the increased minute ventilation induced by the CO₂, the fall in FEV₁ when breathing air or 3% CO₂ was similar for the first 10 minutes after exercise. This suggests that an increased bronchoconstrictor stimulus from the increased minute ventilation (greater airway drying leading to greater mediator release) was being countered by a direct relaxant effect of the increased CO₂ on airway smooth muscle. After the CO₂ was discontinued, this direct relaxant effect of CO₂ was removed, allowing the increased bronchoconstriction to manifest as a sharp and sustained fall in FEV₁.

A recent randomised controlled trial of BBT in asthmatic patients found that, for the BBT group compared with the control group, there was a significant reduction in minute ventilation and β₂-agonist use and a substantial reduction (49%) in inhaled corticosteroid use in the BBT group at three months. Despite this reduction in medication use among the BBT group, there was no decline in morning peak expiratory flow or FEV₁. End-tidal CO₂ was similar in both groups throughout the study.

Could changes in airway CO₂ explain the apparent improvement in asthma following BBT? This seems unlikely, for several reasons:

- we were unable to show that EIA is reduced in subjects breathing 3% CO₂
- end-tidal CO₂ is not increased in subjects who have undertaken BBT
- breathing 6% CO₂ is required to abolish EIA after exercise challenge. To achieve a similar effect by voluntary hypoventilation would require several minutes of profound hypoventilation or apnoea.

Whatever the mechanisms for the benefits of BBT, they are unlikely to result from direct effects of CO₂ on the airway. Nevertheless, further study of hypoventilation exercises and the effects of CO₂ in asthma are warranted given the results of the randomised controlled trial of BBT and our findings that CO₂ does affect airflow obstruction.

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