Is lactic acidosis a cause of exercise induced hyperventilation at the respiratory compensation point?

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Methods: During a first ramp-like exercise test on a cycle ergometer, RCP (range: 2.51–3.73 l·min⁻¹ oxygen uptake) was determined from gas exchange measurements in five healthy subjects (age 26–42; body mass index (BMI) 20.7–23.9 kg·m⁻²; VO₂peak 51.3–62.1 ml·min⁻¹·kg⁻¹). On the basis of simultaneous determinations of blood pH and base excess, the necessary amount of bicarbonate to completely buffer the metabolic acidosis was calculated. This quantity was administered intravenously in small doses during a second, otherwise identical, exercise test.

Results: In each subject sufficient compensation for the acidosis, that is, a pH value constantly above 7.37, was attained during the second test. A delay but no disappearance of the hyperventilation was present in all participants when compared with the first test. RCP occurred on average at a significantly (p = 0.043) higher oxygen uptake (+0.15 l·min⁻¹) compared with the first test.

Conclusions: For the first time it was directly demonstrated that exercise induced lactic acidosis is causally involved in the hyperventilation which starts at RCP. However, it does not represent the only additional stimulus of ventilation during intense exercise. Muscle afferents and other sensory inputs from exercising muscles are alternative triggering mechanisms.
Exercise induced hyperventilation and lactic acidosis

RCP was determined from the VE-VCO2 plot by two experienced investigators who were blind to the subject under investigation. They determined RCP independently by visually estimating the point of departure from linearity.

To determine the onset of pH decline (defined as >0.02 compared to the resting pH without increasing again), arterialised blood was sampled during exercise from the hyperaemised earlobe at intervals of 2 min starting after the warm up, that is, at minutes 3, 5, 7, 9, etc, as well as 3 min after cessation of exercise (postexercise data not shown). Determinations were carried out using an ion selective electrode (Blutgassystem 288, CIBA Corning, Fernwald, Germany). Heart rate (from the written ECG) and lactate concentrations (enzymatic UV method from whole blood, Greiner, Flacht, Germany) were registered on a minute basis.

Intervention
During the second test, sodium bicarbonate (8.4%) was injected through an antecubital venous catheter to buffer the resulting acidosis at the end of exercise. The total dose was determined using the formula:

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[HCO_3^-] = 24 \text{ mmol} \cdot \text{l}^{-1} \cdot (\text{min } HCO_3^- \text{ standard} \times 0.2 \times \text{ body weight})
\]

where \([HCO_3^-]\) is the total amount of sodium bicarbonate to be injected, min HCO_3^- standard is standard bicarbonate 3 min after cessation of the first ramp test, and 0.2 l'kg^{-1} is the estimated extracellular volume (volume of distribution).

From the pH course in the first test, an appropriate temporal distribution of injection volumes was determined without an interindividually fixed pattern. A pretrial in one of the subjects aided the development of proper injection schedules. In addition to online ECG control, immediate serum potassium measurements (results available approximately 1 min after blood sampling) were carried out simultaneously with pH determinations to ensure the subjects’ medical safety. Sodium determinations were done in parallel, and the highest recorded values in the five subjects were 146.7, 150.0, 151.5, 150.9, and 152.8 mmol.l^{-1}.

Figure 1 Top panels: pH course in all five subjects in test 1 (no bicarbonate) and 2 (-bicarbonate); bottom panels: plot of minute ventilation (VE, y axis) against carbon dioxide output (VCO2, x axis). The arrows indicate the onset of bicarbonate injection.

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respectively (ruling out relevant disturbances in osmolarity due to the injections).

**Statistics**

Raw data (ranges) are demonstrated throughout without averaging procedures because of the low number of subjects. We defined the pH dependent change in minute ventilation in relation to carbon dioxide output as the main outcome variable, that is, the difference between the VE-VCO2 plots of both tests. The only statistical testing procedure for differences between the first and the second trial was a Wilcoxon test conducted between the RCPs (corresponding VO2).

**RESULTS**

All tests were medically uneventful, and no hypokalaemia or ECG abnormalities were recorded. Curves for VO2, heart rate, and lactate were almost identical between trials and demonstrated clearly that there was no interference from training or habituation effects. In each subject sufficient compensation of the acidosis, that is, a constant pH value above 7.37, was achieved during exercise (fig 1).

A delay in but no disappearance of the hyperventilation was present in all participants when injected with bicarbonate. Plots of pH v exercise time and VE v VCO2 are presented for all five subjects (fig 1). In the bicarbonate trial, RCP occurred at a significantly higher oxygen uptake (by 0.15 l min⁻¹; p = 0.043).

**DISCUSSION**

Several studies have demonstrated the presence of a second rise in ventilation during incremental exercise, RCP, which is clearly distinguishable from the ventilatory threshold¹¹⁻¹⁴ and must, hence, be based on different physiological mechanisms.¹⁵⁻¹⁷ There are indications from other studies that RCP occurs in response to an initial decrease in blood pH which represents the beginning of failure of the body’s buffering capacity. However, experimental proof was lacking. The present investigation indicates that blood pH is a relevant stimulus for the hyperventilation starting at RCP. However, other mechanisms must also be partly responsible for the hyperventilation.

To our knowledge, this investigation represents the first attempt to elucidate the physiological basis of RCP by directly, that is, intravenously, manipulating blood pH in human beings. Due to the invasiveness of the procedures, only a small number of subjects were recruited. However, their response to the bicarbonate intervention was uniform. Therefore, under the constraints of the designed it could be demonstrated that a decline in blood pH due to insufficient buffering of exercise induced lactic acidosis represents an important stimulus for hyperventilation during intense exercise. Apart from the bicarbonate injection, all other circumstances were held constant between the two incremental tests which implies that the observed changes between the tests have to be attributed to the different pH course. This is even more likely because of the short biological half life of sodium bicarbonate itself which rules out enduring bicarbonate effects on various receptors.

It became evident that even under conditions of maintained resting pH during incremental exercise all subjects showed a delayed (instead of an absent) hyperventilatory response compared to the pretest. As pH was held constant, there must be additional factors that stimulate ventilation under high intensity exercise. Candidates for this function are local muscle mechanoreceptors or metaboreceptors,¹⁰⁻¹¹ pain perception,¹² neuronal impulses of other origin,¹³ and serum potassium.¹⁴ However, acidosis due to failure of lactate buffering seems to be a major determinant for exercise hyperventilation. This is in accordance with results from Schneider and Berwick¹⁵ who observed an increased ventilatory response (despite a decreased VCO2) in relation to VO2 during an incremental exercise test which was preceded by 60 s of maximal cycling. This short bout of intense exercise presumably led to decreased pH values throughout the subsequent incremental test when compared to a reference test which was conducted without prior exhaustive exercise. However, a close coupling between VE and VCO2 was maintained during submaximal stages but the VE/VCO2 ratio switched to a higher level.

In conclusion, for the first time it was directly demonstrated that exercise induced metabolic acidosis is causally involved in the onset of hyperventilation at RCP. However, it is probably not the only additional stimulus of ventilation during intense exercise. Muscle afferents and other sensory inputs from exercising muscles are alternative triggering mechanisms.

**What is already known?**

There is a certain workload during incremental exercise at which the onset of hyperventilation occurs. This is called the respiratory compensation point (RCP). There are theoretical indications that the failure of bicarbonate buffering and the consequent fall in blood pH lead to the occurrence of RCP.

**What this study adds**

This study demonstrates that RCP is delayed when exercise induced blood acidosis is prevented by intravenously injecting bicarbonate. This is the first conclusive experimental evidence that changes in blood pH are involved in the initiation of RCP. However, other physiological stimuli for hyperventilation seem to be present.

**REFERENCES**


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