Kinetics of Excess CO₂ Output during and after Intensive Exercise

Takahiro YUNOKI, Masahiro HORIUCHI, and Tokuo YANO

Laboratory of Human Movement Sciences, Faculty of Education, Hokkaido University, Kita-ku, Sapporo, 060-0811 Japan

Abstract: In order to clarify the kinetics of excess CO₂ output during and after intensive exercise, six male subjects were each instructed to perform 40-, 60- and 80-s cycle ergometer exercises (282±9 W, 90 rpm). Ventilation and gas exchange parameters were recorded breath-by-breath, and lactate concentration (La) was repeatedly measured with blood samples from a finger tip. The increase in La from the resting value to peak value and the duration of exercise showed a significant linear relationship (r=0.91, p<0.01) passing through zero, indicating that lactic acid was produced at a constant rate in working muscles from the beginning of exercise. However, in contrast to this increase in La, excess $\dot{V}CO_2$, defined as the difference between $\dot{V}CO_2$ and $\dot{V}O_2$, showed a temporary negative value after the start of exercise. Subsequently, excess $\dot{V}CO_2$ became positive, reaching a peak at 60 s post-exercise, and then decreased down to zero at about 9 min after the end of the 80-s exercise. End-tidal CO₂ rose above the pre-exercise level during exercise and at about 3 min post-exercise, and thereafter remained below the pre-exercise level. Excess CO₂, calculated by the sum of excess $\dot{V}CO_2$ from the start of exercise to the 10th min after the end of exercise, was significantly correlated with the increase in La from resting to 10 min post-exercise ($r=0.88$, $p<0.01$). These results suggest that although excessive CO₂ output (excess CO₂) in response to intensive exercise is related to the increase in lactic acid, the time course of excessive CO₂ output (excess $\dot{V}CO_2$) is delayed, relative to the production of lactic acid, and is affected by hyperventilation. [Japanese Journal of Physiology, 49, 139–144, 1999]

Key words: intensive exercise, lactate, excessive CO₂ output, hyperventilation.

It has been reported that as part of the CO₂ produced at the onset of constant load exercise is stored in the body (CO₂ stores), the respiratory exchange ratio (RER) temporarily decreases [1, 2]. This change in CO₂ stores during exercise can be estimated from the change in mixed venous CO₂ pressure ($Pv_{CO_2}$), because it has been theoretically and experimentally shown that change in CO₂ stores brings about a change in the level of $Pv_{CO_2}$ [3–5]. Actually, $Pv_{CO_2}$ during constant load exercise is reported to increase for the first 2–3 min and then maintain a constant level [6–8]. Furthermore, it has been confirmed that there is a correspondence between the change in CO₂ stores, estimated from the change in RER, and the change in $Pv_{CO_2}$ at that time [8]. Thus, CO₂ output during constant load exercise is thought to be affected by a change in the CO₂ stores accompanied by a change in CO₂ pressure ($PCO_2$).

In constant load exercise above the anaerobic threshold (AT), the response of $O_2$ uptake to the load is delayed compared with that below the AT, but the kinetics of CO₂ output indicate no clear change [2, 9]. This constancy in CO₂ output kinetics is considered to be due to the addition of CO₂ produced by buffering lactic acid to CO₂ aerobically produced in the early stage of exercise [9]. Thereafter, Stringer et al. [10] carried out detailed measurements of the arterial acid–base balance relative to changes in lactic acid

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Correspondence should be addressed to: Takahiro Yunoki, Laboratory of Human Movement Sciences, Faculty of Education, Hokkaido University, Nishi 7, Kita 11, Sapporo, 060-0811 Japan. Tel: +81-11-706-3422, Fax: +81-11-706-5433, E-mail: yunoki@edu.hokudai.ac.jp
during and after 6-min constant load exercises (two intensities between a level above AT and below maximal O₂ uptake).

During relatively heavy constant load exercise, it is thought that lactate concentration in the blood is not always identical with that in the working muscle due to the influence of lactic acid diffusion, and therefore examination of the relevance of lactate and HCO₃⁻ in the working muscle is thought to be necessary. However, previous studies [11–14] have primarily been concerned with measurement during recovery after exercise, since the duration of exercise in previous studies has been short. Furthermore, although they serve as a reference, these studies on acid–base balance have not directly examined the kinetics of CO₂ output, and there has been very little quantitative investigation of intensive exercise [15]. Additionally, it is unthinkable that all of the CO₂ produced by buffering lactic acid during exercise would be expired during intensive exercise if the duration of exercise is short. In this study, therefore, in order to clarify the kinetics of excess CO₂ output in response to intensive exercise, we measured pulmonary gas exchange and blood lactate levels during and after intensive exercise, and we examined the correlation between these values.

METHODS

1. Experimental procedures. The subjects were six active males who did not train regularly. Their mean (SD) age, height, and weight were 23.0 (1.9) years, 170.5 (6.1) cm, and 66.1 (2.9) kg, respectively. Each subject was informed of the purpose of the study, the experimental procedure, and the risks associated with the experiments before consent was obtained. Furthermore, they were instructed to refrain from heavy exercise on the day before the experiment, not to take a meal within 3 h before the experiment, and to remain in a resting state for 1 h before the start of the experiment.

Initially, each subject performed an incremental exercise test in order to estimate maximal O₂ uptake (VO₂max) using a cycle ergometer controlled by an eddy current (Ergometer 232C: Combi) at 60 rpm. Each subject exercised for 4 min at unloaded work after a 5-min rest, and the work was then increased by a ramp pattern (20 W/min) until exhaustion.

On separate days after the incremental exercise test, each subject performed a cycling exercise with maximal effort for 30 s at a load (kp) corresponding to 7.5% × body weight (Wingate test) [16] using a cycle ergometer controlled by an eddy current (Powermax-VII: Combi). During the exercise, the power output was measured every 5 s from an imposed load and cycling rate (rpm), and the mean power output (mean power) for 30 s of exercise was obtained. A few days later, each subject, after resting on the cycle ergometer for 5 min, exercised at a constant load for 80 s at 90 rpm (282 ± 9 W), corresponding to 50% of the mean power exerted in the Wingate test. After the end of this exercise, the subjects sat on a chair in a resting state for 30 min. In order to assess the process of change in blood lactate concentration during 80-s exercise and the change in kinetics of CO₂ output with different durations of exercise, 40- and 60-s exercises at the same load were also performed on separate days using the same protocol (intensive exercise test).

Data on ventilation (VE), oxygen uptake (VO₂), carbon dioxide output (VCO₂), end-tidal carbon dioxide (EtCO₂) were obtained breath-by-breath using a respiratory gas analyzer (Aeromonitor AE-280S, Minato) during intensive and incremental exercise tests. These data were averaged over a 20-s period. O₂ concentration and CO₂ concentration were measured by a zirconium sensor and infrared absorption analyzer, respectively. These gas analyzers were calibrated by known standard gases. PetCO₂ was measured by a hot-wire flow meter, and the flow meter was calibrated by flowing room air at a constant rate (2 liters per 2 s) using a 2-l calibration syringe. Blood lactate concentration (La) was measured by an automatic analyzer (1500 sport, YSI) using 25 μL of blood sampled from a finger tip with a capillary tube at rest before exercise, immediately after the end of exercise, and at 5, 10, 20 and 30 min post-exercise. The analyzer was calibrated with a standard liquid (5 mM of lactate).

According to the method of Cerretelli and Di Prampero [15], excessive CO₂ output per unit of time (excess VCO₂) was calculated by subtracting VO₂ from VCO₂ during intensive exercise tests. The total of excessive CO₂ output (excess CO₂) was calculated by the addition of values of excess VCO₂ from the start of exercise until 10 min post-exercise.

2. Statistical analysis. Differences in variables obtained in the three intensive exercise tests were analyzed using analysis of variance (ANOVA). A post hoc test (Turkey’s test) was then conducted to assess the differences. The strength of the relationship between dependent and independent variables was expressed by a single correlation coefficient of Pearson. The level of significance was p<0.05. Results are expressed as mean±standard deviation.
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RESULTS

Maximal O₂ uptake (\(\dot{V}O₂_{\text{max}}\)) obtained in the incremental exercise test was 2.7±0.4 l/min. Maximal and mean powers during the Wingate test were 726±54 and 564±18 W, respectively. The powers exerted in the 40-, 60- and 80-s intensive exercise tests were similar. The power exerted in the 80-s intensive exercise test corresponded to 108±11.5% of the power (268±33.5 W) at exhaustion in the incremental exercise test.

The time courses of excess \(\dot{V}CO₂\), \(ET_{CO₂}\) and \(\dot{VE}/\dot{V}CO₂\) in the 80-s intensive exercise test are shown in Fig. 1. The plots indicate mean values per 20 s for all subjects. Excess \(\dot{V}CO₂\) showed a peak negative value at 40 s after the start of exercise and then became positive. This positive value showed a peak at 60 s after the end of exercise and then dropped to zero at about 9 min post-exercise. \(ET_{CO₂}\) increased up to 20 s after the end of exercise and then returned to its pre-exercise value at about 3 min post-exercise. \(ET_{CO₂}\) continued to decrease gradually up to about 5 min post-exercise and then became stable over the whole recovery range. The changes in \(\dot{VE}/\dot{V}CO₂\) and \(ET_{CO₂}\) showed a relationship with the reflected image. During 40- and 60-s intensive exercise tests, excess \(\dot{V}CO₂\) showed a temporary negative value at 40 s after the start of exercises. Subsequently, excess \(\dot{V}CO₂\) became positive, reaching a peak at about 60–80 s post-exercise, and then dropped to zero at about 7 and 8 min after the end of the 40- and 60-s exercises, respectively. The changes in \(ET_{CO₂}\) and \(\dot{VE}/\dot{V}CO₂\) during the 40- and 60-s intensive exercise tests were similar to those during the 80-s test.

Figure 2 shows the changes in \(La\) in the intensive exercise tests. The plots indicate mean values for all subjects. The values immediately after the end of the

**Fig. 1.** Excess \(\dot{V}CO₂\), \(ET_{CO₂}\), and \(\dot{VE}/\dot{V}CO₂\) at rest and during and after 80-s intensive exercise. Vertical bars represent the exercise period. Values are means±SD.

**Fig. 2.** Changes in blood lactate concentration at rest and during recovery of 40 (■), 60 (△) and 80 s (○) of intensive exercises. Values are means±SD.
40-, 60- and 80-s exercises were $3.49\pm0.82$, $5.30\pm0.38$ and $6.75\pm1.29$ mM, respectively. Peak La values, which were observed at 5 min post-exercise, were $4.06\pm0.42$, $6.00\pm0.62$ and $7.74\pm0.85$ mM, respectively. The increases in La from immediately after the end of exercises to 5 min postexercise were $0.58\pm0.85$, $0.70\pm0.79$ and $0.99\pm1.07$ mM, respectively. Figure 3 shows the relationship between the maximal increase in La after the end of intensive exercise (difference between La at rest and peak La: $\Delta$La peak) and the duration of exercise. There was a significant correlation between the duration of exercise and $\Delta$La peak ($r=0.91$, $p<0.01$). Extrapolating this regression line to zero of $\Delta$La peak, the estimated time was around zero.

The total excessive CO$_2$ output (excess CO$_2$), which was the sum of the values of excess VCO$_2$ from the start of exercise to 10 min post-exercise, and $\Delta$La (difference between La at rest and at 10 min post-exercise) were calculated. As shown in Fig. 4, excess CO$_2$ per body weight (excess CO$_2$/kg) obtained in the intensive exercise tests was significantly related to $\Delta$La ($r=0.88$, $p<0.01$). On the other hand, the decreases in $ET_{CO_2}$ (%) at 10 min post-exercise (differences between averaged $ET_{CO_2}$ during 4–5 min at rest and 9–10 min post-exercise) in the 40-, 60- and 80-s exercise tests were $-0.51\pm0.20$, $-0.70\pm0.34$ and $-0.57\pm0.29$%, respectively. These differences were not significant.

**Discussion**

In this study, 40-, 60- and 80-s exercises were performed in order to clarify the kinetics of excess CO$_2$ output during and after intensive exercise. The following results were obtained: (1) values of peak La obtained after the end of exercise increased linearly accompanying an increase in the duration of exercise; (2) excess VCO$_2$ showed a temporary negative value during exercise, then became positive, reaching a peak at 60's post-exercise, and subsequently decreased down to zero at about 9 min post-exercise in the 80-s exercise test; and (3) excess CO$_2$ per body weight (excess CO$_2$/kg) increased in proportion to the increase in La ($\Delta$La).

As lactic acid formed in the working muscles takes time to become uniformly distributed throughout the whole body, the peak value of La is observed at a few minutes after the end of exercise. Although this uniform value seems to indicate a difference between the amount effused out of working muscle and the amount diffused to other tissue and consumed, as the removal of lactic acid is relatively slow, peak La after the end of exercise is considered to reflect the magnitude of lactic acid produced in the working muscles. When these values were plotted as a function of duration of exercise (Fig. 3), it was inferred that lactic acid had been produced at a constant rate in the working muscles from the beginning of exercise.

As the lactic acid produced in working muscles is fully ionized, an equimolar amount of hydrogen ions (H$^+$) is dissociated. This dissociated H$^+$ is then absorbed by the physicochemical action of muscle protein and the breakdown of creatine phosphate, and it is buffered by a leftward shift in the equation of the bicarbonate buffer system [17]:

$$CO_2 + H_2O \rightleftharpoons H^+ + HCO_3^-. \quad (1)$$

However, if the CO$_2$ formed due to this buffering is
not fully eliminated, P\textsubscript{CO\textsubscript{2}} increases. Similarly, the metabolically produced CO\textsubscript{2} is not temporarily removed from the body, CO\textsubscript{2} is stored in the body, resulting in an increase in P\textsubscript{CO\textsubscript{2}}. Actually, it has been demonstrated that the femoral venous P\textsubscript{CO\textsubscript{2}} increased dramatically with maximal cycling exercise [11, 18].

The increased tissue P\textsubscript{CO\textsubscript{2}} induces an increase in P\textsubscript{aCO\textsubscript{2}} and consequently an increase in CO\textsubscript{2} transport from the tissue to the lung. In this case, if ventilation fitting for the CO\textsubscript{2} transport is conducted and CO\textsubscript{2} is eliminated, it is thought that arterial CO\textsubscript{2} pressure (P\textsubscript{aCO\textsubscript{2}}) does not change. Based on the results of the kinetics of P\textsubscript{E}/P\textsubscript{CO\textsubscript{2}} (Fig. 1), elimination of CO\textsubscript{2} by the lung is considered to have been insufficient during exercise. As a result, $\Delta$T\textsubscript{CO\textsubscript{2}} increased. These increases in P\textsubscript{aCO\textsubscript{2}} and $\Delta$T\textsubscript{CO\textsubscript{2}} induce a rightward shift in Eq. 1. Therefore, the increase in HCO\textsubscript{3}\(^{-}\) is masked, and consequently excess P\textsubscript{CO\textsubscript{2}} would have shown a temporary negative value.

After an initial increase, $\Delta$T\textsubscript{CO\textsubscript{2}} showed a decreasing phase. This is because, as shown in the kinetics of P\textsubscript{E}/P\textsubscript{CO\textsubscript{2}}, the amount of CO\textsubscript{2} reduced by ventilation is larger than that transported to the lung. This decrease in $\Delta$T\textsubscript{CO\textsubscript{2}} decreases the venoarterial P\textsubscript{CO\textsubscript{2}} difference and could promote the elimination of CO\textsubscript{2} from the tissues. This decrease in tissue P\textsubscript{CO\textsubscript{2}} simultaneously induces a decrease in venous P\textsubscript{CO\textsubscript{2}}. In that case, Eq. 1 shifts leftward, and the excess P\textsubscript{CO\textsubscript{2}} that had been masked during the period of increase in P\textsubscript{CO\textsubscript{2}} could appear during the period of decrease in P\textsubscript{CO\textsubscript{2}}. Thereafter, $\Delta$T\textsubscript{CO\textsubscript{2}} fell below the pre-exercise level. This is thought to be due to excessive elimination of CO\textsubscript{2} by continuous hyperventilation. However, as the venous P\textsubscript{CO\textsubscript{2}} decreases accompanying the decline in CO\textsubscript{2} stores in the tissues, elimination of CO\textsubscript{2} from the tissues soon stops.

There are other factors that are related to the delay of excess CO\textsubscript{2} output from the production of lactic acid. The first is related to the resynthesis of creatine phosphate. The breakdown of creatine phosphate involves absorption of H\(^{+}\) [17]. Therefore, the influence of the increase in H\(^{+}\) accompanying the increase in lactic acid on the excess CO\textsubscript{2} output is inhibited during exercise. However, as the reverse reaction occurs after the end of exercise, H\(^{+}\) increases even if lactic acid does not increase. Consequently, in Eq. 1, the HCO\textsubscript{3}\(^{-}\) decrement due to lactic acid production decreases during exercise and then the volume corresponding to the diminished amount could appear after the end of exercise.

Another factor is diffusion of lactic acid. The bicarbonate buffer system is more dominant in extracellular fluid than in intracellular fluid. If lactic acid in the muscle flows into the extracellular fluid, the ratio of the amount of lactic acid buffered by the bicarbonate system becomes high. In this study, La increased by 0.99±1.07 mM from the end point to 5 min after the end of the 80-s intensive exercise. Furthermore, as it has been demonstrated that shifts of strong ions, including those of lactate, between compartments of body fluids induce an increase in blood H\(^{+}\) concentration [11, 12, 18, 19–21], these factors could be related to the delay of excess CO\textsubscript{2} output.

Excess CO\textsubscript{2}, calculated as the total of excess P\textsubscript{CO\textsubscript{2}} was significantly related to $\Delta$La. As mentioned above, excess P\textsubscript{CO\textsubscript{2}} is affected by changes in H\(^{+}\) accompanying the diffusion of lactic acid into the whole body and the reaction of creatine phosphate and change in P\textsubscript{CO\textsubscript{2}}. Therefore, these effects must be considered to understand the effect of only diffused lactic acid on excess CO\textsubscript{2}. However, as lactic acid is diffused into the whole body at about 5 min after the end of exercise, the excess CO\textsubscript{2} obtained is thought to reflect the effect of lactic acid equilibrating to the whole body. As creatine phosphate decreases during exercise and recovers at 2–6 min after the end of exercise [22, 23], the effect of creatine phosphate on the excess CO\textsubscript{2} could be counteracted. On the other hand, although $\Delta$T\textsubscript{CO\textsubscript{2}} increases during exercise and recovers after the end of exercise, the recovery is below the resting level. Therefore, excess CO\textsubscript{2} obtained in the present study could include the amount affected by the change in P\textsubscript{CO\textsubscript{2}}.

These results suggest that although excessive CO\textsubscript{2} output (excess CO\textsubscript{2}) in response to intensive exercise is related to the increase in lactic acid, the time course of the excessive CO\textsubscript{2} output (excess P\textsubscript{CO\textsubscript{2}}) is delayed, relative to the production of lactic acid, and is affected by hyperventilation.

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