Kinetics of Excess CO_2 Output during and after Intensive Exercise

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Abstract: In order to clarify the kinetics of excess CO_2 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 CO_2 rose above the pre-exercise level during exercise and at about 3 min post-exercise, and thereafter remained below the pre-exercise level. Excess CO_2, 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 CO_2 output (excess CO_2) in response to intensive exercise is related to the increase in lactic acid, the time course of excessive CO_2 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]

It has been reported that as part of the CO_2 produced at the onset of constant load exercise is stored in the body (CO_2 stores), the respiratory exchange ratio (RER) temporarily decreases [1, 2]. This change in CO_2 stores during exercise can be estimated from the change in mixed venous CO_2 pressure ($P\bar{v}_{CO_2}$), because it has been theoretically and experimentally shown that change in CO_2 stores brings about a change in the level of $P\bar{v}_{CO_2}$ [3–5]. Actually, $P\bar{v}_{CO_2}$ 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 CO_2 stores, estimated from the change in RER, and the change in

$P\bar{v}_{CO_2}$ at that time [8]. Thus, CO_2 output during constant load exercise is thought to be affected by a change in the CO_2 stores accompanied by a change in CO_2 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 CO_2 output indicate no clear change [2, 9]. This constancy in CO_2 output kinetics is considered to be due to the addition of CO_2 produced by buffering lactic acid to CO_2 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

during and after 6-min constant load exercises (two intensities between a level above AT and below maximal O_2 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 HCO_3^- 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 CO_2 output, and there has been very little quantitative investigation of intensive exercise [15]. Additionally, it is unthinkable that all of the CO_2 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 CO_2 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 O_2 uptake ($\dot{V}O_{2\,max}$) 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 CO_2 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 ($\dot{V}E$), oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$) and end-tidal carbon dioxide (ET_{CO_2}) 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. O_2 concentration and CO_2 concentration were measured by a zirconium sensor and infrared absorption analyzer, respectively. These gas analyzers were calibrated by known standard gases. $\dot{V}E$ was measured by a hot-wire flow meter, and the flow meter was calibrated by flowing room air at a constant rate (2 l/about 1 s) using a 2-l calibrator 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 CO_2 output per unit of time (excess $\dot{V}CO_2$) was calculated by subtracting $\dot{V}O_2$ from $\dot{V}CO_2$ during intensive exercise tests. The total of excessive CO_2 output (excess CO_2) was calculated by the addition of values of excess $\dot{V}CO_2$ 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.

RESULTS

Maximal O_2 uptake ($\dot{V}O_{2\,max}$) obtained in the incremental exercise test was 2.7 ± 0.4 l/min. Maximal and mean powers during the Wingate test were 726 ± 54
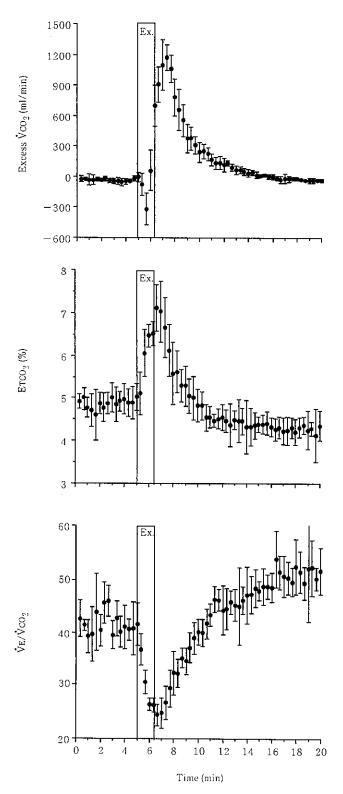

and 564 ± 18 W, respectively. The powers exerted in the 40-, 60- and 80-s intensive exercise tests were similar. The power exerted in the 80-s intensive exercise test corresponded to $108\pm11.5\%$ of the power (268 ± 33.5 W) at exhaustion in the incremental exercise test.

The time courses of excess $\dot{V}CO_2$, ET_{CO_2}, and $\dot{V}E/\dot{V}CO_2$ in the 80-s intensive exercise test are shown in Fig. 1. The plots indicate mean values per 20 s for all subjects. Excess $\dot{V}CO_2$ 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_{CO_2} 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_{CO_2} continued to decrease gradually up to about 5 min postexercise and then became stable over the whole recovery range. The changes in $\dot{V}E/\dot{V}CO_2$ and ET_{CO_2} showed a relationship with the reflected image. During 40- and 60-s intensive exercise tests, excess $\dot{V}CO_2$ showed a temporary negative value at 40 s after the start of exercises. Subsequently, excess $\dot{V}CO_2$ 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_{CO_2} and $\dot{V}E/\dot{V}CO_2$ 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
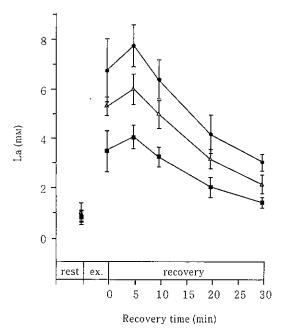

Fig. 1. Excess $\dot{V}CO_2$, ET_{CO_2}, and $\dot{V}E/\dot{V}CO_2$ at rest and during and after 80-s intensive exercise. Vertical bars represent the exercise period. Values are means±SD.

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.
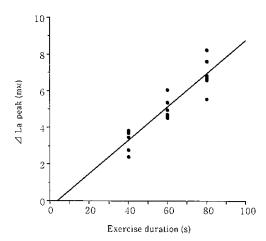
Fig. 3. Relationship between duration of exercise and increase in blood lactate concentrations (difference between blood lactate concentrations at rest and peak) in three intensive exercises.

Fig. 4. Relationship between excess CO_2 per body weight and increase in blood lactate concentration (difference between blood lactate concentrations at rest and at the 10th min after the end of exercise) in intensive exercises.

40-, 60- and 80-s exercises were 3.49 ± 0.82, 5.30 ± 0.38 and 6.75 ± 1.29 mM, respectively. Peak La values, which were observed at 5 min post-exercise, were 4.06 ± 0.47, 6.00 ± 0.62 and 7.74 ± 0.85 mM, respectively. The increases in La from immediately after the end of exercises to 5 min postexercise were 0.58 ± 0.85, 0.70 ± 0.79 and 0.99 ± 1.07 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: ΔLa peak) and the duration of exercise. There was a significant correlation between the duration of exercise and ΔLa peak ($r=0.91$, $p<0.01$). Extrapolating this regression line to zero of ΔLa 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 $\dot{V}CO_2$ from the start of exercise to 10 min post-exercise, and ΔLa (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 ΔLa ($r=0.88$, $p<0.01$). 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 ± 0.20, -0.70 ± 0.34 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 ob-
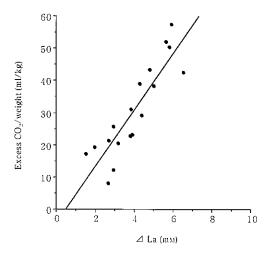
tained after the end of exercise increased linearly accompanying an increase in the duration of exercise; (2) excess $\dot{V}CO_2$ showed a temporary negative value during exercise, then became positive, reaching a peak at 60 s post-exercise, and subsequently decreased down to zero at about 9 min post-exercise 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 (ΔLa).

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]:

$$CO_2+H_2O \rightleftarrows H^+ +HCO_3^-. \qquad (1)$$

However, if the CO_2 formed due to this buffering is

not fully eliminated, P_{CO_2} increases. Similarly, if metabolically produced CO_2 is not temporarily removed from the body, CO_2 is stored in the body, resulting in an increase in P_{CO_2}. Actually, it has been demonstrated that the femoral venous P_{CO_2} increased dramatically with maximal cycling exercise [11, 18].

The increased tissue P_{CO_2} induces an increase in $P\bar{v}_{CO_2}$ and consequently an increase in CO_2 transport from the tissue to the lung. In this case, if ventilation fitting for the CO_2 transport is conducted and CO_2 is eliminated, it is thought that arterial CO_2 pressure (Pa_{CO_2}) does not change. Based on the results of the kinetics of $\dot{V}E/\dot{V}CO_2$ (Fig. 1), elimination of CO_2 by the lung is considered to have been insufficient during exercise. As a result, ET_{CO_2} increased. These increases in $P\bar{v}_{CO_2}$ and ET_{CO_2} induce a rightward shift in Eq. 1. Therefore, the decrease in HCO_3^- is masked, and consequently excess $\dot{V}CO_2$ would have shown a temporary negative value.

After an initial increase, ET_{CO_2} showed a decreasing phase. This is because, as shown in the kinetics of $\dot{V}E/\dot{V}CO_2$, the amount of CO_2 eliminated by ventilation is larger than that transported to the lung. This decrease in ET_{CO_2} increases the venoarterial PCO_2 difference and could promote the elimination of CO_2 from the tissues. This decrease in tissue PCO_2 simultaneously induces a decrease in venous PCO_2. In that case, Eq. 1 shifts leftward, and the excess $\dot{V}CO_2$ that had been masked during the period of increase in PCO_2 could appear during the period of decrease in PCO_2. Thereafter, ET_{CO_2} fell below the pre-exercise level. This is thought to be due to excessive elimination of CO_2 by continuous hyperventilation. However, as the venous PCO_2 decreases accompanying the decline in CO_2 stores in the tissues, elimination of CO_2 from the tissues soon stops.

There are other factors that are related to the delay of excess CO_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_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_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_2 output.

Excess CO_2, calculated as the total of excess $\dot{V}CO_2$, was significantly related to ΔLa. As mentioned above, excess $\dot{V}CO_2$ 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 PCO_2. Therefore, these effects must be considered to understand the effect of only diffused lactic acid on excess CO_2. However, as lactic acid is diffused into the whole body at about 5 min after the end of exercise, the excess CO_2 obtained is thought to reflect the effect of lactic acid equipoising 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_2 could be counteracted. On the other hand, although ET_{CO_2} increases during exercise and recovers after the end of exercise, the recovery is below the resting level. Therefore, excess CO_2 obtained in the present study could include the amount affected by the change in PCO_2.

These results suggest that although excessive CO_2 output (excess CO_2) in response to intensive exercise is related to the increase in lactic acid, the time course of the excessive CO_2 output (excess $\dot{V}CO_2$) is delayed, relative to the production of lactic acid, and is affected by hyperventilation.

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