Effect of acute sodium bicarbonate ingestion on excessive CO_2 output during incremental exercise

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Summary. The effect of bicarbonate ingestion on total excess volume of CO_2 output (CO_2 excess), due to bicarbonate buffering of lactic acid in exercise, was studied in eight healthy male volunteers during incremental exercise on a cycle ergometer performed after ingestion (0.3 g · kg $^{-1}$ body mass) of $CaCO_3$ (control) and $NaHCO_3$ (alkalosis). The resting arterialized venous blood pH ($P< 0.05$) and bicarbonate concentration ($[HCO_3^-]_b$) ($P< 0.01$) were significantly higher in acute metabolic alkalosis (AMA) (pH; 7.44±0.03, $[HCO_3^-]_b$; 29.4±1.5 mmol· l^{-1}) than in control (pH; 7.39±0.03, $[HCO_3^-]_b$; 25.5±1.0 mmol· l^{-1}). The blood lactate concentrations ($[La^-]_b$) during exercise below the anaerobic threshold (AT) were not affected by AMA, while significantly higher La^- levels at exhaustion (12.29±1.87 vs 9.57±2.14 mmol· l $^{-1}$, $P< 0.05$) and at 3 min after exercise (14.41±1.75 vs 12.26±1.40 mmol· l $^{-1}$, $P<0.05$) were found in AMA compared with control. The CO_2 excess increased significantly from control (3,177±506 ml) to AMA (3,897±381 ml) ($P< 0.05$). The CO_2 excess per body mass (CO_2 excess· mass^{-1}; ml· kg^{-1}) was found to be significantly correlated with both increase of $[La^-]_b$ from rest to 3 min after exercise ($\Delta [La^-]_b$) ($r= 0.926$, $P< 0.001$) and decrease of $[HCO_3^-]_b$ from rest to 3 min after exercise ($\Delta [HCO_3^-]_b$) ($r=0.872$, $P< 0.001$), indicating that CO_2 excess· mass^{-1} could increase linearly with the changes in both $\Delta [La^-]_b$ and $[HCO_3^-]_b$.
As a consequence, CO_2 excess· mass^{-1} per unit increase of $[La^-]_b$ (CO_2 excess· mass^{-1}· $\Delta [La^-]_b$) was similar for the two conditions. The present results suggest that the relationship between CO_2 excess (ml· kg^{-1}) and blood lactate accumulation could be unaffected by acute metabolic alkalosis, due to the same relative contribution of bicarbonate buffering of lactic acid as control.

Key words: CO_2 excess - acute metabolic alkalosis - bicarbonate - blood pH - blood lactate accumulation

INTRODUCTION

During a progressive incremental exercise below the anaerobic threshold (AT), the changes of expired carbon dioxide ($\dot{V}CO_2$) are assumed to be nearly equal to the exercise-induced metabolic changes in muscles, whereas above the AT, $\dot{V}CO_2$ consists not only of aerobically produced $\dot{V}CO_2$, but also of the excess carbon dioxide output (excess $\dot{V}CO_2$) derived from bicarbonate buffering of lactic acid (Beaver and Wasserman 1991; Hirakoba et al. 1990, 1992; Jones 1980; Yano 1987).

It has been shown that the relationship between the integrated excess $\dot{V}CO_2$ with respect to time from the AT to the end of a progressive incremental exercise (defined as CO_2 excess) and blood lactate accumulation varies among subjects due to different states of fitness (Hirakoba et al. 1990, 1992) and to specificity of the training such as aerobic and anaerobic training (Yano 1987). In addition, it has been indicated that the relationship between CO_2 excess and blood lactate accumulation during incremental exercise above the AT are determined by the rates of buffering in bicarbonate and nonbicarbonate systems for lactic acid (Yano 1987). Hence, it may be expected that ingestion of bicarbonate would result in greater CO_2 excess, probably owing to the larger capacity of the bicarbonate system to buffer the hydrogen ion (H^+) dissociated from lactic acid. The purpose of the present study, therefore, was to investigate the effect of acute metabolic alkalosis (AMA) due to ingestion of sodium bicarbonate ($NaHCO_3$) on the relationship between CO_2 excess and blood lactate accumulation.

METHODS

Subjects. Eight healthy male volunteers, who were physical education students, participated in this study. The average values (±SD) ~~in~~ of their age, height, body mass, and maximal oxygen uptake per body mass ($\dot{V}O_{2max}$) were 20.1±1.2 yrs, 170.4 ±4.7 cm, 57.0±5.5 kg, and 58.3±2.8 ml· kg $^{-1}$ · min^{-1}, respectively. All the subjects gave their informed consent after having been explained the procedures and potential risks of the experiments.

Protocol. The experiments were carried out on two separate occasions within a week. The subjects were asked to refrain from drinking alcohol and doing any intense exercise in the 24 h prior to the experiment, but allowed a light meal. The subjects reported to the laboratory in the late morning or early afternoon at least 3 h before testing, and then ingested gelatin capsules ~~including~~ containing calcium carbonate ($CaCO_3$; control) or sodium bicarbonate ($NaHCO_3$; alkalosis), amounting to a total dose of 0.3 g · kg^{-1} body mass, according to Jones et al. (1977). The last capsule was taken 1 h before the onset of exercise testing. The order of administration was randomized and the experiment was performed in a double blind manner, with at least three days interval between the two conditions.

During the period in which subjects ingested each ~~drug~~ salt a 21-gauge butterfly needle was inserted into a superficial dorsal hand vein for blood sampling and then the hand was placed in a plastic box heated (~~about~~ 42-45°C) by a hair-dryer, in order to "arterialize" the venous blood (Forster et al. 1972). The hand for blood sampling was kept resting in the box fixed to a handle of the ergometer until the collection of the last blood sample. Arterialization of the venous blood was verified by achieving blood oxygen partial pressure (PO_2) $\geq$ 70 mmHg (Forster et al. 1972; Wilkes et al. 1983); the averages of PO_2 at rest in control and AMA were 78.9 and 74.9 mmHg, respectively, with no significant difference between the two acid-base conditions. The resting blood samples were taken 1 h following ingestion of the last capsule.

An incremental exercise test, which has been described previously (Hirakoba et al. 1992), was carried out under both control and alkalotic conditions. Briefly,

after 4 min unloaded pedaling, each subject performed on a cycle ergometer (Monark-Crescent AB, Varverg, Sweden), a 1-min incremental exercise test with an increase of work rate of 30 W every minute until each subject's exhaustion.

During the tests, expired gas was collected in an automatic gas analyzer (Aerobics Processor 391, San-ei Instruments, Tokyo, Japan) containing a small mixing chamber from a Hans Rudolph two-way mask through a low-resistance low-dead space intake hose. Minute ventilation ($\dot{V}_E$, l· min^{-1}), oxygen uptake ($\dot{V}O_2$, ml· min^{-1}) and carbon dioxide output ($\dot{V}CO_2$, ml· min^{-1}) were calculated with a microcomputer-based system. This gas analysis system uses a heated wire flowmeter (Minato Medical Science, Osaka, Japan) to measure expired flow, an infrared absorption analyzer to measure CO_2, and a polarographic method for measuring O_2. The flowmeter was calibrated by a 2-liter calibrator syringe and the gas analyzer by known standard gases immediately before and after each test.

Blood samples for lactate analysis were collected at rest, every minute during exercise from the 4th min to exhaustion, and at 3 min after exercise. After the blood was deproteinized in cold perchloric acid, blood lactate concentration ($[La^-]_b$, mmol· l^{-1}) was measured using an enzymatic method (Hadjivassiliou and Pieder 1968). In addition, blood samples for blood gases were anaerobically taken in a heparinizied syringe at rest and 3 min after exercise and were kept on ice. Blood pH and carbon dioxide partial pressure (PCO_2, mmHg) were measured by using a pH/blood gas analyzer (Model 170, Corning) within half an hour after blood sampling. Blood bicarbonate concentration ($[HCO_3^-]_b$, mmol· l^{-1}) was calculated according to the Henderson-Hasselbalch equation.

CO_2 excess (ml) was calculated according to the method previously described by Yano (1987) and Hirakoba et al. (1992).

CO_2 excess $= \int$ excess $\dot{V}CO_2 = \int(\dot{V}CO_{2,\,measured} - \dot{V}CO_{2,\,predicted})$ with respect to time

where excess $\dot{V}CO_2$ is the difference between actually measured $\dot{V}CO_2$ ($\dot{V}CO_{2,\,measured}$) and predicted $\dot{V}CO_2$ ($\dot{V}CO_{2,\,predicted}$) at exercise intensities above the AT.

$\dot{V}CO_{2,\ predicted}$ is the value obtained from an extrapolation of the $\dot{V}CO_2$-$\dot{V}O_2$ relationship at exercise intensities below the AT.

The AT was detected by the gas exchange parameters ($\dot{V}_E$, $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$) and blood lactate concentrations (Davis et al. 1979; Wasserman et al. 1973). The summarized criteria of the AT detection are given elsewhere (Hirakoba et al. 1992).

Statistics: All values are expressed as means±SD. The statistical significance of difference between control and AMA was tested by the paired Student's t-test (two- tailed test) and Person product correlation was used to assess the strength of the relationship between variables. Significance level was accepted at $P < 0.05$ for all tests.

RESULTS

The acid-base data revealed that resting blood pH ($P< 0.05$) and $[HCO_3^-]_b$ ($P< 0.01$) were significantly higher in AMA due to the acute ingestion of $NaHCO_3$, as compared with control (Table 1).

The $[La^-]_b$ increase during submaximal exercise below the AT was not affected by AMA, while it was found to be larger in AMA than in control during exercise above the AT; the $[La^-]_b$ at exhaustion ($P< 0.05$) and 3 min after exercise ($P< 0.05$) in AMA were significantly higher compared with control (Table 1). Therefore, the increase of $[La^-]_b$ ($\Delta [La^-]_b$) due to incremental exercise (measured as the difference between $[La^-]_b$ at rest and that at 3 min after exercise) showed a tendency to be greater in AMA (13.16 mmol· l^{-1}) than in control (11.40 mmol· l^{-1}); the difference between the two conditions was approximately 2 mmol· l^{-1}. The decrease of $[HCO_3^-]_b$ ($\Delta [HCO_3^-]_b$) due to incremental exercise (measured as the difference between $[HCO_3^-]_b$ at rest and that at 3 min after exercise) in control and AMA were 10.4 and 11.8 mmol· l^{-1}, respectively, which corresponded roughly to $\Delta [La^-]_b$ in these two conditions. Therefore, the $\Delta [La^-]_b$ was significantly related to the $\Delta [HCO_3^-]_b$ ($r=0.844$, $P<0.001$, Fig. 1).

The submaximal $\dot{V}CO_2$-$\dot{V}O_2$ relationships, in the two acid-base conditions, below the AT were found to be well fitted by a linear regression line, with mean correlation coefficients (r) of $r=0.981\pm0.023$ (control) and $r=0.989\pm0.007$ (AMA). The slope and intercept of the submaximal $\dot{V}CO_2$-$\dot{V}O_2$ relationship below the AT for AMA were the same as those for control (Table 2). Similarly, there were no significant differences in the peak values for $\dot{V}O_2$ and $\dot{V}_E$ at exhaustion between these two conditions. On the other hand, the peak $\dot{V}CO_2$ obtained in AMA was significantly higher ($P< 0.05$) compared with control as listed in Table 2.

Mean values (±SD) of CO_2 excess, CO_2 excess per unit of body mass (CO_2 excess· $mass^{-1}$) and CO_2 excess· $mass^{-1}$ per unit increase of $[La^-]_b$ (CO_2 excess · $mass^{-1}$· $\Delta [La^-]_b$) are given in Table 3. CO_2 excess (ml) and CO_2 excess · $mass^{-1}$

(ml· kg^{-1}) were found to be significantly higher in AMA than in control ($P<0.05$). Nevertheless CO_2 excess· $mass^{-1}$· Δ $[La^-]_b$ was similar for control (4.80±0.39 ml· kg^{-1}· $mmol^{-1}$· l^{-1}) and AMA (5.07±0.46 ml· kg^{-1}· $mmol^{-1}$· l^{-1}).

Table 3.

Figure 2 shows the relationships between CO_2 excess · $mass^{-1}$ and both Δ $[La^-]_b$ and Δ $[HCO_3^-]_b$ in control and AMA. The CO_2 excess · $mass^{-1}$ was found to be significantly correlated with both Δ $[La^-]_b$ ($r=0.926$, $P<0.001$) and Δ $[HCO_3^-]_b$ ($r=0.872$, $P< 0.001$).

DISCUSSION

Acute ingestion of sodium bicarbonate produced metabolic alkalosis (AMA) with elevated pH and $[HCO_3^-]_b$. In addition to higher blood pH and $[HCO_3^-]_b$, many investigators (Bouissou et al. 1988; Jones et al. 1977; Kowalchuk et al. 1984; Sutton et al. 1981; Wilkes et al. 1983) reported that bicarbonate ingestion resulted in a greater increase of blood lactate accumulation during exercise. In this study $[La^-]_b$ levels during exercise above the AT were also found to be higher in AMA, with a greater $\Delta [La^-]_b$ in AMA (13.16 mmol· l^{-1}) compared with control (10.4 mmol· l^{-1}). These results could be explained either by an increased rate of efflux of La^- from muscle due to an elevated extracellular buffer concentration (Hirche et al. 1975; Mainwood et al. 1972; Mainwood and Worsely-Brown 1975; Spriet et al. 1986), or by an increase of La^- formation within exercising muscle due to less inhibition of glycolitic enzymes such as phosphorylase and phosphofructokinase (Bouissou et al. 1988; Sutton et al. 1981). Since muscle La^- and pH were not measured in this study, ~~it is, therefore, not known which~~ the mechanism ~~might be the explanation.~~ is not known.

It is accepted that the excess volume of CO_2 is derived from bicarbonate buffering of the H^+ dissociated from lactic acid (Beaver et al. 1986; Sutton and Jones 1979; Jones 1980; Wasserman et al. 1981). In addition, it has been pointed out that the CO_2 excess depends on blood lactate accumulation, so that a greater CO_2 excess would imply an increase of bicarbonate buffering of lactic acid (Beaver and Wasserman 1991; Hirakoba et al. 1990, 1992; Yano et al. 1984; Yano 1987). The CO_2 excess (ml) and CO_2 excess· $mass^{-1}$ (ml· kg^{-1}) obtained in AMA showed significantly higher values compared with control. These results suggest that bicarbonate buffering of lactic acid may be increased by extracellular alkalinization.

On the other hand, it is possible that the CO_2 excess may be affected by a change of the submaximal $\dot{V}CO_2$-$\dot{V}O_2$ relationship, because the CO_2 excess is calculated as the integral of the differences between the measured $\dot{V}CO_2$ and predicted $\dot{V}CO_2$ from the submaximal $\dot{V}CO_2$ -$\dot{V}O_2$ relationship below the AT

(Beaver and Wasserman 1991; Hirakoba et al. 1992; Yano 1987). The slope and intercept of the submaximal $\dot{V}CO_2$-$\dot{V}O_2$ relationship were found to be similar for control and AMA (Table 2), which is consistent with the study of Kowalchuk et al. (1984) who reported that the submaximal $\dot{V}CO_2$-$\dot{V}O_2$ relationship was not affected by acute metabolic alkalosis. It seems, therefore, unlikely that the higher CO_2 excess (ml) and CO_2 excess· mass^{-1} (ml· kg^{-1}) in AMA could be accounted for by the change of $\dot{V}CO_2$-$\dot{V}O_2$ relationship. In contrast with the submaximal $\dot{V}CO_2$ responses, peak $\dot{V}CO_2$ was found to be significantly higher in AMA (3,861±499 ml · min^{-1}) than in control (3,686±392 ml· min^{-1}). Since it is inferred from a similar $\dot{V}O_2$ peak value in control and AMA that aerobically produced $\dot{V}CO_2$ would be unchanged between these two conditions, this higher peak $\dot{V}CO_2$ appears to be mainly due to a large excess volume of CO_2 generated from bicarbonate buffering of lactic acid in AMA, which was also accompanied by greater Δ $[La^-]_b$. This would be supported by a significant relationship between Δ $[La^-]_b$ and Δ $[HCO_3^-]_b$ in the two acid-base conditions ($r=0.844$, $P<0.001$, Fig. 1).

Fig. 1

This study was undertaken mainly to determine the effect of changes in perfusing HCO_3^- on the contribution of bicarbonate buffering to the H+ of lactic acid. It is, therefore, necessary to estimate the excess volume of CO_2 per unit of body mass per unit change of blood lactate accumulation (CO_2 excess· mass^{-1}· Δ $[La^-]_b$) to determine the above mentioned effect, because CO_2 excess (ml) increases or decreases by the change of Δ $[La^-]_b$ as previously mentioned. Further, the CO_2 excess· mass^{-1}· Δ $[La^-]_b$ is thought to reflect the relative contribution of bicarbonate system to the H+ buffering at the same amount of lactate production. Since the H+ of lactic acid must be buffered ~~at~~ near the site of its formation, intramuscular HCO_3^- in the exercising muscle has been considered to be the major source of CO_2 excess output (Beaver and Wasserman 1991). If the elevated extracellular bicarbonate concentration due to bicarbonate ingestion would be associated with an enhancement of intramuscular HCO_3^- buffer capacity, it is possible that the CO_2 excess· mass^{-1}· Δ $[La^-]_b$ could be increased by bicarbonate ingestion, presumably owing to the increase of intramuscular HCO_3^- buffering of

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lactic acid produced in exercising muscle and to faster efflux of CO_2 than of La^- from muscles (Cechetto and Mainwood 1978; Kowalchuk et al, 1988; Steinhagen et al, 1976). However, It was found to be a similar CO_2 excess· mass^{-1}· Δ $[La^-]_b$ for control (4.80±0.39) and AMA (5.07±0.46) as indicated by the relationship between CO_2 excess· mass^{-1} and Δ $[La^-]_b$ in the two acid-base status examined in this study (Fig. 1). Costill et al. (1984) reported that despite the alkalinization of the extracellular fluid, there was no measurable effect on intracellular pH. Similarly, Rupp et al. (1983) also showed that the administration of bicarbonate had no effect on resting muscle pH. These findings are in agreement with Heisler's study (1975) in which the intracellular pH remained unchanged over a pH range from 7.4 to 7.15 of the incubation medium. It has been pointed out that this difference in pH between the intra- and extracellular fluids may be due to the impermeable nature of the muscle membrane to HCO_3^- (Robin 1961). According to the previous studies (Costill et al. 1984; Parry-Billings and MacLaren 1986; Wilkes et al 1983), it is also expected in this study that intramuscular HCO_3^- buffer capacity could not be enhanced by acute bicarbonate ingestion. Consequently, it is indicated that intracellular CO_2 production (due to intramuscular HCO_3^- buffering) at the same lactate concentration and/or CO_2 efflux from muscle to blood may be similar for control and AMA, which would lead to a similar CO_2 excess· mass^{-1}· Δ $[La^-]_b$ in the two acid-base conditions.

As shown in Figure 2, high correlations were found between CO_2 excess· mass^{-1} and both Δ $[La^-]_b$ ($r=0.926$, $P< 0.01$) and Δ $[HCO_3^-]_b$ ($r=0.872$, $P< 0.01$), indicating that CO_2 excess· mass^{-1} is closely associated with the changes in $[La^-]_b$ and $[HCO_3^-]_b$, regardless of acid-base changes; it increases linearly with changes in Δ $[La^-]_b$ and the corresponding changes in Δ $[HCO_3^-]_b$. This finding supports the contention of Beaver and Wasserman (1991) that CO_2 excess may be a useful estimate of HCO_3^- buffering of the H+ of lactic acid and of lactate accumulation. On the other hand, these results reveal that the excess volume of CO_2 generated from bicarbonate buffering of lactic acid in AMA is the same as control, when comparing at the identical lactate accumulation.

It is, therefore, suggested that the relationship between CO_2 excess· mass^{-1} and blood lactate accumulation could be unaffected by acute metabolic alkalosis, and that the relative contribution of bicarbonate system to the H+ buffering of lactic acid may be remained constant between control and acute metabolic alkalosis .

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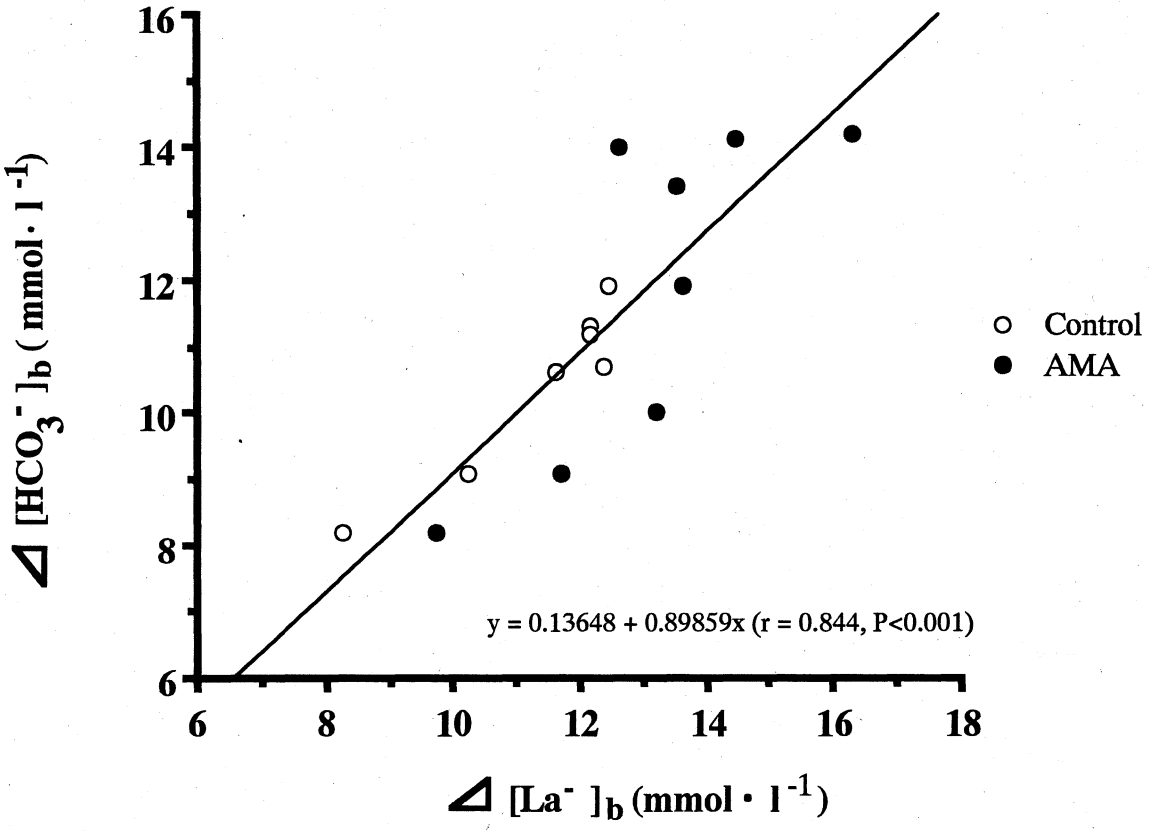
LEGEND

Fig. 1. Relationship between $\Delta [La^-]_b$ and $\Delta [HCO_3^-]_b$ due to incremental exercise in control and acute metabolic alkalosis (AMA). Blood gas samples (pH and $\Delta [HCO_3^-]_b$) were taken from seven of the subjects in control. For definitions in Table 1.

Fig. 2. Relationships between $CO_2 \cdot mass^{-1}$ and both $\Delta [La^-]_b$ and $\Delta [HCO_3^-]_b$ due to incremental exercise in control and acute metabolic alkalosis (AMA). Blood gas samples (pH and $\Delta [HCO_3^-]_b$) were taken from seven of the subjects in control. For definitions in Table 1 and 3.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Δ [HCO3-]b (mmol· l -1)
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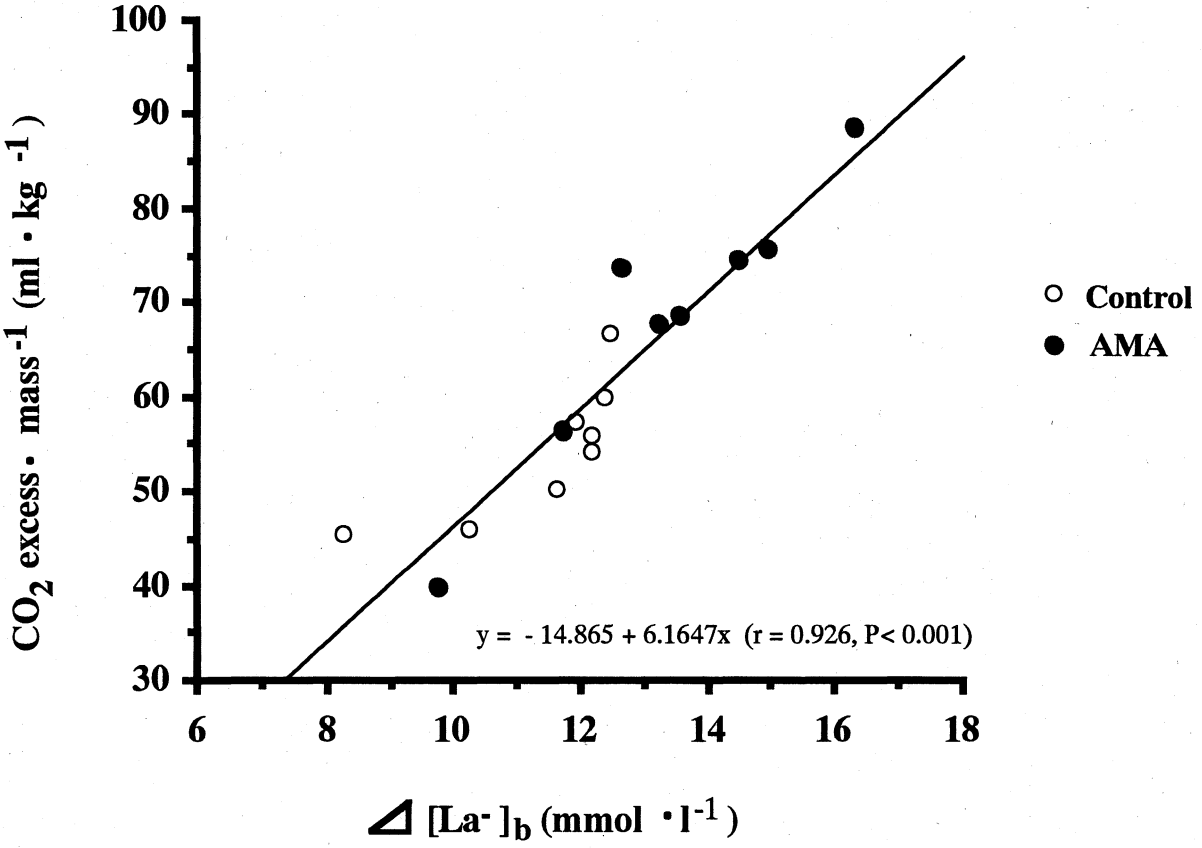
Control
AMA
y = 0.13648 + 0.89859x (r = 0.844, P<0.001)

Fig. 1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CO_2 excess • mass^{-1} (ml • kg^{-1})
⊿ [La$^-$]$_b$ (mmol • l^{-1})
y = - 14.865 + 6.1647x (r = 0.926, P< 0.001)
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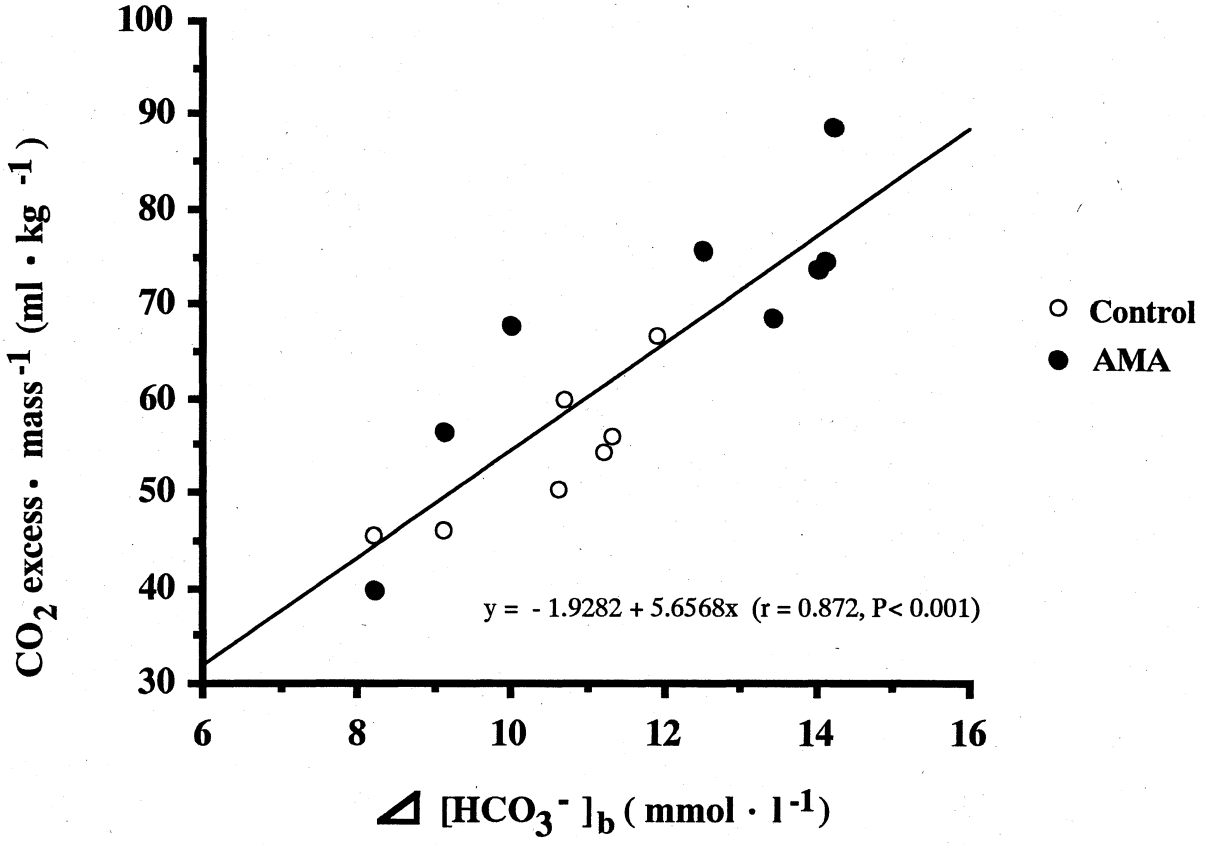
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CO_2 excess • mass^{-1} (ml • kg^{-1})
⊿ [HCO_3^-]$_b$ (mmol • l^{-1})
y = - 1.9282 + 5.6568x (r = 0.872, P< 0.001)
Control
AMA

Fig. 2.

Table 1. Blood bicarbonate and lactate concentrations at rest, anaerobic threshold and 3 min after exercise in control and acute metabolic alkalosis (AMA).

		Control			AMA		
		pH@	$[HCO_3^-]_b$@	$[La^-]_b$	pH@	$[HCO_3^-]_b$@	$[La^-]_b$
			(mmol· l^{-1})			(mmol· l^{-1})	
Rest	Mean	7.394	25.5	0.86	7.444*	29.4**	1.25*
	SD	0.027	1.0	0.17	0.029	1.5	0.38
AT	Mean	--	--	1.75	--	--	1.86
	SD			0.28			0.40
Exh.	Mean	--	--	9.57	--	--	12.29*
	SD			2.14			1.87
Rec.	Mean	7.230	15.1	12.26	7.298*	17.6	14.41*
	SD	0.033	1.6	1.40	0.055	2.7	1.75

$[HCO_3^-]_b$, blood bicarbonate concentration; $[La^-]_b$, blood lactate concentration; AT, anaerobic threshold; Exh., exhaustion; Rec. , 3 min after exercise. @Blood samples for pH and $[HCO_3^-]_b$ were taken from seven of the subjects in control. The values shown are mean of seven.
* $P< 0.05$, ** $P< 0.01$, Significantly different from control.

Table 2. Comparisons of the slope and intercept of the submaximal $\dot{V}CO_2$-$\dot{V}O_2$ relationship below the anaerobic threshold (AT) and of the peak values of the gas exchange parameters at exhaustion between control and acute metabolic alkalosis (AMA).

		$\dot{V}CO_2$ vs $\dot{V}O_2$ curve below AT		Peak values		
		Slope	Intercept	$\dot{V}O_2$ ($ml \cdot min^{-1}$)	$\dot{V}CO_2$ ($ml \cdot min^{-1}$)	$\dot{V}_E$ ($l \cdot min^{-1}$)
Control	Mean	0.858	-107.41	3323	3686	92.4
	SD	0.032	52.60	308	392	12.5
AMA	Mean	0.867	-128.65	3427	3861*	92.9
	SD	0.049	66.35	410	499	12.5

$\dot{V}O_2$, oxygen uptake; $\dot{V}CO_2$, carbon dioxide output; $\dot{V}_E$, minute ventilation (STPD).

*$P < 0.05$, Significantly different from control.

Table 3. Comparison of excess volume of CO_2 due to blood lactate accumulation during incremental exercise between control and acute metabolic alkalosis (AMA).

	Control		AMA	
	mean	SD	mean	SD
CO_2 excess (ml)	3117	506	3897*	381
CO_2 excess $\cdot$ mass^{-1} (ml $\cdot$ kg^{-1})	54.5	6.6	68.2*	13.6
CO_2 excess $\cdot$ mass^{-1} $\cdot$ Δ [La$^-$]$_b$ (ml $\cdot$ kg^{-1} $\cdot$ mmol $\cdot$ l^{-1})	4.80	0.39	5.07	0.46

CO_2 excess, the integrated excess $\dot{V}CO_2$ with respect to time from the anaerobic threshold to the end of exercise; CO_2 excess $\cdot$ mass^{-1}, CO_2 excess per unit of body mass; CO_2 excess $\cdot$ mass^{-1} $\cdot$ Δ [La$^-$]$_b$, CO_2 excess per unit of body mass per unit increase of blood lactate (Δ [La$^-$]$_b$)

*$P < 0.05$, significantly different from control.