Hyperkalemia During Progressive Dynamic Exercise

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Serum potassium levels, catecholamines, and plasma renin activity are elevated during maximal dynamic exercise. Catecholamines and plasma renin activity have been shown to rise nonlinearly during exercise and to parallel changes in venous blood lactate. Since the hyperkalemia of exercise is modulated by catecholamines, we studied the changes in serum potassium in relation to attaining the exercise intensity associated with a rise in blood lactate (the lactate threshold). Eight healthy male subjects 25 to 30 years of age underwent progressive cycle ergometry (PE) at increments of 25 W/4 min. During PE, absolute levels of peripheral venous potassium increased significantly only after the lactate threshold was exceeded ($P < .01$). In a control study (TC), subjects exercised to their lactate threshold and remained at that work rate for a time equal to that of PE. During TC, there were no significant increases in potassium until the final four minutes of exercise ($P < .05$). Plasma aldosterone levels rose comparably during PE and TC. These results demonstrate that significant potassium elevation during dynamic exercise begins at the lactate threshold. This threshold response of potassium may have clinical implications for exercise prescription in patients with impaired potassium homeostasis.

INTRODUCTION

Rapid potassium changes are a well-documented effect of intense dynamic exercise,[1-6] and catecholamines have been shown to be important modulators of the rapid potassium shifts.[7] Catecholamine levels increase with progressive dynamic exercise,[8-10] as do levels of other hormones whose release is stress related.[11-14] Norepinephrine and epinephrine levels during exercise are closely related to changes in mixed venous blood lactate,[15-18] with abrupt changes evident at the lactate threshold, that point during progressive dynamic exercise at which mixed venous blood lactate rises abrubtly.[19]

The present authors have investigated the possibility that potassium changes during exercise are also related to the lactate threshold. The findings may have important implications for evaluating different methods of exercise prescription, with particular reference to patients who have difficulty handling potassium loads, but who may benefit from an exercise program.

SUBJECTS AND METHODS

Eight normotensive untrained men (age, 27 ± 1 yr) served as subjects. There was no history of hypertension, cardiovascular disease, or electrolyte disturbances. Written, informed consent was obtained, and the protocol was approved by the Research and Publications Committee of Lenox Hill Hospital.

All studies were performed between 8 AM and 10 AM on two nonconsecutive days within a two-week period. Subjects reported to the laboratory after having only clear fluids and toast for breakfast. No caffeinated beverages were permitted. Venous blood samples were obtained by cannulation of a forearm vein. A 1-L solution of D5W with 2000 units of

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heparin served as a flush for the intravenous line.

The protocol for the exercise bouts has been reported previously.[20] Progressive exercise (PE) was always performed first to determine the lactate threshold. Subjects sat next to a mechanically calibrated Collins Pedalmate cycle ergometer for 20 minutes before resting blood samples were obtained. Subjects then began exercising on the ergometer while measurements of oxygen consumption ($\dot{V}O_2$) were being made by use of the Beckman MMC (Beckman Instruments, Fullerton, CA), and while the ECG (leads V_5, aV_F) and blood pressure (BP) were being recorded. Rate–pressure product ([RPP], heart rate [HR] × systolic blood pressure [SBP]) was computed as an indirect index of myocardial oxygen consumption.[21] Initial work rate was 25 W and this was increased by 25 W every four minutes. Blood samples were obtained after the third minute of each stage. Subjects continued in this manner until they could no longer maintain a 60-RPM pedaling rate. The lactate threshold was defined as that point during exercise after which a nonlinear increase in lactate occurred.

During the control study (TC), subjects performed incremental exercise in the same manner as in the PE study. When they attained the work rate of the previously determined lactate threshold, they maintained this work rate until they had exercised for as long (28 ± 2 min) as they had in the PE study (Figure 1). Blood samples were obtained in a manner identical with that in the PE study.

Serum potassium levels were measured in triplicate by flame photometry. Blood lactate concentration was measured by a Roche 640 lactate analyzer (Roche Bio-Electronics, Basel, Switzerland). Plasma aldosterone concentration was measured by the method of Buhler and colleagues[22] with a normal range in our laboratory of 5–20 ng/dL.

Values are expressed as means ± standard error of the mean. We used repeat measures analysis of variance to detect differences between consecutive work stages.[23] We also used linear regression analysis and we compared slopes by a test for differences between regression coefficients.[24] Paired *t* tests were used to test for differences between time control and progressive exercise.[23]

RESULTS

Values at the lactate threshold were not different between the PE and TC studies (Table I). During PE, subjects attained a peak HR of 189 ± 4 beats/min, rate–pressure product of 36,300 ± 1500, and $\dot{V}O_2$ of 2.74 ± .10 L/min. Corresponding values at the end of the TC study were 148 ± 5, 255 ± 17,

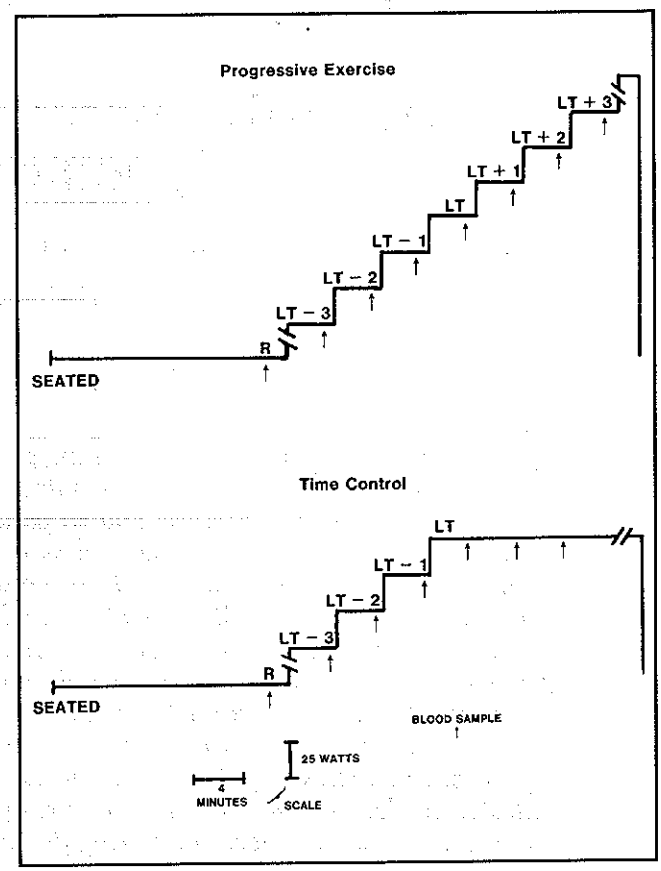

Figure 1. Schematic diagram of the protocol used in the progressive exercise (PE) and time control (TC) studies. Work rates were increased by 25 W every four minutes in both studies. During the TC study, once subjects had attained the previously determined lactate threshold, they maintained this work rate until the total time spent exercising during PE was accomplished. Blood samples were obtained at three minutes of each work rate. R = resting; LT = lactate threshold; LT − 1 = one work rate below LT; LT + 1 = one work rate above LT, etc. Values are given as means ± standard error of the mean.

TABLE I
HEMODYNAMIC AND OXYGEN CONSUMPTION VARIABLES

Variable	Rest	LT	End	
HR (beats/min)	78 ± 2	140 ± 7	189 ± 4	PE
	75 ± 2	130 ± 4	148 ± 5†	TC
RPP (X 10^{-2})	99 ± 5	243 ± 18	363 ± 15	PE
	88 ± 3*	215 ± 13	255 ± 17†	TC
$\dot{V}O_2$ (L/min)	.35 ± .04	1.48 ± .09	2.74 ± .10	PE
	.31 ± .02	1.40 ± .09	1.48 ± .09†	TC

Values are given as means ± standard error of the mean.
*$P < .05$
†$P < .01$ for PE vs TC.
LT = lactate threshold; PE = progressive exercise studies; TC = time control studies; HR = heart rate; RPP = rate-pressure product; $\dot{V}O_2$ = oxygen consumption.

TABLE II
BLOOD AND PLASMA VARIABLES

Variable	Rest	LT	End	
K^+ (mEq/L)	4.1 ± .1	4.6 ± .1	5.5 ± .1	PE
	4.3 ± .1	4.6 ± .1	4.9 ± .1*	TC
La (mmol/L)	1.29 ± .04	2.39 ± .20	7.89 ± .47	PE
	1.29 ± .08	2.53 ± .14	3.69 ± .36*	TC
ALDO (ng/.1L)	3.9 ± 0.7	7.8 ± 1.2	18.3 ± 1.9	PE
	3.7 ± 0.7	9.3 ± 1.3	17.1 ± 2.0	TC

Values are given as means ± standard error of the mean.
*$P < .01$ for PE vs TC.
LT = lactate threshold; K^+ = potassium; La = lactate; ALDO = aldosterone; PE = progressive exercise studies; TC = time control studies.

and 1.48 ± .09 L/min, ($P < .01$ for all, by comparison with progressive exercise).

Changes in potassium, venous blood lactate, and plasma aldosterone levels are shown in Table II. Levels of potassium and lactate were higher at the end of PE than at the end of the TC study (potassium, 5.5 ± .1 vs 4.9 ± .1 mEq/L, and lactate, 7.89 ± .47 vs 3.69 ± .36 mmol/L, both $P < .01$). There were no significant differences between the lactate thresholds during the stages of PE or, during the same stages of the TC study, between the thresholds for serum potassium or lactate (K^+, 4.6 ± .1 vs 4.6 ± .1, and lactate 2.39 ± .20 vs 2.53 ± .14). There were no significant differences between the PE or TC studies when aldosterone levels were compared. Even though work load was held constant at the lactate threshold during TC, there were small increases in $\dot{V}O_2$ with time.

Changes in lactate are shown in Figure 2. The graph clearly shows the lactate threshold during PE. During TC there was a gradual increase in lactate concentration with time even though work did not exceed the lactate threshold. There was no abrupt increase in lactate levels as there was during PE. The intent of the study design was to make this evident.

Serum potassium levels increased nonsignificantly over time below the lactate threshold (Figure 3) during both PE and TC studies. During PE, there were significant increases in potassium levels above the lactate threshold levels with each increase in work rate ($P < .01$). During TC, there were no significant increases in potassium levels until the final four minutes of exercise were maintained at the lactate threshold ($P < .05$).

The aldosterone response was not different between PE and TC studies. Aldosterone concentrations increased significantly, commencing two work rates below the lactate threshold in both tests, and no difference between slopes of the lines above the lactate threshold could be demonstrated (2.98 for PE and 2.32 for TC, not statistically significant).

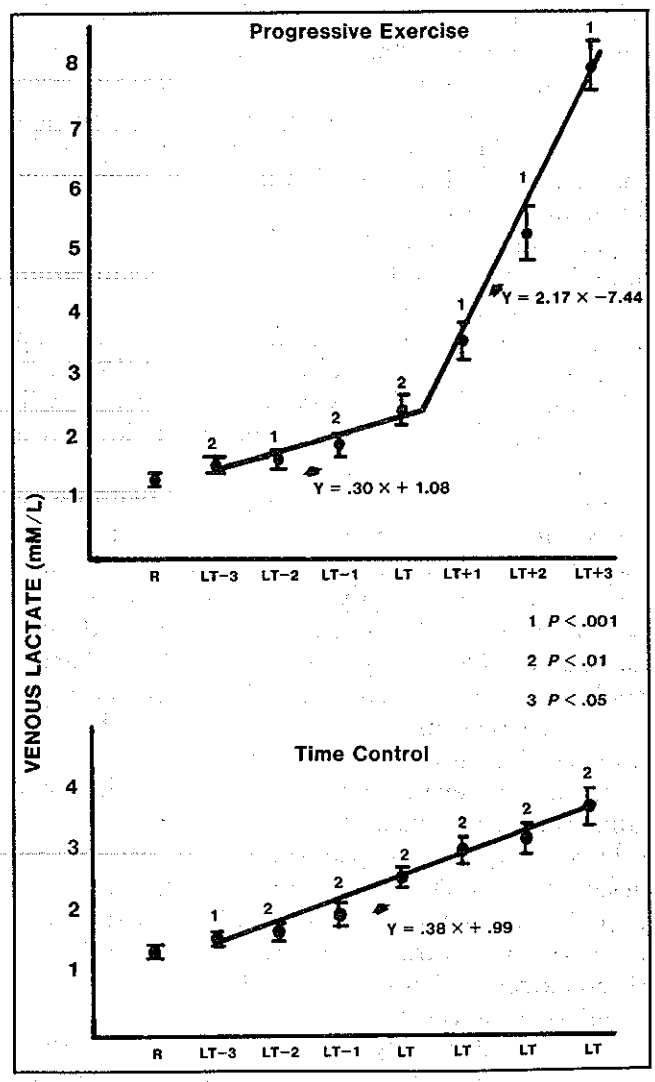

Figure 2. Mixed venous blood lactate is plotted as a function of work rate normalized for the lactate threshold. The slope of the line above the lactate threshold in progressive exercise is significantly greater than that below the lactate threshold and in the time control (TC) study. Significance symbols indicate that the level attained differs from those preceeding it. R = resting; LT = lactate threshold; LT − 1 = one work rate below LT; LT + 1 = one work rate above LT, etc. In the TC study, work rate was held constant at LT once this level was attained. Values are given as means ± standard error of the mean.

DISCUSSION

This study tested the hypothesis that serum potassium levels would show a nonlinear rise during incremental dynamic exercise. The results show that serum potassium levels do not rise significantly until the lactate threshold has been surpassed, which suggests a threshold effect for potassium level changes.

Serum potassium concentration is known to rise during dynamic exercise.[1-6] The origin of this increase is almost certainly from exercising muscles.[1] Most studies however, have not addressed the relation of changes in potassium concentration to stages of incremental exercise.[2,3,6,7,25] By combining data obtained at 9, 14, and 19 minutes of exercise at different intensities, a correlation between changes in potassium concentration and percentage of maximum $\dot{V}O_2$ has been shown.[4] Our results demonstrate that if exercise is maintained at the lactate threshold long enough, a significant increase in potassium concentration will eventually be obtained (Figure 3, TC). It may well be that exercise at any intensity will result in significant increases in potassium levels if it is maintained for a sufficient period.

Several factors appear to regulate the rate of potassium release and reuptake during exercise. With the onset of muscular contraction, local venous potassium levels promptly increase. This initial rise in potassium may well play a role in the augmented blood flow that is evident in working muscles.[26] Rats that are made hypokalemic before muscle stimulation experience a decrease in blood flow and evidence of muscle necrosis. Changes in peripheral venous potassium are dependent on several factors, including the degree of admixture with blood from nonworking muscles, cellular reuptake of potassium, and pH. As we observed in our TC study, there was no significant rise in peripheral venous potassium until the final stage of exercise. In contrast, exercise above the lactate threshold resulted in a prompt and significant increase in mixed venous potassium levels.

Although this study was not designed to address the mechanism for the increase in serum potassium concentration at the lactate threshold, catecholamines are known to modulate potassium levels.[3,7] The demonstration of a threshold increase in the levels of both epinephrine and norepinephrine as well as in plasma renin activity prompted our examination of serum potassium at the lactate threshold.[15,16,20] This point during progressively increasing dynamic exercise is likely to represent augmented sympathetic nervous system activity. In fact, increases in the levels of epinephrine and norepinephrine may actually cause the lactate threshold by stimulating muscle phosphorylase and promoting lactate production.[27,28] An increase in the levels of norepinephrine at the lactate threshold could inhibit potassium uptake by skeletal muscle, most likely through an alpha adrenergic mechanism.[29] Although the relation of peripheral venous lactate to catecholamines has been shown repeatedly, and catecholamines are known to affect potassium homeostasis, it is also possible that the increases in potassium levels noted at the lactate threshold are purely coincidental.

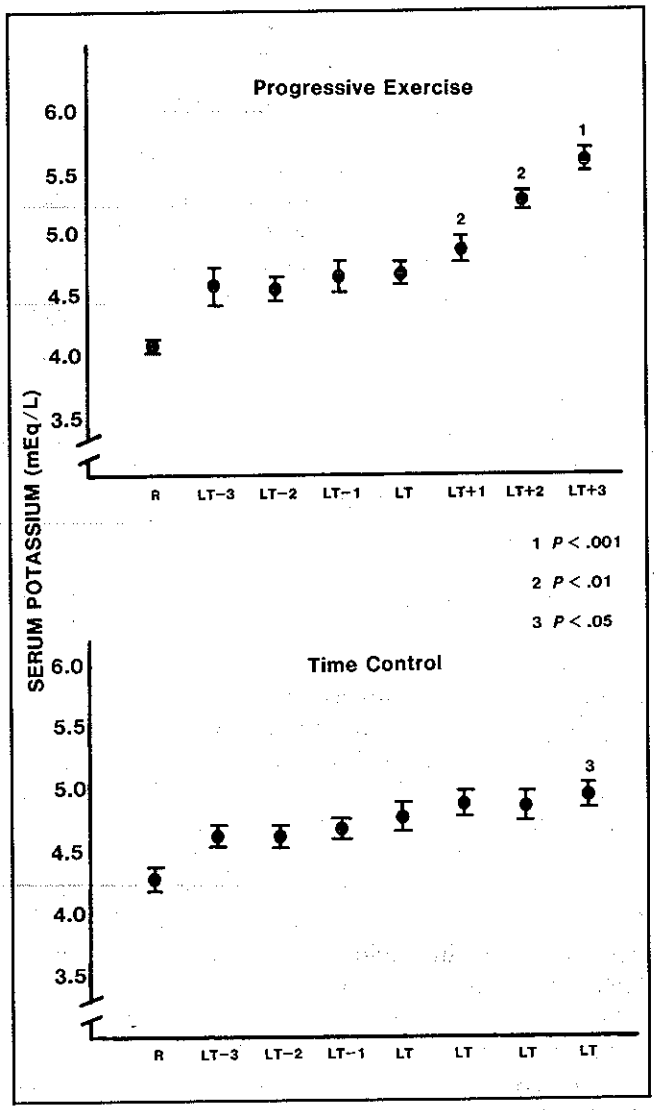

Figure 3. Serum potassium plotted as a function of work rate normalized for the lactate threshold. There was no significant increase in potassium level until the lactate threshold of progressive exercise was reached. The final time period of the time control study also showed a significant increase. Significance symbols indicate that the level attained differs from those preceeding it. R = resting; LT = lactate threshold; LT − 1 = one work rate below LT; LT + 1 = one work rate above LT, etc. Values are given as means ± standard error of the mean.

Since lactate levels continued to increase significantly at each sampling time in the TC study—but potassium levels did not—it seems unlikely that lactic acidosis is the cause of the increase in serum potassium levels. This is further supported by the observation that changes in blood pH appear to play a minor role in the rise in serum potassium concentration associated with exercise in trained or untrained subjects.[7,30] In addition, it has been dem-

onstrated that changes in the levels of insulin and blood glucose do not explain the increase in potassium levels at the end of maximal exercise.[7,30] As demonstrated previously, hemoconcentration during exercise does not account for the increased levels of serum potassium during progressive exercise.[20]

Aldosterone levels were not different between the PE and TC studies. Since potassium levels rose above the lactate threshold it does not appear that aldosterone release is responding to the increase in serum potassium concentration during dynamic exercise. Similarly, since plasma renin activity also increased above the lactate threshold,[20] it does not appear that aldosterone is responding to increased activity of the renin-angiotensin system. Aldosterone release during exercise may be in response to very subtle changes in potassium or angiotensin II concentration, or to other stimuli such as ACTH.[31]

In conclusion, this study has shown that exercise above the lactate threshold of dynamic exercise is associated with consistent and significant increases in levels of serum potassium. The rise in serum potassium level that occurs when exercise exceeds the lactate threshold may be deleterious, especially in patients who have difficulty handling a potassium load (e.g., in renal failure, diabetes mellitus), or in patients who are being treated with diuretics. Such problems may be avoided by determining the lactate threshold, or its ventilatory approximation,[32] and prescribing exercise below this point.

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