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Lactate Dehydrogenase Activity and Insulin and Lactate Levels at an Altitude Below Sea Level (−350 m) Compared to Those at an Altitude Above Sea Level (620 m) After Exercise

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Abstract—This study was designed to investigate the effect of exercise at 350 m below sea level altitude (−350 m) on the serum levels of lactate dehydrogenase (LDH), insulin, and lactate. The study was carried out on ten trained adult males with mean age of 23.3 ± 3.4 years following a 21-km noncompetitive run. Venous blood was withdrawn from the subjects before exercise and 5 min post exercise. For comparison purposes, a similar study was performed with the same subjects but at 620 m above sea level (+620 m). The results show a significant increase in LDH and lactate levels after exercise only at low altitude (−350 m). Serum insulin levels decreased significantly after exercise at both altitudes. These changes in serum levels of LDH, insulin, and lactate at different altitudes suggest that a type of metabolic adjustment is present that meets energy requirements during exercise.

Key words: exercise, low altitude, lactate dehydrogenase, insulin, lactate

It is well known that an increase in blood level of lactate in response to exercise is higher at hypoxic altitude (i.e., at high altitude) than that at sea level [1]. This increase in lactate levels is blunted by acclimatization [2] and is due to variations in lactate release [3]. The significance of this metabolic adjustment was suggested to involve the regulation of glycolysis and phosphorylation [4, 5]. To date there are no reports of acute effects of exercise on lactate dehydrogenase (LDH; EC 1.1.1.27), lactate, and insulin concentrations at below sea level altitudes. Therefore, we decided to investigate the effect of such exercise on serum levels of LDH, lactate, and insulin at 350 m below sea level in the Jordan Valley (−350 m). LDH, insulin, and lactate were chosen as parameters to measure in order to investigate carbohydrate metabolism during exercise. For comparison, serum levels of LDH, insulin, and lactate were also measured following exercise at 620 m above sea level (+620 m) in the city of Irbid.

MATERIALS AND METHODS

Ten healthy male adults with ages ranging from 19 to 30 years participated in this study. They were all in training and had practiced running regularly. Data on their physiological characteristics are given in Table 1. A noncompetitive 21-km run took place at +620 m and at −350 m altitudes on two separate days in the first week of May 1998. However, it was required to finish the race within 90 min of starting the exercise. The temperature was approximately 20°C at the above sea level location and approximately 30°C at the below sea level location. Water was available for all runners during the race. A small amount of water just to moisten the mouth was advised. The weights of all participants were recorded before the race. Venous blood samples (from the antecubital vein) were drawn before the race at each altitude as controls and 5 min following the race and placed on ice. The samples were centrifuged, and the serum was kept at −20°C. Both experiments were performed in the morning. All the measurements were done in duplicate. The samples of all subjects in both experiments were analyzed in the same run. LDH activity was measured using a commercial kit from Lab Kit (Barcelona, Spain). Since LDH activity is directly proportional to NADH consumption, NADH was determined photometrically at 25°C, pH 7.5. Absorbance was measured at 339 nm. The method is described by Bergmeyer [6]. Insulin was determined by radioimmunoassay using the commercially available kit from DPC (Los Angeles, USA). The sensitivity of the insulin assay was 1.2 μU/ml and the coefficient of intra-assay variation was 4.9%.

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Table 1. Physiological and descriptive data on the subjects who participated in the study

Parameter	Age, year	Weight, kg	Height, cm	Blood pressure, mm/Hg	Pulse rate, per minute	Training experience, years
Mean	23.3	62.5	172.2	126.7/73.2	57.2	4.8
Standard deviation	3.4	7.1	4.7	5.1/11.6	7.4	3.2

Lactate levels were determined using a Microzym-L Biosensor Analyzer (S. G. I., Toulouse, France). Data are expressed as mean ± standard deviation (SD).

Statistical significance was tested using the Student *t*-test for paired data; p values of < 0.05 were considered significant.

RESULTS

The results in Table 2 show the levels of lactate dehydrogenase activity, lactate, and insulin. The basal level of LDH significantly decreased from 184 ± 15 U/liter at high altitude to 168 ± 11 U/liter at low altitude ($p < 0.01$). After exercise the level increased significantly only at low altitude, from 168 ± 11 U/liter to 206 ± 19 U/liter ($p < 0.001$). The basal serum level of lactate at +620 m was significantly higher than that at −350 m altitude ($p < 0.04$). The results also show the serum levels of lactate at both altitudes increased after exercise, but the increase was statistically significant only at −350 m altitude ($p < 0.01$).

Table 2. LDH activity, lactate concentration, and insulin level before and after exercise at locations above sea level (+620 m) and below sea level (−350 m)

Altitude	Metabolite level	
	before running	after running
Lactate dehydrogenase activity, U/liter		
+620 m	184 ± 15	187 ± 1
−350 m	168 ± 11*	206 ± 19**
Lactate, mM		
+620 m	1.43 ± 0.12	1.51 ± 0.17
−350 m	1.25 ± 0.11	1.69 ± 0.13**
Insulin, μU/liter		
+620 m	10.4 ± 2.9	7.6 ± 2.4***
−350 m	11.5 ± 3.6	9.1 ± 2.9****

Note: Results are presented as mean ± SD, $N = 10$.
* $p < 0.04$ (when compared to before exercise at +620 m).
** $p < 0.01$ (when compared to before exercise at − 350 m).
*** $p < 0.003$ (when compared to before exercise).
**** $p < 0.04$ (when compared to before exercise).

Lactate increased from 1.25 ± 0.11 mM before to 1.69 ± 0.13 mM after exercise, while those at above sea level were little affected. The results in Table 2 show the levels of insulin at both altitudes before and after exercise. The difference between the basal (pre-exercise) levels of serum insulin at both altitudes was not significant. At both altitudes, the levels of insulin decreased significantly following exercise ($p < 0.003$ for +620 m and $p < 0.04$ for −350 m). However, the magnitude of the decrease in insulin after exercise at both altitudes was similar.

DISCUSSION

The decreased basal serum level of lactate at low altitude compared to that above sea level (Table 2) suggests a depression of anaerobic glycolysis upon transfer of the subjects from above sea level to below sea level. Such a decrease in glycolytic flux rate could occur due to a change in the availability of a substrate, namely glucose-6-phosphate (G-6-P). A decrease in glucose levels at low altitude, compared to above sea level was reported by Khrasha [7]. Reduced glucose levels at low altitude could result in a decrease in availability of G-6-P, which could lead to a decrease in flux through fructose-6-phosphate/fructose-1,6-bisphosphate. This flux is controlled by the activity of phosphofructokinase-1 (PFK-1), the major rate-limiting enzyme in glycolysis [8]. In a previous study performed in our laboratories [9], we found transfer from +620 m level to −350 m to cause a significant decrease in PFK-1 activity and a significant increase in serum ATP. Thus, the decrease in serum levels of lactate at low altitude could be due to decreased glycolytic flux rate due to PFK-1 inactivation and/or a decrease in glucose availability. Another possible reason for the decreased level of lactate at low altitude, yet to be investigated, could be an increased rate of lactate clearance. Exercise produced a significant increase in lactate, but only at −350 m (Table 2). This increase in serum lactate following exercise at low altitude is most likely due to the increase in LDH that is demonstrated in this study (Table 2). The increase in LDH after exercise was found to be significant only at −350 m altitude. LDH is known to convert pyruvate to lactate in muscle during intense activ-

ity [10]. Serum levels of insulin and other counter-regulatory hormones may have a role in this shift in energy metabolism. Insulin level decreased in serum during exercise at low altitude (Table 2), but this decrease is unlikely to be responsible for the greater production of lactate because the decrease was observed following exercise at both altitudes. However, a change in the sensitivity of cells to insulin at the different altitudes cannot be ruled out. The role of growth hormone, one of the major counter-regulatory hormones, which is known to increase following exercise, is another possibility, but this increase was observed at both +620 m and −350 m altitudes [2]. On the other hand, post-exercise levels of adrenocorticotropic hormone (ACTH) and cortisol, other counter-regulatory hormones, were shown to increase only at low altitudes [11]. It is likely, therefore, that changes in ACTH and cortisol may play a role in the increase in serum levels of lactate in response to exercise at low altitude. Another possible explanation is an increase in the rate of glycogenolysis due to increased secretion of epinephrine during exercise [12], thus leading to increased lactate production. Increased glycogenolysis would lead to an increase in muscle glycolysis (anaerobic) and a subsequent increase in the serum level of lactate. If the amount of epinephrine secreted at −350 m is greater, then the amount of lactate produced would be also greater. Also, at the low altitude of −350 m there might be a mismatch between the increased rate of pyruvate formation and the decreased rate of electron transport and oxidative phosphorylation. The outcome of this mismatch is the reduction of pyruvate to lactate to provide the needed NAD^+ to continue glycolysis. This possibility, at least in part, may contribute to the increase in lactate following exercise. However, a partial shift in energy metabolism under this experimental condition to β-oxidation of fatty acids also could not be excluded. A high concentration of acetyl-CoA would inhibit pyruvate dehydrogenase, leading to more pyruvate reduced to lactate.

LDH activity increased significantly after exercise only at −350 m. It increased little at +620 m. Also, the basal activity before exercise was significantly reduced at low altitude. It is not clear what causes the changes in LDH activity under such conditions. The decrease in the basal concentration of lactate at such altitude (Table 2) may be a factor. Should the level of lactate have a negative feedback effect on the activity of LDH, which catalyzes the production of lactate from pyruvate under severe exercise [10], the inhibition imposed on LDH would become reduced when lactate level decreases, thus increasing basal LDH activity at −350 m before exercise. The increase in LDH activity after exercise could be related to increased use of fat as a fuel, which would lead to increased production of acetyl-CoA, thus inhibiting pyruvate dehydrogenase and increasing LDH activity. Some possible factors that cannot be excluded are the effect of the high barometric pressure and increased temperature (30°C) at −350 m altitude. As to the changes in insulin, the results show a significant decrease in insulin level at both altitudes after exercise. The extent of decrease was similar at both altitude levels. The decrease in insulin as a result of exercise, which is due to an inhibition of insulin release from the pancreas by sympathetic stimulation during exercise, is well documented [13].

In summary, it appears that some regulatory mechanisms that need further elucidation emerge below sea level where there are acute hyperoxic, hyper-barometric, and high temperature conditions. These mechanisms may involve a shift in energy metabolism to maintain ATP homeostasis. The ratio of insulin/counter-regulatory hormones may be an important factor in such change of energy metabolism at low altitude.

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