

Brief Report

Lactic Acidosis Complicating the Acquired Immunodeficiency Syndrome

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Lactic acidosis, characterized by metabolic acidosis and a blood lactate level higher than 5 mmol/L, is generally classified as either anaerobic (type A) or aerobic (type B) (1). In type A lactic acidosis, tissue hypoxia and anaerobic metabolism have a definite clinical cause, such as pulmonary edema, cardiopulmonary arrest, or shock. Examples of type B lactic acidosis include that associated with malignancy, glycogen storage diseases, or certain myopathies, where tissue hypoxia is not apparent. In cases where the blood lactate level exceeds about 9 mmol/L, mortality may exceed 75% (2). Patients with human immunodeficiency virus (HIV) infection may develop type A lactic acidosis associated with tissue hypoxia related to sepsis, shock, or cardiac arrest (3). During a 2-year period, however, we encountered seven HIV-infected patients who developed severe lactic acidosis in the absence of hypoxemia or another obvious cause.

Methods

Between July 1989 and June 1991, seven patients with confirmed HIV infection (six with AIDS; one with AIDS-related complex) (4) developed lactic acidosis. The patients presented with the following symptom complexes: nausea, emesis, and anorexia with weight loss ($n = 4$); fever and malaise ($n = 2$); and tachypnea with dyspnea ($n = 3$) (Table 1). Metabolic acidosis was diagnosed in three patients at admission to the hospital because of dyspnea, whereas dyspnea or a decrease in the blood bicarbonate level led to evaluation of arterial blood gases in four other patients (Table 1). The control group included nine age-matched patients admitted to the same intensive care unit over the same interval who had placement of a pulmonary artery catheter (5) for close monitoring of volume status. When studied, all controls were normovolemic (normal cardiac output and pulmonary artery pressure), and none had metabolic acidosis, hypoxia, or clinical evidence of a mixed acid-base disorder. The cardiac output was determined by

thermodilution (5); the blood lactate level, oxygen delivery, and oxygen utilization were assessed as previously reported (6, 7). Data are expressed as mean \pm SD. The unpaired Student *t*-test was used for comparisons.

Results

When lactic acidosis was diagnosed, six of the seven patients were lucid and generally had no symptoms except hyperventilation (see Table 1). Other causes for elevated anion gap metabolic acidosis, such as diabetic ketoacidosis, malignancy, sepsis, uremia, thyrotoxicosis, or exogenous intoxication were ruled out by appropriate laboratory tests and diagnostic procedures and by autopsy in four cases. No single drug was being taken by all seven patients: Four patients were receiving zidovudine, one patient was receiving ganciclovir, and one patient was receiving clofazimine. Values at the time of diagnosis of lactic acidosis (see Table 1) were as follows: arterial oxygen saturation, $98\% \pm 1\%$; arterial lactate, 14.3 ± 2.6 mmol/L (controls, 1.6 ± 0.8 mmol/L; $P < 0.001$); and anion gap, 28 ± 5 mmol/L (controls, 11 ± 2 mmol/L; $P < 0.001$). The oxygen extraction ratio $\{100 \times (\text{arterial } O_2 - \text{venous } O_2) / \text{arterial } O_2\}$ (O_2 expressed as mL O_2 /100 mL blood) was $24.9\% \pm 6.0\%$, which did not differ from that of controls ($19.5\% \pm 7.8\%$; $P = 0.2$).

In three patients, the cardiac index was 3.20 ± 0.21 L/min per m^2 body surface area (control value 3.19 ± 1.38 L/min per m^2 ; $P > 0.2$) when the blood lactate level was 14.2 mmol/L. The systemic oxygen delivery was 938 ± 118 mL/min (controls, 1137 ± 490 mL/min; $P > 0.2$) and oxygen utilization was 211 ± 51 mL/min (controls, 213 ± 87 mL/min; $P > 0.2$). Thus, cardiac output, oxygen extraction, and both oxygen delivery and utilization were in the normal range (7, 8) and did not differ in controls (Figure 1).

Four patients died of cardiovascular collapse secondary to progressive metabolic acidosis (see Table 1). In all four, the arterial pH fell below 6.85 and the lactate level was higher than 15 mmol/L before death. However, in the other three patients, arterial pH and blood levels of lactate did not change substantially during hospitalization, and all were discharged in a lucid and ambulatory state. Within 15 months, all had died of other complications of AIDS (see Table 1).

Discussion

In seven patients with HIV infection who did not have shock, sepsis, malignancy, or other causes of systemic hypoxemia, lactic acidosis developed suddenly

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Table 1. Seven Patients with Human Immunodeficiency Virus Infection and Lactic Acidosis*

Patient	Clinical Presentation	Age	Blood Pressure	Arterial Lactate	Arterial pH
		y	mm Hg	mmol/L	
1	Homosexual man with Kaposi sarcoma, admitted with weakness, fatigue and wasting; blood gases evaluated because of fall in bicarbonate after 1 week in the hospital	46	110/70	10.4	7.27
2	Homosexual man with adrenal insufficiency, admitted with nausea, emesis and dyspnea, tachypnea; dyspnea led to blood gas measurements on hospital day 2	42	160/90	17.6	7.28
3	Homosexual man with duodenal ulcer and esophagitis, admitted for sudden tachypnea and dyspnea; blood gases measured at admission to hospital	40	100/75	12.4	7.26
4	Heterosexual man contracted AIDS from blood transfusions; admitted for fever, wasting, and fatigue; blood gases evaluated on day 2 because of tachypnea and a fall in bicarbonate	29	120/75	13.1	7.09
5	Homosexual man admitted with dyspnea and tachypnea; on day 2, blood gases were evaluated because of a low bicarbonate in the absence of symptoms	54	100/75	17.4	7.15
6	Heterosexual woman contracted AIDS from blood transfusions; admitted with dyspnea and anorexia; lactic acidosis diagnosed after admission blood gas evaluation	43	144/82	15.0	7.22
7	Heterosexual woman contracted AIDS from a male bisexual lover; admitted with malaise, nausea, emesis, dyspnea, and anorexia; lactic acidosis was diagnosed after admission blood gas evaluation	46	104/60	14.2	7.27
Mean ± SD		43 ± 8		14.3 ± 2.6	7.22 ± 0.07

* AIDS = the acquired immunodeficiency syndrome.

† Four patients died in the hospital, and three were discharged from the hospital.

and without obvious cause. In these patients, the arterial P_{O_2} , cardiac index, oxygen delivery, oxygen utilization, and oxygen extraction ratio were not significantly different from those of controls, providing no evidence

for systemic hypoxemia or tissue hypoxia. Although oxygen delivery and utilization were evaluated in only three patients, the normal oxygen extraction ratio strongly suggests that all had normal oxygen utilization.

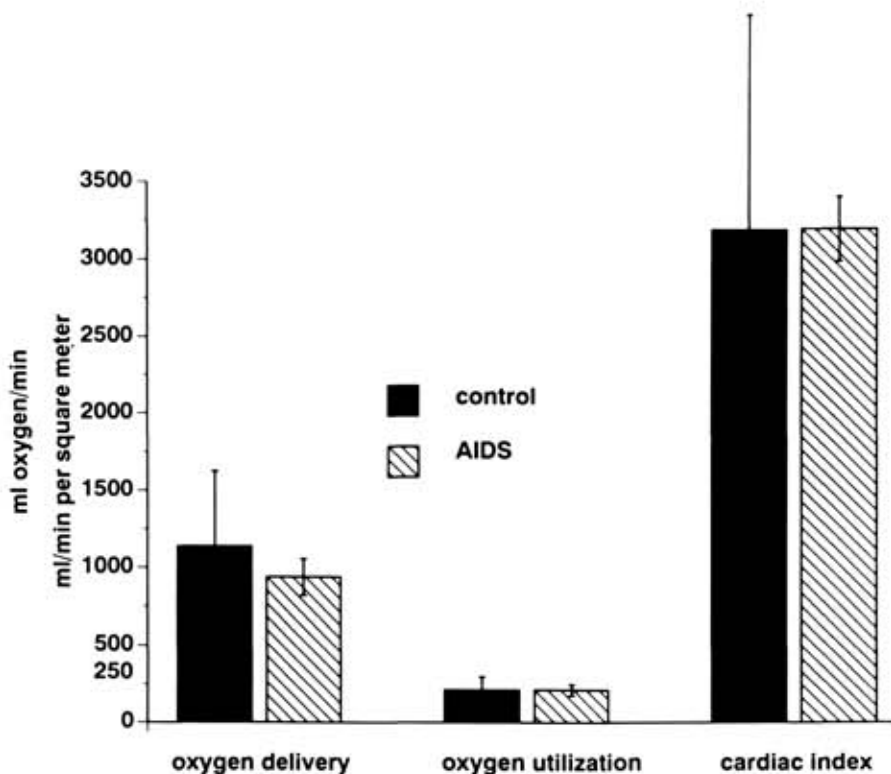


Figure 1. Oxygen delivery, oxygen utilization, and cardiac index in three patients with the acquired immunodeficiency syndrome (AIDS) and lactic acidosis and in nine control patients. The cardiac index and oxygen delivery and utilization are all within one standard deviation (SD) of the control values. Data are presented as mean ± SD.

Table 1—Continued

Arterial P_{CO_2}	Arterial P_{O_2}	Arterial Bicarbonate	Arterial Oxygen Saturation	Unmeasured Anion	Outcome†
mm Hg	mm Hg	mmol/L	%	mmol/L	
16	106	7.4	97	21	After 4 weeks in the hospital, died of cardiovascular collapse secondary to metabolic acidosis, with arterial pH below 6.85
11	132	5.1	98	32	Died of cardiovascular collapse secondary to metabolic acidosis on hospital day 5, with arterial pH below 6.85; autopsy revealed no reason for lactic acidosis
21	96	9.3	98	26	Discharged from hospital after 5 days; died 6 months later and autopsy revealed no reason for lactic acidosis
16	150	5.4	98	25	Died of cardiovascular collapse secondary to metabolic acidosis on hospital day 5, when arterial pH was below 6.85
10	168	3.5	99	32	After 2 weeks, lactic acidosis resolved spontaneously with no specific therapy; discharged free of lactic acidosis but died after 15 months of AIDS-related complications
21	152	8.8	99	33	Discharged from hospital after 4 weeks with lactic acidosis; died of unrelated causes 5 weeks later; autopsy revealed no reason for lactic acidosis
21	100	9.6	97	26	After 3 weeks, suddenly had worsening of lactic acidosis; died of cardiovascular collapse, with arterial pH below 6.85
17 ± 5	129 ± 29	7.0 ± 2.4	98 ± 1	28 ± 5	

All had normal blood pressure with no evidence of shock or sepsis, so that substantial shunting of blood was clinically unlikely.

The disorder in the patients resembled adult Reye syndrome, in that type B lactic acidosis was associated with a probable infectious cause (9). Increased production of lactate may also have been associated with a myopathy related to zidovudine therapy. Such a myopathy can cause a decrease of muscle respiratory chain capacity in some patients with AIDS (10). Lactic acidosis was a major comorbid event in four patients, but the other three survived an average of 32 weeks, suggesting a heterogeneous cause.

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