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LETTER TO THE EDITOR

Consecutive blood lactate assessment in HIV-infected children: correlation with therapy and clinical characteristics

The issue of blood lactate in HIV-infected children treated with antiretrovirals has recently been addressed.[1] Hyperlacticacidemia is increasingly being recognized as a serious concern among HIV-infected patients and is fatal in some cases, but there are no firm data regarding differences by age, sex, race or exposure to different antiretroviral therapies or to particular risk factors.[2—7] Hyperlacticacidemia and lactic acidosis do occur in both adults and children, but it is unclear whether severe lactic acidosis is preceded by a period of increased plasma lactate level (PLL) and prospective studies of the prevalence of lactate levels are lacking.[8]

The plasma lactate level was evaluated in two different blood samples taken one year apart (mean 12.4 months, range 7—18 months) in children attending the infectious diseases clinic at the University of Genoa. The purpose of the determination after 12 months was to assess the eventual occurrence of increased PLL in children with previously normal values. Children who had altered values at the first determination had normal or stable values in the following determination after four to eight weeks. All patients underwent regular clinic visits and laboratory assessments every four to eight weeks and their compliance with antiretroviral therapy was considered good. PLL was first determined between 1 January and 31 March 2002 and then again between 1 January and 31 March 2003.

Fifty-one children (28 males, 23 females) were evaluated, with a mean age of 11.02 years (range 1—19 years); 49/51 children (27 males, 22 females) underwent both lactate assessments. According to CDC staging, 31/51 (61%) patients were symptomatic (stage B or C) and 20 (39%) were asymptomatic (stage A or N). Fat redistribution, identified by physical signs of central fat accumulation, peripheral lipoatrophy or both, was observed at baseline in 14/51 children (27%). Baseline characteristics did not differ between the two determinations regarding CDC staging and fat redistribution.

Possible risk factors for increased PLL were considered to be: gender, fat redistribution, CDC stage and current antiretroviral therapy. In particular, regimens containing didanosine (DDI), stavudine (D4T), DDI + D4T, protease inhibitors (PIs) and DDI + D4T + PI were considered. Plasma lactate level was considered normal below 2.0 mmol/l.

None of the children showed clinical signs or symptoms related to hyperlacticacidemia at the first lactate determination. PLL was increased in 23/51 patients (45%) at the first assessment and in 11/49 (22%) at the second assessment.

At the time of the two blood samples, antiretrovirals were being administered to 45/51 (88%) and 45/49 children (92%) respectively: nine (18%) and ten patients (20%) received dual nucleoside reverse transcriptase inhibitors (NRTI) or a PI-sparing therapy; 36 (70%) and 35 (71%) received a PI-containing therapy. Mean duration of their current therapy was 27.4 months (range 0—66) and 35.2 months (range 0—77) respectively, while the cumulative time of exposure to the different antiretrovirals was 80.6 months (range 0—164) and 94.2 months (range 0—178).

PLL was studied as the primary variable. All the comparisons between groups were carried out using the χ^2 test (Table 1). In both determinations, increased lactate levels were observed more frequently in females, in patients with more advanced infection, those affected by lipodystrophy and those treated with PI and less frequently in those only treated with NRTIs. An association with duration of treatment was not found. Increased PLL in the second sample occurred significantly more frequently in children with previously altered values ($p = 0.039$).

Recently, several studies have implicated therapy with stavudine and/or didanosine as a risk factor for

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Table 1 Association of plasma lactate levels (PLL) with all considered risk factors.

1st assessment (51 patients) PLL 1st sample	Total number of cases	Normal PLL N	%	Increased PLL N	%	*p* values
PLL 1st sample						
Females	23	10	43.5	13	56.5	0.114
Males	28	18	64.3	10	35.7	
CDC stage B or C	31	16	51.6	15	48.4	0.383
CDC stage A or N	20	12	60	8	40	
Lipodystrophy	14	6	42.9	8	57.1	0.227
No lipodystrophy	37	22	59.5	15	40.5	
Antiretroviral	45	24	53.3	21	46.7	0.434
No antiretroviral	6	4	66.7	2	33.3	
DDI	19	11	57.9	8	42.1	0.485
No DDI	32	17	53.1	15	46.9	
D4T	27	15	55.6	12	44.4	0.572
No D4T	24	13	54.2	11	45.8	
DDI + D4T	16	9	56.3	7	43.8	0.570
No DDI + D4T	35	19	54.3	16	45.7	
PI	36	18	50	18	50	0.218
No PI	15	10	66.7	5	33.3	
DDI + D4T + PI	16	9	56.3	7	43.8	0.570
No DDI + D4T + PI 2nd assessment (49 patients)	35	19	54.3	16	45.7	
PLL 2nd sample						
Females	22	16	72.7	6	27.3	0.348
Males	27	22	81.5	5	18.5	
CDC stage B or C	31	23	74.2	8	25.8	0.357
CDC stage A or N	18	15	83.3	3	16.7	
Lipodystrophy	14	7	50	7	50	0.007
No lipodystrophy	35	31	88.6	4	11.4	
DDI	23	16	69.6	7	30.4	0.180
No DDI	26	22	84.4	4	15.4	
D4T	29	21	72.4	8	27.6	0.248
No D4T	20	17	85	3	15	
DDI + D4T	17	12	70.6	5	29.4	0.307
No DDI + D4T	32	26	81.3	6	18.8	
PI	35	25	71.4	10	28.6	0.103
No PI	14	13	92.9	1	7.1	
DDI + D4T + PI	15	11	73.3	4	26.7	0.450
No DDI + D4T + PI	34	27	79.4	7	20.6	
Altered PLL 1st sample	22	14	63.6	8	36.4	0.039
Normal PLL 1st sample	27	24	88.9	3	11.1	

DDI: didanosine; D4T: stavudine; PI: protease inhibitor; CDC: Centers for Disease; Control; PLL: plasma lactate level.

hyperlacticacidemia or lactic acidosis; in this study, a correlation with elevated PLL was especially found with the use of PIs. This study found increased PLL in treated children and those with lipodystrophy, as is also described elsewhere.[1,9]

It has been found that increased PLL does not appear to be predictive either of consecutive altered values or of severe hyperlacticacidemia in HIV-infected children: one patient had fatal lactic acidosis and her previous PLL was normal.[10]

Consecutive follow-up and larger cohorts of children will allow better identification of the risk factors for elevated PLL and for hyperlacticacidemia.

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