Lactic Acidosis in HIV Infected Children Due to Antiretroviral Therapy

Lactic acidosis is predominantly seen in patients receiving nucleoside reverse transcriptase inhibitors (NRTI)(1). It presents as malaise, nausea, vomiting along with abdominal pain, hyperventilation, hepatomegaly, and muscle weakness. Laboratory parameters reveal hyperlactemia and metabolic acidosis with increased anion gap(2,3). Obesity, female gender, prolonged use of NRTI, a combination of stavudine and didanosine especially during pregnancy and stavudine based regimes are known risk factors(4,5). We present 2 HIV infected children who developed lactic acidosis on prolonged antiretroviral therapy (ART) and were on stavudine at the time of lactic acidosis.

A 5½-year-old HIV infected girl had chicken pox, failure to thrive (weight = 12 kg, < 5th centile), generalized lymphadenopathy and hepatosplenomegaly. She was started on ART due to clinical deterioration and immunological suppression. Her serial CD4 and virological parameters with ART regimes are depicted in *Table I*. At 9½ years of age, she had positive Mantoux test (20 × 15 mm) with weight loss and normal *X*-ray chest. She was started on antituberculous therapy (ATT) consisting of isoniazid and rifampicin for 6 months and ART regime was changed in view of clinical, immunological and virological deterioration (*Table I*). At 10 years of age, she presented with vomiting, hyperventilation, severe metabolic acidosis (pH = 7.09, HCO_3 = 3.7 mmol/L), hyperbilirubinemia (5.1 mg/dL) and normal transaminases Serum lactate was 30 mg/dL. Ultrasound of abdomen revealed hepatomegaly.

Similarly, another 4½-years-old HIV infected boy suffering from pulmonary tuberculosis, on ATT since 6 months had recurrent fever and cough since 2 years. On examination, he was malnourished (weight = 8 kg, <5th centile and height = 85 cm, <5th centile), had hepatosplenomegaly with

TABLE I–*Serial Immunological and Virological Parameter of Both Patients.*

	CD4 count (cells/cumm)	CD percent (%)	Viral load (copies/mL)	ART regimes started
Patient 1				
Baseline	318	11	102508	AZT + 3TC
After 2 years	987	21	47164	AZT + 3TC
After 3 years	533	18	72544	D4T + 3TC + NVP
After 4 years	682	22	2355	D4T + 3TC + NVP
After 4½ years	370	15	46606	D4T + ddI + EFV
Patient 2				
Baseline	418	7.4	–	AZT + 3TC + NVP
After 6 months	1106	18.36	–	AZT + 3TC + NVP
After 1 year	200	11.8	–	D4T + 3TC + EFV

AZT= Zidovudine, 3TC = Lamivudine, NVP = Nevirapine, d4T = Stavudine, ddI = Didanosine, EFV= Efavirenz

bilateral otorrhea, right sided crepitations and clubbing. His baseline immunological workup was suggestive of severe immune suppression (*Table I*). He was started on 3 drugs ART. After 6 months of ART, his weight had increased by 3 kgs, *X*-ray chest showed improvement and his immunological parameters improved (*Table I*). ATT was stopped after 1 year of therapy. At 6½ years of age, he had pyogenic meningitis, which responded to IV antibiotics. ART regime was changed in view of a severe infection and immunological deterioration (*Table I*). At the age of 7½ years, he had severe breathlessness. His blood gases revealed metabolic acidosis (HCO_3 = 15.6 mmol/L) and serum lactate was elevated (37 mg/dL).

Both patients were treated with bicarbonate infusions, thiamine, riboflavin and carnitine to which they responded and ART was continued. Both were advised protease inhibitors when changing the ART regime due to regime failure but could not afford the same. Also, ART regime has been adjusted on clinical and immunological parameters due to unavailability of drug resistance testing.

Severe decompensated lactic acidosis may be fatal and requires urgent management. The clinician should suspect the same on clinical symptoms as well as other laboratory abnormalities.

Ira Shah,
Department of Pediatric HIV Clinic,
B. J. Wadia Hospital for Children,
Parel, Mumbai 400 012, India.
E-mail: irashah@pediatriconcall.com

REFERENCES

1. Fortgang IS, Belitsos O, Chaisson R, Moore RD. Hepatomegaly and steatosis in HIV-infected patients receiving nucleoside analogue antiretroviral therapy. Am J Gastroenterol 1995; 90: 1433-1436.
2. Brinkman K, ter Hofstede HI. Mitochondrial toxicity of nucleoside analogue reverse transcriptase inhibitors : lactic acidosis, risk factors and therapeutic options. AIDS 1999; 1: 141-148.
3. Boxwell DE, Styrt BA. Lactic acidosis in patients receiving nucleoside reverse transcriptase inhibitors. 39th Inter science Conference on Antimicrobial Agents and Chemotherapy. San Francisco, CA,1999. Abstract 1284.
4. Lonergan JT, Behling C, Pfander H, Hassanein TI, Mathews WC. Hyperlactatemia and hepatic abnormalities in 10 human immunodeficiency virus - infected patients receiving nucleoside analogue combination regimens. Clin Infect Dis 2000; 31: 162-166.
5. Chen C, Vazquez - Padua M, Cheng Y. Effect of anti-human immunodeficiency virus nucleoside analogues on mitochondrial DNA and its implications for delayed toxicity. Mol Pharmacol 1991; 39: 625-628.