Letter to the editor

Severe metabolic acidosis and Fanconi syndrome during stavudine and abacavir therapy in a resource-limited setting

Dear Editor,

Lactate acidosis due to mitochondrial toxicity has been particularly associated with stavudine and didanosine, but has also been reported in regimens with nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), which are considered to have less mitochondrial toxicity.\(^1,2\) Lactate acidosis presents with malaise, nausea, vomiting, fatigue, tachypnoea, liver involvement, and dysrhythmia, and can be lethal.\(^1\) Obesity and female gender are considered risk factors.\(^1,3\) Tenofovir, NRTI, is associated with Fanconi syndrome, which is characterized by metabolic acidosis, hypophosphatemia, hypokalemia, proteinuria, glucosuria, polyuria and renal failure.\(^3\) Cases of Fanconi syndrome associated with NRTIs have been published.\(^4\) Mitochondrial toxicity may contribute to nephrotoxicity.\(^4\) Concomitant lactate acidosis and Fanconi syndrome with NRTIs has been reported.\(^3,5\) The first-line antiretroviral regimen in Suriname contains zidovudine, lamivudine, and nevirapine. Available replacement drugs are stavudine, abacavir, didanosine, tenofovir, and efavirenz. Lactate measurements are unavailable in our resource-limited setting.

A compliant HIV-infected obese East-Indian woman (BMI 46.4 kg/m\(^2\)) in her mid-thirties received a regimen consisting of abacavir, stavudine and lamivudine after the development of nevirapine hepatotoxicity and zidovudine-related anemia. She came to the emergency room three months after the start of this changed regimen with development of dyspnea, weakness, constipation, and vomiting. She was dyspneic and had a respiratory rate of 42 breaths/minute, blood pressure of 150/90 mmHg, heart rate of 110 bpm, temperature of 36.5 °C and oxygen saturation measured by pulse oximetry of 88%. Venous blood analyses revealed a pH of 7.21, base excess of -14.3 mmol/L, bicarbonate value of 13.3 mmol/L, hypokalemia (2.5 mmol/L; normal range 3.6-5.0), hypophosphatemia (0.50 mmol/L; normal range 1.00-1.60), and elevated LDH (1,031 IU/L; normal range 240-480). She had proteinuria. Previous values were normal. Her CD4 count was 175 cells/\(\mu\)L (initial count 110 cells/\(\mu\)L). Chest X-rays were normal. Ultrasonographic abdominal examination revealed possible abnormalities of the kidney parenchyma and hepatic steatosis. Initial intensive care unit (ICU) admittance was not possible due to limited capacity. Antiretroviral therapy was stopped, and she received bicarbonate intravenously, vitamin B supplementation, supportive fluids, and oxygen. Metabolic acidosis persisted, with arterial pH values reaching 7.2. Furthermore, she had polyuria, with a mean urine output of 6.1 L/day. Despite ICU admission on the 11\(^{th}\) day, she died after 12 days of hospitalization.

The presence of severe metabolic acidosis and hepatic steatosis in our case, despite discontinuation of antiretroviral therapy, is suggestive of stavudine toxicity.\(^1\) A contribution of abacavir is possible. Lamivudine is less suspected. Hypokalemia, hypophosphatemia, and polyuria, in our case, are suggestive of Fanconi syndrome and should most likely be ascribed to stavudine and possibly abacavir.\(^3,4\) We thus show the development of severe metabolic acidosis and Fanconi syndrome due to possible combined stavudine and abacavir toxicity. An earlier case of stavudine-associated metabolic acidosis in our setting had a better outcome. Eliminating stavudine from first-line regimens limits the possibility of using fixed-dose combinations in Suriname. These cases support the policy for resource-limited settings of using stavudine as a last-resort treatment option. We emphasize that continuous education is necessary despite limited resources.

Conflict of interest

All authors declare to have no conflict of interest.

REFERENCES


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