Letters to the Editor

Hyperlactatemia and Human Immunodeficiency Virus Infection: Lessons from the Era of Antiretroviral Monotherapy

Lactic acidosis is a life-threatening complication of antiretroviral therapy with nucleoside reverse transcriptase inhibitors (NRTIs) (2, 3), and there is a spectrum of conditions associated with lactic acid elevation, ranging from moderate asymptomatic hyperlactatemia to life-threatening lactic acidosis. Identification of the compounds responsible for hyperlactatemia is uneasy, because most patients now receive combination therapies (8). Isolated case reports have suggested the role of single-NRTI treatment in the development of hyperlactatemia, but little is known about the role of human immunodeficiency virus (HIV) infection (1, 7). Data obtained in the era of single-agent antiretroviral therapy could be helpful in assessing the roles of individual NRTIs and of HIV itself.

Between May 1991 and December 1992, we measured lactic acid in blood from 53 unselected HIV-infected patients evaluated in a specialized unit. Testing for blood lactate was part of a routine clinical and biological evaluation of HIV disease. None of them had sepsis, fever, acute disease, respiratory or cardiac failure, recent surgery, or recent traumatism or engaged in intense physical activity. Both asymptomatic (20 of 53) and symptomatic (33 of 53) patients were evaluated. Symptomatic patients had fatigue, myalgia, or proximal weakness. Thirty-five patients were receiving NRTIs; 31 were receiving zidovudine (200 to 1,000 mg/day), and 4 were receiving didanosine (250 to 400 mg/day). Eighteen patients were not treated by NRTIs. Zidovudine receivers had no history of lactic acidemia. Zidovudine receivers had no history of treatment with another NRTI. The total cumulated dose of zidovudine was 35 to 660 g (median, 230 g). The CD4 count was 0 to 540 (median value, 100/mm\(^3\)) for patients receiving NRTIs and 10 to 1,000 (median value, 380/mm\(^3\)) for untreated patients. Venous blood samples were collected with the patients at rest between 8:30 and 10:30 a.m. after an overnight fast. Samples were obtained by direct venipuncture without venostasis or hand clenching. The samples were frozen, stored at −20°C, and assayed within 4 days. Lactic acid was measured from the supernatant (4). Lactatemia was abnormal if higher than 1.5 mmol/liter (reference values obtained using the same technique and blood draw protocol from 45 subjects in whom the diagnosis of mitochondrial disorder could be excluded were 0.3 to 1.5 mmol/liter [mean ± 2 standard deviations]).

Hyperlactatemia was found in 18 patients (18 of 53 [34%]; 1.6 to 7.5 mmol/liter [median, 2.0 mmol/liter]) of whom 17 (94%) were receiving NRTIs (zidovudine, 14; didanosine, 3). The proportion of patients with hyperlactatemia was higher for patients treated with NRTIs than for untreated patients (17 of 35 versus 1 of 18; \(P = 0.002\) [Fisher's exact test]). Lactatemia correlated with the total cumulated dose of zidovudine received (Spearman correlation coefficient, \(r = 0.54\); \(P = 0.002\) ) and, to a lesser extent, with the duration of treatment by NRTIs (\(r = 0.39\); \(P = 0.02\) ). We tested the influence of the stage of disease on lactatemia: no correlation was found between the CD4 count and lactatemia (\(r = -0.13\); \(P = 0.36\)).

Following strict criteria for blood sampling, lactic acid determination, and comparison to normal values, we found that hyperlactatemia in HIV-infected patients was commonly associated with treatment by zidovudine or didanosine. The correlation between lactatemia and the total received dose of zidovudine is another argument for considering this compound to be responsible for hyperlactatemia. Such a correlation was not evaluated with didanosine receivers because of the small number of patients. Lactate elevation was uncommon among untreated HIV-infected patients. The absence of correlation of lactatemia and CD4 counts suggests that the comparison between treated and untreated patients is appropriate even though median CD4 counts are different.

There is evidence that combination therapy may exacerbate some metabolic toxicities (5, 6). Our findings of relatively common hyperlactatemia in patients on zidovudine or didanosine monotherapy strengthen the association between this condition and nucleoside analogues.

This study was supported by a grant to P. Chariot from Sidaction (Paris, France).

REFERENCES


Patrick Chariot*
Nacer Bourokba
Department of Legal Medicine
Hôpital Raymond-Poincaré
92380 Garches
France

Isabelle Monnet
Department of Pneumology
Centre Hospitalier Intercommunal
94010 Créteil, France

Romain Gherardi
Department of Pathology
Hôpital Henri-Mondor
94010 Créteil, France

*Phone: 33 1 47 10 76 97
Fax: 00 33 1 47 10 76 99
E-mail: patrick.chariot@rpc.ap-hop-paris.fr