SCIENTIFIC LETTER

Stavudine dosage reduction: Effect on symptomatic hyperlactataemia and lactic acidosis in patients at Dr George Mukhari Hospital, Pretoria

To the Editor: A range of studies have demonstrated that symptomatic hyperlactataemia and lactic acidosis are associated with antiretroviral combinations containing stavudine.[1,2] The HIV treatment programme in Khayelitsha, Cape Town, which began using stavudine as a first-line therapy in 2003, reported approximately 10% of patients switching from stavudine to the alternative drug after 12 months due to hyperlactataemia.[3] Following a meta-analysis showing that lower doses of stavudine are safer and as effective, the World Health Organization (WHO) issued a statement that only a low dose of stavudine (30 mg) should be used.[4]

This retrospective review included patients treated at the adult HIV clinic at Dr George Mukhari Hospital, Pretoria, South Africa. The study was approved by the Medunsa Research Ethics Committee (reference MP 156/2005). The records of 86 patients (aged 27 - 59 years) initiated on stavudine-containing antiretroviral therapy regimens between 2004 and 2006 were analysed: 66 females (29 received 40 mg stavudine; 37 received 30 mg stavudine) and 20 males (7 received 40 mg stavudine; 13 received 30 mg stavudine). Lactate levels were not routinely determined for all patients (only when a clinician suspected lactic acidosis or symptomatic hyperlactataemia on the basis of clinical symptoms). A serum lactate level >2.0 mmol/l was considered to be elevated. Lactic acidosis was defined by persistently increased blood lactate levels (>5 mmol/l) in association with acidosis (pH <7.35) and a bicarbonate level ≤ 20 mmol/l.[5]

Among female patients, elevated lactate levels developed in 18/29 (62%) treated with 40 mg stavudine, but only 13/37 (35%) treated with 30 mg of stavudine (range 2.3 - 9.8 mmol/l). Among male patients, elevated lactate levels developed in 2/14 (14%) treated with 30 mg stavudine and 2/7 (29%) treated with 40 mg stavudine.

Thirty-five patients (41%) had elevated lactate levels with signs or symptoms that obliged clinicians to cease treatment. The relative odds of developing elevated lactate levels when commencing treatment were 2.92 times higher in the group receiving 40 mg stavudine than in the group receiving 30 mg stavudine (95% confidence interval 1.10 - 2.51). The relative risk (RR) ratio was higher for female patients, with a greater risk for developing hyperlactataemia than males (RR 2.17 for 40 mg stavudine; RR 2.28 for 30 mg stavudine) (Table 1).

The onset of the first symptoms of elevated lactate levels occurred from 2 to 18 months following treatment initiation. Of the 35 patients with elevated lactate levels, 43% (*n*=15) were obese and 4 (11%) died due to complications of lactic acidosis.

This analysis demonstrated that stavudine dose reduction increased the odds of patients being more stable on treatment with fewer reported side-effects. Stavudine-containing regimens should be avoided in obese female patients. Low-dose stavudine (20 mg) may offer alternative solutions in poor or resource-limited settings, with a lower associated risk of toxicity and side-effects; however, virological non-inferiority to the first-line treatment option should be established.

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Table 1. Elevated lactate level in patients receiving 30 mg or 40 mg stavudine

	40 mg stavudine	30 mg stavudine	OR (95% CI)
Female, *n* (%)			3.02 (1.10 - 8.29)
Elevated lactate levels	18 (27)	13 (20)	
Normal lactate levels	11 (17)	24 (36)	
Total	29 (44)	37 (56)	
Male, *n* (%)			2.20 (0.24 - 20.00)
Elevated lactate levels	2 (10)	2 (10)	
Normal lactate levels	5 (25)	11 (55)	
Total	7 (35)	13 (65)	

OR = Odds ratio; CI = confidence interval.

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