**Absence of Sustained Hyperlactatemia Among HIV-Infected Patients with Risk Factors for Mitochondrial Toxicity**

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**Background:** Published reports of the prevalence of asymptomatic hyperlactatemia among HIV-infected individuals have ranged from 4-36%. The variability in the reported asymptomatic hyperlactatemia prevalence may reflect cohort differences in risk factors for hyperlactatemia and/or techniques for venous lactate collection.

**Methods:** We examined the prevalence of elevated venous lactate levels among HIV-infected, nucleoside reverse transcriptase inhibitor-treated subjects with one or more of the following risk factors associated with hyperlactatemia: previous hyperlactatemia; anion gap >15 mmol/L; \( \text{HCO}_3^- <20 \text{ mmol/L} \); d4T use for >6 months; recently elevated ALT, CK or LDH; mild-moderate nausea, fatigue or abdominal discomfort; peripheral neuropathy; lipoatrophy or osteopenia/porosis. Venous lactate levels were collected in accordance with strict Adult AIDS Clinical Trials Group (AACTG) guidelines without tourniquet or fist clenching. *Sustained hyperlactatemia was defined as two consecutive elevated nonexercise, venous lactate levels greater than or equal to 1.5 X the upper limit of normal (ULN) and less than or equal to 4 X ULN, the second of which must be fasting and measured no more than 30 days apart.*

**Results:** 83 subjects (14% women, 65% non-white) were enrolled. At entry, 71% were receiving d4T, 63% had increased anion gap, 17% had ALT > upper limit of normal (ULN), 14% self-described lipoatrophy, 11% peripheral neuropathy, 6% low \( \text{HCO}_3^- \) and 2% osteopenia. Mild abdominal discomfort
was reported in 10% and nausea in 2%. Two thirds of the subjects had 2 or more risk factors with 11% having greater than 4. The median initial venous lactate levels for the cohort was 1.2 mmol/L (range 0.7 – 5.1 mmol/L). Two subjects had a lactate level > 1.5 X ULN during the study: a subject with a value of 2.1 X ULN at entry and a week 2 level of 1.2 X ULN and a subject with a week 2 value of 1.9 X ULN but an entry lactate level of 1.4 X ULN. The latter subject developed symptomatic lactic acidosis 3 weeks following study discontinuation (less than 6 weeks from the entry visit). Therefore, during the study, no cases of sustained asymptomatic hyperlactatemia (above 1.5 X ULN) or symptomatic lactate elevation were detected although, one case of evolving lactic acidosis was diagnosed after completion of the study.

**Conclusions:** Sustained asymptomatic hyperlactatemia among subjects with risk factors previously associated with hyperlactatemia was not observed when venous lactate levels were measured in a standardized fashion. However, one case of hyperlactatemia, which evolved into symptomatic lactic acidosis was diagnosed soon after the completion of the study. Our findings indicate that asymptomatic hyperlactatemia is either very rare or an artifact of collection technique.

There were no episodes of symptomatic hyperlactatemia or lactic acidosis during the study. A 95% confidence interval for the prevalence of hyperlactatemia given our data (i.e., 0 out of 83) is (0, 3.54%). In other words, the true prevalence of hyperlactatemia as defined by this study is likely to be less than 3.54%.

95% CI = (0, 1−"n") = (0, 3.54%)