The Influence of Antiretroviral Therapy on the QTc Interval in an African Cohort

To the Editor—Cardiovascular disease in human immunodeficiency virus (HIV) infection encompasses a wide range of pathologic entities, including myocardial, pericardial, and endocardial disease, atherosclerosis, arrhythmias, and vasculitis. The most common manifestations of HIV-associated heart disease in sub-Saharan Africa are pericarditis, cardiomyopathy, and pulmonary hypertension [1]. Coronary artery disease, lipodystrophy, and metabolic syndrome, although common in developed countries, are traditionally thought to be less clinically significant problems in the African subcontinent [2]. It is well known that prolongation of the QT_C interval can predispose patients to potentially fatal ventricular tachyarrhythmias, particularly torsades de pointes, and thus is an independent predictor of cardiovascular morbidity and mortality [3].

The aim of this study was to determine whether there is an association between antiretroviral (ARV) therapy and prolonged QT in HIV-positive ARV-treated patients in Nairobi, Kenya. HIV-positive adults from both inpatient and outpatient departments at Aga Khan Teaching Hospital, Nairobi, were enrolled with exclusion criteria including any known cardiac disease. Patients were enrolled into either the "ARV-experienced" or "ARV-naive" arm of the study. The study was approved by the local ethics committee, and written informed consent obtained from all patients.

A standard 12-lead electrocardiogram was obtained in each patient, and a QTc interval of >440 ms was considered prolonged. A total of 299 HIV-positive patients were screened, 157 in the ARV-experienced arm and 142 in the ARV-naive control arm. A total of 27 patients in the ARV-experienced arm and 12 in the ARV-naive arm were excluded due to protocol violations, leaving 130 patients in each arm of the study (Table 1). QT_C interval prolongation was observed in 16.2% of patients in the ARV-experienced group, compared with 6.9% in the ARV-naive control group ($\chi 2 = 5.43$; $P = .01$); the odds ratio was calculated as 2.5 with a 95% confidence interval (1.01–6.67; $P = .02$). The overall prevalence of QTc prolongation across the whole subject cohort (ARV-experienced and ARV-naive) was 11.5%. When patients were divided by sex, prolongation was observed in 11.3% of male and 11.8% of female patients. The majority of patients with QTc prolongation had QTc intervals of 440–469 ms, and none had QTc intervals >500 ms (Table 2). There did not appear to be any significant difference in prevalence of QT_C prolongation between patients receiving a nonnucleoside analogue reverse-transcriptase inhibitor–based regimen and those receiving a protease inhibitor–based regimen ($P = .78$). In addition, there was no significant difference in prevalence of QTc prolongation between patients with World Health Organization stage I/II HIV infection and those with stage III/IV infection ($\chi 2 = 0.52$; $P = .47$), nor were there correlations with CD4 cell count ($r = -0.043$), in contrast to findings of other studies [4–6].

Literature on the association of QTc prolongation and ARV therapy is surprisingly sparse [7–10]. Our study shows that ARV therapy does appear to confer a significant increased risk of QT_C prolongation in HIV-positive patients, compared with ARV-naive controls. The increased risk has the potential to predispose otherwise medically stable patients to the development of potentially fatal ventricular arrhythmias, although the exact significance of an acquired asymptomatic QT_C prolongation in clinical practice is yet to be established.

These results should remind physicians of the importance of measuring and monitoring the QT_C interval for patients receiving ARV therapy and tailoring management accordingly, to successfully minimize cardiovascular morbidity and mortality as ARV drugs become readily available.

Notes

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Table 1. Baseline Characteristics of Study Patients

Patient characteristic	ARV-experienced patients	ARV-naive patients	*P*
Age, mean ± SD (range), y	42.0 ± 8.15 (23–72)	42.5 ± 8.17 (27–84)	.60
Sex ratio, M-F	0.97:1	1:1.13	.62
Weight, mean ± SD (range), kg	67.4 ± 12.8 (42–123)	66.9 ± 15.0 (40–112)	.77
Hypertension, no. (%)	30 (23.1)	34 (26.2)	.67
Diabetes mellitus, no. (%)	4 (3.1)	7 (5.4)	.54
Excess alcohol intake, no. (%)	1 (0.8)	12 (9.2)	.004
Current smoker, no. (%)	1 (0.8)	9 (6.9)	.02
CD4 cell count, mean ± SD, cells/mm^3	344 ± 269 (4–1308)	288 ± 331 (3–2000)	.14
Mean potassium level, mean ± SD, mmol/l	3.9 ± 0.47	4.0 ± 0.46	.09
eGFR, mean ± SD, mL/min	90.7 ± 23.7	83.9 ± 18.9	.03

Abbreviations: ARV, antiretroviral; eGFR, estimated glomerular filtration rate; SD, standard deviation.

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