
Acknowledgments

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References


QT Interval Prolongation and Antiretroviral Treatment: Another Point of Interest

To the Editor—In their recent brilliant article, Owens and Nolin [1] described how the QT interval can be prolonged by use of antimicrobials, such as macrolides and ketolides, certain fluoroquinolones and antimalarials, pentamidine, and the azole antifungals. The antimicrobials mentioned by Owens and Nolin [1] are widely administered worldwide, although for limited periods of time. On the other hand, ∼2 million persons are continuously exposed to antiretroviral therapy worldwide, and this number will probably increase as the HIV epidemic continues to spread and as antiretroviral therapy becomes available for more people, especially in developing countries. Indeed, from 2001 to 2005, the number of persons receiving antiretroviral therapy in low- and middle-income countries increased >5-fold from 240,000 to ∼1.3 million [2].

In recent years, there has been increasing concern with regard to QT interval prolongation in HIV-infected patients. Indeed, an increased prevalence of QT interval prolongation and a longer QT interval have been described in HIV-infected patients, compared with HIV-uninfected subjects [3–5]. QT interval prolongation in HIV-positive patients has been associated with alterations in cardiac innervation as a result of autonomic neuropathy [4, 6]. Moreover, several drugs administered to HIV-infected patients can cause a prolongation of the QT interval, including pentamidine [7], pyrimethamine [8], trimethoprim-sulfamethoxazole [9], methadone [10], clarithromycin [11], and ciprofloxacin [12, 13]. Furthermore, among antiretroviral drugs, efavirenz [14] and protease inhibitors [15, 16] have been reported as potential QT interval prolongers.

In a recent case-control study conducted at our institute, we were able to demonstrate an association between the administration of efavirenz or nelfinavir and the development of QT interval prolongation in HIV-infected individuals [17]. Moreover, we provided evidence that the risk of QT prolongation increased when efavirenz or nelfinavir therapy was combined with zidovudine therapy. In our opinion, clinicians who care for HIV-infected persons should be aware of the risk of QT interval prolongation, particularly if antiretroviral therapy is combined with drugs with known potential to prolong the QT interval.

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Reply to Chinello and Petrosillo

The interest and comments expressed by Chinello and Petrosillo [1] regarding our recent article about antimicrobial-associated QT interval prolongation in HIV-infected patients are greatly appreciated. Because of space constraints, we omitted any discussion regarding antivirals in our article [2]. We would like to echo the concerns raised in the letter by Chinello and Petrosillo [1], chief among them to emphasize the awareness of QT and metabolic liability of antiretroviral therapy among practicing clinicians involved in the care of HIV-infected patients [3]. Chinello and Petrosillo [1] mention that there is a high magnitude of patients receiving antiretroviral drugs, some of which have QT liability and/or metabolic liability (table 1); HIV infection may predispose patients to QT interval prolongation; and finally, a plethora of drugs are now identified to carry QT liability, many of which are likely to be administered to patients with HIV.

What makes the aforementioned findings clinically important is the fact that these drugs collide to create “multiple hits” to an individual’s repolarization reprograming clinically important is the fact that these drugs collide to create “multiple hits” to an individual’s repolarization reprograming clinically important is the fact that these drugs collide to create “multiple hits” to an individual’s repolarization. Considering the fact that nonnucleoside reverse-transcriptase inhibitors and protease inhibitors are also cytochrome P450 (CYP) substrates and notable inhibitors of CYP3A4 (table 1), the additional risk of interactions with numerous drugs warrants significant attention. For example, concurrent administration of drugs that inhibit CYP3A4 activity (e.g., macrolides and azole antifungals) with efavirenz or protease inhibitors, which are CYP3A4 substrates with QT liability, may lead to increased exposure of the latter, to QT

References