Management of antiretroviral-related neuropsychiatric adverse effects

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The introduction of highly active antiretroviral therapy has led to sustained suppression of viral replication, immune reconstitution and improved clinical outcomes. Clinical trials (1,2) have informed recommendations for specific regimens as preferred therapy in treatment-naïve HIV-infected individuals. Observational cohort studies (3-5) have indicated that the rate of viral rebound after initial suppression to an undetectable (less than 50 copies/mL) viral load varies according to specific antiretroviral agents. In these cohort studies, efavirenz in combination with a dual nucleoside backbone continues to be an effective third agent. In addition, clinical trials (6-8) have demonstrated that efavirenz can be combined in a nucleoside-sparing regimen with boosted protease inhibitors, and can be successfully substituted for protease inhibitors and maintain viral suppression (9). Efavirenz is generally well tolerated, with the most frequent side effects being neuropsychiatric, including dizziness, insomnia, somnolence, impaired concentration and vivid dreams. These symptoms are usually mild to moderate, usually self-limiting, and resolve after the first two to four weeks of efavirenz use. In one clinical trial (10), central nervous system (CNS) symptoms occurred in more than 50% of efavirenz-treated patients. In a substudy of the ACTG 5095 trial (A5095 [11]) in which patients were randomly assigned to receive efavirenz with or without abacavir, 6% of those patients receiving efavirenz experienced CNS symptoms or mood disorders that led to discontinuation of the agent. Symptoms occurred within the first week of therapy in those on efavirenz; however, these resolved within the first month with no evidence of significant differences in neuropsychological performance. No significant changes in anxiety or depressed mood were found (11-14). Longer term toxicity has been observed with persistence of neuropsychiatric disorders after a mean of two years on efavirenz. In one study (15) in which 20% of African-American patients (18-20). CYP2B6 genotypic effects. The neuropsychiatric toxicities have been associated with a CYP2B6 (G516T) genotype and other polymorphisms, which affect drug clearance, resulting in higher blood concentration levels. The CYP2B6*16 TT genotype may be found in 20% of African-American patients (18-20). CYP2B6 genotyping can lead to recognition of patients at risk of neuropsychiatric symptoms and to targeted interventions with the initiation of efavirenz therapy. The role of therapeutic drug monitoring to decrease the incidence of these symptoms requires evaluation.

REFERENCES


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