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Stepped-Dose vs. Full-Dose Efavirenz for HIV Infection and Neuropsychiatric Adverse Events: A Randomized Trial.

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BACKGROUND: More than 50% of patients who start efavirenz treatment develop limiting neuropsychiatric adverse events (NPAEs). OBJECTIVE: To assess whether a stepwise dose of efavirenz decreases the incidence and severity of NPAEs while maintaining virologic efficacy.

DESIGN: Randomized, double-blind, controlled trial. SETTING: 7 HIV clinics in Spain.

PATIENTS: 114 HIV-infected patients eligible for efavirenz treatment plus 2 nucleoside or nucleotide reverse transcriptase inhibitors. INTERVENTION: Random assignment (by computer-generated sequence) to efavirenz, 200 mg/d on days 1 through 6, 400 mg/d on days 7 through 13, and 600 mg/d on day 14 and after, or to efavirenz, 600 mg/d, from day 1 plus 2 nucleoside or nucleotide reverse transcriptase inhibitors chosen by patient's physician.

MEASUREMENTS: Neuropsychiatric symptoms and sleep quality were assessed by questionnaires at 0, 7, 14, and 30 days. Primary outcome was efavirenz-related NPAEs during the first 2 weeks, and secondary outcome was plasma HIV RNA level at 24 weeks.

RESULTS: Compared with the stepped-dose group, the full-dose group presented higher incidence and severity of dizziness (66.0% vs. 32.8%; P = 0.001), hangover (45.8% vs. 20.7%; P = 0.008), impaired concentration (22.9% vs. 8.9%; P = 0.038), and hallucinations (6.1% vs. 0%; P = 0.056) during the first week. From week 2, the incidence of efavirenz-related NPAEs was similar in both groups, although the severity was higher in the full-dose group. Virologic and immunologic efficacy seemed similar in both groups. Limitations: The sample size was calculated by selecting a high absolute difference in rates of efavirenz-related NPAEs between the groups. A lower absolute difference and a greater sample size could have made the differences between groups reach statistical significance beyond the first week. In addition, the sample size does not allow confirmation of similar efficacy between treatment groups.

CONCLUSION: A stepwise dose of efavirenz over 2 weeks reduces the incidence and intensity of efavirenz-related NPAEs while maintaining efficacy.

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