Lack of efficacy of low dose oral interferon alfa in symptomatic HIV-1 infection: a randomised, double blind, placebo controlled trial

Abstract:

BACKGROUND: Interferon alfa (IFN-alpha) exhibits dose related in vitro activity against human immunodeficiency virus (HIV), with complete inhibition of HIV replication at IFN-alpha concentrations > or = 256 IU/ml. In mid-1990, Kenyan investigators reported that oral administration of an extremely low dose (150 IU/day) of natural human (nHu) IFN-alpha resulted in complete alleviation of AIDS related complex and AIDS symptoms and resolution of opportunistic infections without additional treatment. Moreover, loss of HIV antibody seropositivity was reported in approximately 10% of treated patients. Subsequent small studies failed to substantiate these spectacular claims, but controversy on the efficacy of this treatment persisted. METHODS: We studied 559 adult Ugandan patients with WHO stage 2-4 HIV infection and a Karnofsky performance score of more than 50, who had not received any drugs with antiretroviral activity in the previous 3 months. The patients were randomly assigned in a double blind fashion either to 150 IU oral nHuIFN-alpha/day or placebo. The duration of treatment was extended from 28 weeks to 60 weeks 9 months after enrollment had started. At that time 112 subjects had already received 28 weeks of treatment and been discontinued from the study. RESULTS: Both study groups were comparable with respect to all baseline characteristics studied, except that the nHuIFN-alpha group had slightly lower absolute CD4+ lymphocyte counts (median 60.7 x 10(6)/l) than the placebo group (median 85.3 x 10(6)/l) ($p = 0.033$). Therefore, all analyses were adjusted for CD4+ lymphocyte counts at entry. In both treatment groups there was relentless progression of HIV disease. Subjects treated with nHuIFN-alpha and placebo had similar mortality, disease progression rates, decline of CD4+ lymphocyte counts and Karnofsky performance scores, and prevalence of symptoms. No patient reverted to HIV-1 seronegative antibody status. Serious adverse events were not seen. Quality control of the study medication documented that the active drug indeed contained IFN-alpha activity. CONCLUSIONS: The current large, randomised, double blind, placebo controlled study did not show any benefit from oral treatment with 150 IU nHuIFN-alpha/day in a population of African patients with symptomatic HIV infection.