Improvement of Depression and Anxiety after Discontinuation of Long-term Efavirenz Treatment.

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Introduction

Efavirenz is part of first-line antiretroviral therapy guidelines of WHO since 2002. The side effects of efavirenz are mainly neuropsychiatric and generally considered to be mild and transient. Recent studies indicate however that discontinuation of chronic efavirenz treatment can be observed in up to 50% of cases, which are mostly related to neuropsychiatric side-effects.

Aim of the study

To 1) assess neuropsychiatric symptoms in HIV-infected patients on long-term efavirenz therapy and 2) study the effect of a switch to non-efavirenz containing anti-retroviral treatment on neuropsychiatric symptoms.

Methods

A consecutive series of 47 HIV-infected participants on long-term efavrenz treatment were included in the present study. All participants were screened for neuropsychiatric symptoms using three self-report questionnaires*. In 24 patients no neuropsychiatric symptoms were noticed and efavirenz was continued. In 23 patients symptoms were found, efavirenz was discontinued, and reassessment using the questionnaires was done 2-weeks and 3-months after the switch of medication (Fig. 1).

*The depression-anxiety-stress-scale (DASS) was used to assess anxiety, depression and stress, the symptom-checklist (SCL-90) to assess a broad range of neuropsychiatric symptoms and the outcome-questionnaire (OQ-45) to assess daily life functioning.

Data were analyzed using repeated measures ANOVA to assess the effect of switching over time. A change in the percentage of patients scoring above norm scores after switching was analyzed using Chi square.

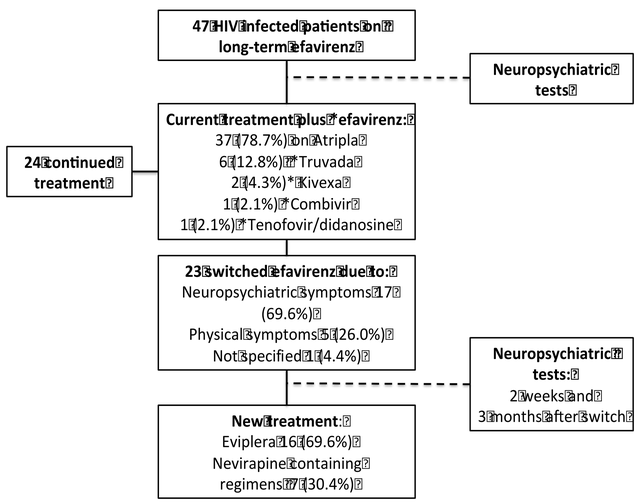


Fig 1 Consort flow chart of participants in the study

Results

The main neuropsychiatric symptoms reported were depressive and anxiety symptoms, insufficiency in thinking and physical symptoms. Comparing efavirenz switchers with those that continued treatment shows that those that switched had higher baseline levels of neuropsychiatric symptoms (on all three questionnaires).

Analyzing the scales separately for the effect of switching over time on the subscales showed improvement (Fig. 2a and 2b) on all subscales of the DASS ($F(2,21)=4,5$, $p=.016$) and SCL-90 ($F(2,21)=5.2$, $p=.010$). For the OQ-45 there was a trend to overall improvement ($F(2,21)=3.1$, $p=.057$) (Fig. 2c).

The total scores on all three questionnaires improved, particularly in those (n=17) switching because of neuropsychiatric symptoms (interaction time by group: $F(2,42)=3.2$, $p=.039$, Fig. 3). This differential effect of switching on neuropsychiatric symptoms was mainly observed on the SCL-90 (interaction time by group: $F(2,42)=4.5$, $p=.017$).

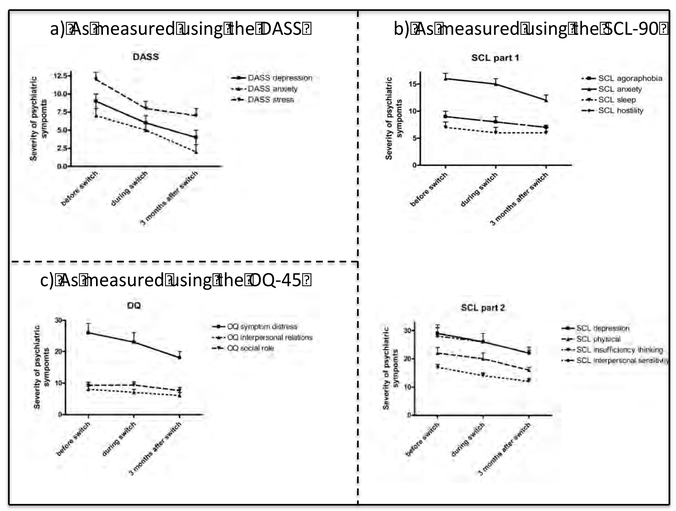


Fig 2 Change in neuropychiatric symptoms after switching from efavirenz, to a non-efavirenz containing treatment regimen

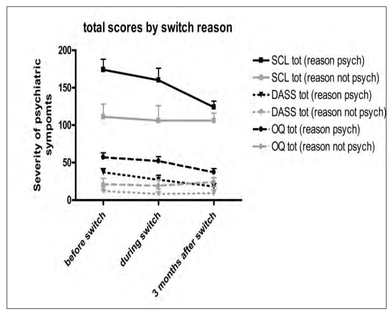


Fig 3 Change in neuropychiatric symptoms after switching from efavirenz to a non-efavirenz containing treatment regimen, based on the reason for switching

Conclusion

Neuropsychiatric symptoms are common among HIV-infected subjects and may be caused by different factors/agents, including long-term efavirenz use. DASS and SCL-90 can be used to identify those that may benefit discontinuation of efavirenz.