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Brief report

Mood, cognition and EEG changes during interferon α (alpha-IFN) treatment for chronic hepatitis C

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Abstract

Background: This study is aim to investigate concurrent long-term psychiatric, cognitive and neurophysiological measures of α-IFN neurotoxicity in the treatment of chronic viral hepatitis.
Methods: Twenty patients with HCV hepatitis were enrolled while treated with α-IFN (3–6 MU t.i.w. for 6–12 months). Neurotoxicity was evaluated by psychiatric [Hamilton Depression Rating Scale (HAM-D), Hamilton Scale for Anxiety (HAM-A), Beck Depression Inventory (BDI) and State-Trait Anxiety Inventory (STAI-Y)], complete cognitive and neurophysiological assessments (EEG spectral analysis, P300). Patients were assessed at baseline (t_0), 2 (t_1) and 6 months (t_2) since the beginning of therapy.
Results: Depression scores significantly increased (HAM-D: t_0=4.4±2.6; t_1=8.9±3.9, p<0.001; and t_2=7.7±3.8, p<0.001). A concurrent increase was shown also for anxiety (HAM-A: t_0=6.0±3.2; t_1=9.6±4.5, p<0.005; and t_2=9.1±4.5, p<0.005). Significant neurophysiological effects were also detected: increase of α power (p<0.05) in frontal derivations, reduction of the mean dominant frequency (p<0.005) and increase of theta power (p<0.05) in parietal derivations. In contrast, no significant cognitive changes occurred.
Limitations: The study was performed on a relative small sample of patients mainly with observational intentions. Biological data (e.g. blood cytokines samples) are not available: they could have given useful information about biological mechanisms related to the alterations observed.

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Conclusions: α-IFN treatment caused a time-dependent induction of symptoms of mild depression, concurrent anxiety and EEG changes. These psychiatric and neurophysiological changes can better explain the pharmacological profile of α-IFN and could help to address research on at risk population and, particularly, during pegylated-IFN therapy.

Keywords: α-interferon; Depression; EEG; Cognition; Chronic hepatitis C

1. Introduction

Interferon α (α-IFN) is a first-choice-treatment of chronic hepatitis C (Chemello et al., 1995). However, it is often hampered by adverse reactions, among which neuropsychiatric ones are frequent and impairing (Dieperink et al., 2000; Trask et al., 2000). Depression incidences range between 0% and 38% (Mulder et al., 2000; Otsubo et al., 1999; Quesada et al., 1986): this variability may be due to lack of standardized methods of investigation, severity of underlying disease, dose of α-IFN administered and reporting of somatic complaints as depressive symptoms.

Few studies up to date dealt with the cognitive effects of α-IFN in patients with hepatitis, mostly relying on rather insensitive tests such as the Mini Mental State Examination (Kamei et al., 2002; Valentine et al., 1998; Smith et al., 1988).

Only one study on long-term neurophysiological findings of α-IFN induced encephalopathy is available (Kamei et al., 2002): this approach could provide objective measures of CNS involvement, similarly to neurophysiological studies of cognitive decline and metabolic encephalopathies (Barrett, 2000; Amodio et al., 1999a,b).

We designed a study aiming to investigate the psychiatric, cognitive and neurophysiological effects of α-IFN in patients with chronic hepatitis C at different time-points: before the beginning (t_0) and after 2 (t_1) and 6 months (t_2) from the start of therapy.

2. Methods

2.1. Patients

Twenty outpatients aged 18–60, with diagnosis of chronic viral hepatitis based on markers positivity (anti-HCV-ELISA/HCVRNA-PCR) and on liver biopsy, were eligible if they have had high serum ALT level on at least two examinations during the last 2 months.

The exclusion criteria were the presence of HIV and/or HBV co-infections, autoimmune diseases, liver cirrhosis with a Child-Pugh score >5. Further criteria were: active psychiatric disorders, current psychotropic drug prescription and/or alcohol or substance abuse (cessation<6 months).

The patients were treated for 6 or 12 months and with a fixed dose of 3 or 6 MU of α-IFN thrice weekly depending on viral genotype. All patients received also a weight-adapted ribavirin dose (15 mg/kg/day). Safety haematological and biochemical analysis were monitored during the treatment.

The study was approved by the local Ethical Committee; all patients gave their consent to the study.

2.2. Psychiatric evaluation

Mini International Neuropsychiatric Interview (MINI) (Sheehan and Lecrubier, 1994) was performed during screening visit to exclude the presence of active psychiatric disorder and/or alcohol or substance abuse. At each time-point, all patients underwent a psychiatric evaluation including the 17-item version Hamilton Depression Rating Scale (HAM-D) (Hamilton, 1960), the Hamilton Scale for Anxiety (HAM-A) (Hamilton, 1959) and two self-administered scales: the Beck Depression Inventory (BDI) (Beck and Word, 1961) and the State and Trait Anxiety Inventory (STAI-Y) (Spielberg, 1983). Structured and semi-structured interviews (MINI, HAM-D and HAM-A) were all administered by a psychiatrist with 4-year clinical experience.

2.3. Electrophysiological assessment

Spontaneous closed eye EEG-activity was recorded by digital EEG equipment (System 98, Micromed,