بسم الله الرحمن الرحيم

Hearing Profile in Hepatitis C Patients Treated With Interferon and Ribavirin

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ABSTRACT:

METHODS: Hearing assessment using pure tone audiometry and TEOAEs was done for 3 adult middle-aged groups: Group **A:** 30 chronic active hepatitis C virus (HCV) patients receiving treatment with PEG- interferon and ribavirin, for at least three months; Group **B**: 30 chronic HCV patients who did not receive treatment; and Group **C**: 10 healthy normal hearers as controls.

OBJECTIVE*:* to study the effect of Interferon and Ribavirin combination on hearing in chronic HCV patients treated with these medications.

RESULTS: Group A showed mild high frequencies sensorineural hearing loss (SNHL) in (63.33%) of cases (unilateral in 36.67% & bilateral in 26.67%). The onset was sudden in 6.67% of cases. Group B showed SNHL which was unilateral in 13.33 % of cases. All subjects in this study had present TEOAE. In group A the TEOAE Pass was 48.33%, and Partial Pass was 51.67% of ears. There was a statistically significant difference among the three groups as regards the hearing threshold at different frequencies and TEOAE overall wave reproducibility. This difference was found between groups A and B and groups A and C in both ears but not between groups B and C. This suggests that HCV itself did not affect hearing or cause outer hair cells damage as much as did the treatment used for the disease. Normal hearing ears of the unilateral SNHL showed lower pass rate (27.27%) than those of the bilateral normal hearing (54.55%), which suggests subtle changes in the cochlea.

CONCLUSION*:* Interferon and ribavirin combination used in treatment of HCV patients, could affect the cochlea causing outer or inner hair cells damage. So we ***recommend*** that the HCV patients should be aware of the possibility of occurrence of clinical hearing loss or sub-clinical cochlear damage from dual therapy with interferon and ribavirin. We recommend that the Egyptian Ministry of Health add

audiological testing and monitoring in the guidelines of treatment and follow-up of treatment in HCV patients, i.e. HCV patients, scheduled for dual therapy with interferon and ribavirin, must have their hearing and inner ears assessed by both TEOAEs and pure tone audiometry before, during and after cessation of treatment, as well as a long term follow-up.

Key Words: audiometry; cochlea; Interferon, hearing; hepatitis C virus (HCV) infections; Ribavirin; transient evoked otoacoustic emissions.

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ABBREVIATIONS

ABR	Auditory Brainstem Response
ALT	Alanine Amino-Transferase
AST	Aspartate Amino-Transferase
ASHA	American Speech Hearing Association
CHC	Chronic Hepatitis C
DPOAE	Distortion Products Otoacoustic Emissions
HAV	Hepatitis A Virus
HBV	Hepatitis B Virus
HCC	Hepato-Cellular Carcinoma
HCV	Hepatitis C Virus
IFN	Interferon
IFN-α	Interferon Alpha
IFN-γ	Interferon Gamma
LDL	Low Density Lipoprotein
NS	Non-Structure Protein
OAE	Otoacoustic Emissions
PCR	Polymerase Chain Reaction
PTA	Pure Tone Audiometry
TEOAE	Transient Evoked Otoacoustic Emissions
SNHL	Sensorineural Hearing Loss
SOAE	Spontaneous Otoacoustic Emissions
WHO	World Health Organization

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INTRODUCTION AND RATIONALE

Interferon alpha **(IFN alpha)** is a cytokine with antiviral, antiproliferative and immunomodulator effects. It has been widely used for the treatment of many systemic disorders, especially in acute and chronic viral Illness **(Woo and Burnakis, 1997)**. The antiviral immune response to the antiviral effect of interferon may also lead to autoimmune pathological consequences, mediated by antibodies formed in response to viral infection, or by immune Complexes produced during an infection **(Tinghitella, 1990)**. Although IFN alpha may have many mild to severe side effects such as flu-like syndrome, anosmia, haematological, infectious, cardiovascular, renal, autoimmune, and psychiatric problems, auditory complaints due to IFN alpha administration are rare and reversible **(Chung and Older, 1997)**. The mechanisms of this side effect are not known, but may be a result of vasculitis affecting small arterioles.

PEG-interferon and ribavirin combination therapy for the treatment of hepatitis C virus (HCV) is well known to be associated with significant adverse effects. Sensorineural hearing loss, that in most cases is unilateral, but may be bilateral **(Piekerska et al., 2007)** has been reported as a consequence of therapy with both non-pegylated and pegylated interferon (PEG-INF) but is not a well-known adverse effect. Sudden hearing loss may occur in about 1% of patients on PEG-IFN/ribavirin combination therapy. This rate was not different to that observed in an untreated population. Possible mechanisms involved include direct ototoxicity of

IFN, autoimmunity, and hematological changes. In contrast to published cases on auditory disability due to standard IFN, hearing loss did not fully resolve after discontinuation of therapy with PEG-IFN. On the other hand, symptoms did not worsen on continued treatment **(Formann et al., 2004 and wong et al., 2005)**. Therefore, the decision whether to continue or to stop the treatment when signs of ototoxicity appear is based on the clinical judgment of the treating physician **(Elloumi et al., 2007).**

Rationale:

In literature, few studies evaluated the effect of these drugs on hearing, and to the best of our knowledge, no studies evaluated the effect of these drugs on cochlear outer hair cells.

Moreover, the Egyptian Minstery of Health guildelines for HCV therapy are not specifying screening of the hearing level by audiometry or monitoring cochlear function in their treatment and follow-up protocol.

So in this study we investigated the effect of dual treatment with interferon and ribavirin on hearing and on cochlear hair cells in chronic hepatitis C virus patients.