

Interferon Alfa and Ribavirin Induced Hair Changes

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ABSTRACT

Combination therapy of Interferon alfa and ribavirin in chronic hepatitis C has well documented cutaneous adverse effects. Most interesting of these has been reported on hair physiology. This study was conducted to determine the frequency and pattern of adverse effects involving hair in patients receiving combination of interferon alfa 2a and ribavirin for chronic hepatitis C. The study was conducted in Department of Dermatology, Division of Medicine Shaikh Zayed Hospital. Thirty Eight patients who completed treatment with interferon alfa (3 MIU subcutaneously thrice weekly) and 1200 mg ribavirin daily for 24 weeks were enrolled in this single-center study. The patient's response and examination finding particularly regarding involvement of hair was noted on a Pro forma. Thirty Two out of thirty eight (84%) patients noted adverse effects involving hair. The most frequent was diffuse hair loss and occurred in 27 patients (71%). Hypertrichosis of eyelashes (trichomegaly) and eyebrows (synophrys) was observed in 18 (47%) and 16 (42%) patients respectively. Graying of hair was noted in 4 patients (11%), while discoloration of moustache hair was seen in 2 patients (5%). Epilation at the site of subcutaneous injection was noted in 10 patients (26%). Alopecia areata was reported in 2 patients (5%). It is concluded that adverse effects involving hair are frequent and varied (hair loss to excess hair growth) during combination therapy with Interferon alfa-2a and Ribavirin for chronic hepatitis C.

INTRODUCTION

The use of interferon has rapidly escalated over the past few years keep in par especially with HCV acquiring endemic proportions worldwide, and it being the most effective therapy in combination with ribavirin¹.

Interferon alfa (INF- α) has well documented cutaneous and extra-cutaneous effects. It has been reported to produce a variety of sequelae involving hair physiology like alopecia², hypertrichosis^{3,4}, changes in hair texture⁵ and colour⁶.

The purpose of this study was to assess the type and frequency of hair involvement caused by INF- α and ribavirin in HCV positive patients in our population.

PATIENTS AND METHODS

The study was conducted from January 2007 to June 2007 in the Department of Dermatology

Division of Medicine at Shaikh Zayed Hospital, Lahore. Thirty eight consecutive HCV positive patients who completed treatment with INF- α 2a plus ribavirin for 24 weeks were included in the study. A thorough clinical history with particular emphasis on hair and skin involvement was taken. The patient's response and examination finding of skin, mucous membrane hair and nails were recorded.

The values of Hb, WBC, Platelet count, ESR, Billirubin, ALT, AST and alkaline phosphatase, taken at baseline and after completion of treatment were compared, and any significant change was recorded.

As it was only a descriptive study only descriptive statistics were used. Ages of patient was expressed as mean \pm standard deviation and male to female patient proportion was expressed as ratio. All analysis was done on statistical program for social sciences (SPSS) version 10.0.

RESULTS

Patients' characteristics

A total of 43 patients were enrolled for the study. Five patients were lost to follow up and study was completed in 38 patients. The mean age of patients was 36 years \pm 10 SD. There were 16 men and 22 women with male to female ratio of 0.72.

Hair changes in patients

Effect of combination therapy of Interferon alfa and Ribavirin in chronic hepatitis C on hair was rather interesting. On one hand there was diffuse thinning of scalp hair and on the other, significant eyelash (Fig. 1) and eyebrow hypertrichosis (Fig. 2) was noted. Loss of hair was also noted at the site where INF- α 2a was injected subcutaneously.

Overall thirty two out of thirty eight patients (84%) developed adverse effects involving hair. The various patterns of hair involvement are shown in Table 1. Most common side effect noted was diffuse hair loss seen in twenty seven patients (71%). Hypertrichosis was next common adverse effect. Trichomegaly developed in eighteen patients (47%) and synophrys was seen in sixteen patients (42%). Epilation at site of injection was seen in ten patients (26%). Other less common side effects were, graying of hair, discolouration of moustache and alopecia areata (Fig. 3) as shown in Table 1.

Table 1: Pattern of hair involvement

Pattern	Number	Percentage
Diffuse hair loss	27	71
Hypertrichosis		
Trichomegaly	18	47
Synophrys	16	42
Epilation	10	26
Graying of hairs	4	11
Discolouration of moustaches	2	11
Alopecia areata	2	5



Fig. 1. Trichomegaly (Hypertrichosis of eyelashes).



Fig. 2. Synophrys (Hypertrichosis of eye brows).



Fig. 3. Alopecia areata.

DISCUSSION

Hair is the keratinized product of the hair follicle, which has a cyclic activity of growth and rest, anagen and telogen, respectively. Normally 80-90% scalp hair is in anagen. Loss of more than 120 hair daily is called alopecia⁷.

Drugs typically cause a diffuse, reversible alopecia by influencing one of the cycles that hair follicles go through. Interference in the hair cycle may be in the form of abrupt cessation of mitotic activity in rapidly dividing hair matrix cells, as caused by chemotherapeutic agents, causing anagen effluvium or by precipitating follicles into premature resting phase causing telogen effluvium. Telogen effluvium, a term first described by Kligman in 1961⁸, has five types⁹, based on the phase of the telogen hair is in.

Hair was the skin adenexa most affected in our study group. Alopecia was the most frequent and distressing complaint. Diffuse hair loss seen in our patients started early i.e. within 1 month of starting treatment and continued throughout the treatment, meaning thereby that the hair was affected in the immediate anagen release phase, in which follicles are stimulated to enter telogen prematurely.

The therapeutic response produced by IFN- α /ribavirin, in HCV infection depends on it being an immunomodulatory and antiproliferative agent. IFN- α specifically promotes the differentiation towards Th1-type response, which is associated with IFN- γ production and the development of cellular immunity¹⁰. IFN- γ has been shown to induce catagen in cultured human hair follicles within just 4 days¹¹, it also up regulates other catagen inducers¹² e.g. transforming growth factor (TGF) beta-2, this could explain the early loss of hair seen in our patients

Alopecia has been frequently described with IFN- α , but most studies have reported involvement in 10-20% of the patients², whereas in our study group 71% experienced significant hair loss. This may be due to the synergistic immunomodulatory effect of this combination and/or mild suppressive effect on the hemoglobin in patients who already may be suffering from some malnourishment in this part of the world. Loss of hair was also noted at the

site where INF- α 2a was injected subcutaneously, showing that the drug has a direct role in hair loss, too.

Though on one hand patients complained of hair loss, on the other hypertrichosis of eyelashes and eyebrows was noted. It is to be noted here that while thinning of scalp hair was commoner in females, eyelash and eyebrow hypertrichosis was more frequent in males. Eyelid and eyebrow trichomegaly has been reported earlier, with this combination in only a few case reports^{13&14}. Similar hair phenomenon has been described in patients taking other immunomodulatory drugs like cyclosporine¹⁵, cetuximab¹⁶ and tacrolimus¹⁷, suggesting a common immune dysregulation.

Rapid graying of hair was also noted in few of our patients, despite the fact that IFN increases the expression of alpha-melanocyte stimulating hormone (MSH) surface receptors¹⁸ which is manifested by generalized darkening of complexion and worsening of melasma.

Two patients in our study group developed alopecia areata, this side effect has been reported earlier and may be extensive¹⁹.

A large number of drugs have been reported to produce hair changes; however it is difficult to establish a definite correlation between the two. The hair changes produced by drugs are mostly reversible after cessation of the drug, but the time it may take to do so and the degree of reversibility may vary for different groups of drugs. Though hair has no vital function, its psychological impact on the quality of life is immense, these side effect must be recognized as they may lead to poor patient compliance.

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