The impact of interferon therapy on the sexual function of hepatitis C male patients

Kamal Abdel Hafez[a], Sheref Kamel[b], Ahmed Abdel Aal[a], Ehab Mansour[c], Ali Mahran[a]

Departments of [a]Dermatology, Venereology, and Andrology, [b]Gastroenterology and Tropical Medicine and [c]Radiology, Assiut University Hospital, Assiut, Egypt

Correspondence to Ali Mahran, M.D., Department of Dermatology, Venereology, and Andrology, Assiut University Hospital, Assiut 71111, Egypt
Tel: +20882414631; Fax: +20882333327; e-mail: alimahran74@yahoo.com

Received 26 December 2018
Accepted 12 February 2019

Journal of Current Medical Research and Practice
September-December 2019, 4:319–321

Objective
To evaluate the impact of interferon therapy on male sexual function.

Patients and methods
One hundred hepatitis C patients were included in the study. Fifty two patients were receiving interferon and 48 patients were not receiving interferon. All participants underwent history taking including International Index of Erectile Function (IIEF-5) score, general and local examination, assessment of hormonal profile, and pharmacopenile duplex Doppler ultrasonography.

Results
The IIEF-5 score of the noninterferon-treated group (18 ± 6.5) was significantly higher than the interferon-treated group (12 ± 4.5) (P = 0.022). Forty (76.9%) patients on interferon reported low sexual desire compared with 22 (45.8%) patients of noninterferon-treated group (P = 0.001). Total testosterone among interferon-treated patients (188 ± 0.32 ng/dl) was significantly lower than noninterferon-treated patients (270 ± 0.52 ng/dl) (P = 0.001). Similarly, free testosterone level among interferon-treated patients (3 ± 0.22 ng/dl) was significantly lower than noninterferon-treated group (7 ± 2.3 ng/dl) (P = 0.05). Estradiol levels among interferon-treated patients (80 ± 3.3 pg/ml) were significantly higher than noninterferon-treated patients (58 ± 2.3 pg/ml) (P = 0.01). However, prolactin level showed no significant difference between the interferon-treated (13 ± 1.3 ng/ml) and the noninterferon-treated groups (12 ± 1.5 ng/ml) (P = 0.59). Thirty eight (73%) patients on interferon showed vasculogenic erectile dysfunction compared with 32 (66.7%) patients not receiving interferon (P = 0.11). Twenty two (42.2%) patients on interferon showed veno-occlusive dysfunction which was significantly higher than noninterferon group (16.6%) (P = 0.03). Eighteen (37.5%) patients of the noninterferon group showed mixed vasculogenic erectile dysfunction compared with eight (15.4%) patients on interferon (P = 0.05).

Conclusion
Interferon had negative impact on libido, IIEF-5 score, and hormonal profile but did not affect penile hemodynamics.

Keywords:
erectile dysfunction, hepatitis, interferon

J Curr Med Res Pract 4:319–321

2357-0121

Introduction

The etiology of erectile dysfunction (ED) might be endocrinal, vascular, psychogenic, neurological, local penile, drug induced, or multifactorial. Liver diseases are among the causes of ED. Some patients with chronic hepatitis C report impaired sexual function whereas others maintain normal sexual performance [1]. The etiology of ED among patients with hepatitis C is multifactorial. It might be endocrinal, psychogenic, or drug induced. The aim of this work is to evaluate the impact of interferon therapy on male sexual function among hepatitis C patients.

Patients and methods

This study was conducted in Assiut University Hospitals, Assiut, Egypt. This work has been carried out on 100 married patients suffering from chronic hepatitis C virus (HCV) infection consecutively recruited after signed consent. Patients with other systemic diseases that might affect sexual function were excluded from the study. The patients were classified into two groups. The first group included 52 (52%) patients on interferon. The other group included 48 (48%) patients who were not on interferon. Patients were subjected to history taking including the abridged form of International Index of Erectile Function questionnaire (IIEF-5), Arabic version [2,3], general and local examination, and assessment of hormonal profile. Serum prolactin, serum estradiol, serum total testosterone (Immunolight

technique) and serum free testosterone (enzyme-linked immunosorbent assay technique) were evaluated. Pharmacopenile duplex ultrasound was performed using a 7.5 MHz linear array transducer and 20 μg of PGE-1 for intracorporeal injection [4]. All patients included in the study provided written informed consent. The ethical committee in Assiut Faculty of Medicine approved the study.

Results

In this study, the IIEF-5 score of the noninterferon-treated group (18 ± 6.5) was significantly higher than the interferon-treated group (12 ± 4.5) (P = 0.022). In addition, the IIEF-5 score was significantly correlated to the interferon therapy duration (r=–0.366, P = 0.01).

Sexual desire was significantly lower among patients on interferon. Low or absent sexual desire was reported in 40 (76.9%) patients on interferon compared with only 22 (45.8%) patients of noninterferon-treated group (P = 0.001).

As regards the impact of interferon on serum testosterone, serum level of total and free testosterone were significantly lower among patients on interferon (188 ± 13.7, 3 ± 0.22 ng/dl, respectively) compared with those noninterferon-treated patients (270 ± 18.6, 7 ± 2.3 ng/dl, respectively) (P = 0.001, 0.05, respectively). Moreover, the serum levels of total and free testosterone were negatively correlated to the interferon therapy duration (r=–0.326, P = 0.001; r=–0.252, P = 0.01, respectively).

On the contrary our results showed that serum estradiol level was significantly higher in patients on interferon therapy (80 ± 3.3 pg/ml) compared with those noninterferon-treated patients (58 ± 2.3 pg/ml) (P = 0.01). It was also clear that the estradiol level is significantly correlated to the duration of interferon treatment (r = 0.337, P = 0.002).

Both groups did not show significant difference as regards prolactin level. The mean level was 13 ± 1.3 ng/ml for interferon-treated patients compared with 12 ± 1.5 ng/ml for nontreated group (P = 0.59). However, there was a positive correlation between serum prolactin level and the interferon therapy duration (r = 0.421, P = 0.03).

As regards penile duplex results, vasculogenic ED was reported in 38 (73%) patients on interferon compared with 32 (66.7%) patients not receiving interferon (P = 0.11). Twenty two (42.2%) patients on interferon showed veno-occlusive dysfunction compared with eight (16.6%) patients among those of noninterferon group (P=0.03). Among the noninterferon group, 18 (37.5%) patients showed mixed vasculogenic ED whereas only eight (15.4%) patients on interferon therapy showed mixed vasculogenic ED (P = 0.05).

Discussion

Hepatitis C is a major health problem in many countries around the world among which is Egypt. It affects about 3% of the world's population [5]. Pathological and psychosexual consequences of the disease may impair the sexual performance in HCV-infected patients [6]. Our current study evaluated the impact of interferon therapy on the sexual function among patients with HCV infection.

In our study we found that there is statistically significant difference between interferon and noninterferon-treated patients as regards sexual desire as interferon-treated patients showed history of markedly lower and/or absent sexual desire than noninterferon-treated group (P = 0.001). Comparable results were reported by El-Atrebi *et al*. [7] whose study included 100 HCV Egyptian patients with mean age of 41.4 years and found some degree of impairment in sexual desire in 22% of male HCV patients before interferon therapy with progressive worsening in patient's sexual desire and erectile function after interferon therapy in 44% of patients.

This coincides with the findings of Dove *et al*. [8] who reported significant declines in all components of sexual health during therapy, in spite of the fact that Dove's study included a larger number (260) of male American patients (Caucasians and Africans) with mean age 48 years. Before therapy, 37% of men reported at least some degree of impairment in sexual desire and 44% reported dissatisfaction with their sexual life, whereas 26% reported impairment in erectile and 22% in ejaculatory function. During therapy, significant declines were observed in all components of sexual health compared with pretreatment. At the end of therapy (24 or 48 weeks), an estimated 38–48% of men reported that overall sexual function was worse than before treatment.

Low sexual desire among patients on interferon in our study might be attributed to lower free and total testosterone and higher estradiol levels compared with noninterferon groups. Furthermore, patients on interferon therapy may report higher depression scores [7] which may participate in loss of libido.

In accordance with Barreca *et al*. [9] and Corssmit *et al*. [10], the present study illustrated the effect of interferon therapy on the hormonal levels and incidence of ED in chronic HCV-infected patients. On studying the serum level of total testosterone among interferon-treated patients, we found decline in its level

with mean ± SD of 188 ± 13.7 and reported statistically significant lower level than noninterferon-treated group (270 ± 18.6) (P = 0.001). Furthermore, serum free testosterone level showed statistically significant lower levels among interferon-treated patients with mean ± SD of 3 ± 1.2 than noninterferon-treated group (7 ± 2.3) (P = 0.05).

These results indicate an effect of interferon therapy on male gonadal steroid biosynthesis. Comparable results were reported by Krauss *et al.* [11] who evaluated sexual dysfunction in men with chronic HCV on antiviral therapy. Researchers illustrated contributions of interferon-induced sex hormone changes to sexual dysfunction as they investigated changes in free testosterone and total testosterone in 34 male patients treated with interferon alpha-2b for 6–12 months. They found that free and total testosterone decreased significantly during antiviral therapy in close correlation with libido/sexual function which coincides with our results. In addition to our study, they measured the degree of depression using the Hospital Anxiety and Depression Scale. They found that depression scores increased during therapy and were also significantly associated with sexual dysfunction. However, androgen levels displayed no significant correlation with depression. El-Atrebi *et al.* [7] noticed sexual dysfunction during interferon and ribavirin treatment in patients with chronic hepatitis C infection and postulated that interferon therapy causes increase in hepatic synthesis of sex hormone binding globulin with resulting suppression of circulating androgens. Also, they reported that chronic hepatitis C patients under interferon therapy show high depression scores which participate in occurrence of ED. Serum estradiol level was statistically significant higher (80 ± 12.3) among interferon-treated group than the noninterferon-treated patients (58 ± 13.3) (P = 0.01) and that coincides with Corssmit *et al.* [10].

Regarding serum level of prolactin, we did not find any significant difference between the two groups. On the contrary, Krauss *et al.* [11] postulated that, during their study period, prolactin blood concentrations rose significantly and this increase was reversible after the end of interferon alpha-2b therapy.

In our study, there was a negative correlation between duration of interferon therapy and serum levels of total and free testosterone which coincides with Corssmit *et al.* [10] and also, there was a positive correlation between duration of interferon therapy and serum levels of prolactin and estradiol which agree with Krauss *et al.* [11].

Regarding IIEF-5 score, we found statistically significant difference between the two groups as the noninterferon-treated group reported statistically significant higher score than the interferon-treated group (P = 0.022) which coincide with Corssmit *et al.* [10]. Moreover, we found statistically significant negative correlation between duration of interferon therapy and IIEF-5 score.

Lower IIEF-5 scores among patients on interferon is probably the outcome of the hormonal and the psychological changes that are associated with interferon administration. Moreover, the IIEF-5 scores showed negative correlation with the duration of interferon therapy among patients included in our study.

Conclusion

Patients on interferon reported loss of libido, lower total and free testosterone levels, higher estradiol level, and lower IIEF-5 score compared with those not receiving interferon. However, interferon did not affect penile hemodynamics.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Soykan A, Boztas H, Idilman R, Ozel ET, Tuzun AE, Ozden A, Kumbasar H. Sexual dysfunction in HCV patients and its correlations with psychological and biological variables. Int J Impot Res 2005; 17:175–179.

2 Rosen RC, Smith MD, Cappelleri JC, Lipsky J. Development and evaluation of an abridged 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. Int J Impot Res 1999; 11:319–326.

3 Shamloul R, Ghanem H, Abou-zeid A. Validity of the arabic version of the sexual health inventory for men among Egyptians. Int J Impot Res 2004; 16:452–455.

4 Aversa A, Bonifacio V, Moretti C. Prostaglandin E1 versus prostaglandin E1 plus phentolamine in male erectile dysfunction: a dynamic colour power Doppler study. Int J Impot Res 2002; 12:33–40.

5 Shereen SH, Amr G, Maan KA, Wahid D. Erectile dysfunction in patients with chronic hepatitis c virus infection. Arab J Gastroenterol 2014; 2:4–6.

6 Ferri C, Bertozzi MA, Zignego AL. Erectile dysfunction and hepatitis C virus infection. J Am Med Assoc 2002; 8:698–699.

7 El-Atrebi KA, El-Atrebi MA, El-Bassyouni HT. Sexual dysfunction in males with hepatitis C virus: Relevance to histopathological changes and peginterferon treatment. Saudi J Gastroenterol 2011; 17:406–410.

8 Dove LM, Rosen RC, Ramcharran D, Wahed AS, Belle SH, Brown RS. Decline in male sexual desire, function, and satisfaction during and after antiviral therapy for chronic hepatitis C. Gastroenterology 2009; 137:873–884.

9 Barreca T, Picciotto A, Franceschini R, Varagona G, Garibaldi A, Valle F, *et al.* Sex hormones and sex hormone-binding globulin in males with chronic viral hepatitis during recombinant interferon-alpha 2b therapy. J Interf Res 1993; 13:209–211.

10 Corssmit EP, Endert E, Sauerwein HP, Romijn JA. Acute effects of interferon-alpha administration on testosterone concentrations in healthy men. Eur J Endocrinol 2000; 143:371–374.

11 Krauss MR, Schafer A, Bentink T, Scheurlen M, Weissbrich B, Al-Taie O, Seufert J. Sexual dysfunction in males with chronic hepatitis C and antiviral therapy, interferon-induced functional androgen deficiency or depression. J Endocrinol 2005; 185:345–352.