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Sexual dysfunctions in HCV patients and its correlations with psychological and biological variables

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The frequency of sexual dysfunction (SD) is not very well known in patients with chronic hepatitis C. In this study, the prevalence of SD and its correlations with psychological and biological variables was assessed in 46 HCV positive patients. The mean age of patients was 46.4 ± 9.4 y; the mean duration of HCV infection was 43.4 ± 34.0 months; 52% were male; 89% were living with a spouse. SD was assessed using the Arizona Sexual Experiences Scale (ASEX), the level of anxiety and depression measured with the Hospital Anxiety and Depression Scale (HADS). Biochemical parameters were also assessed. Overall, as indicated by ASEX criteria, SD was observed in 35% of our patients. Of 24 males, 21% described SD; problems with drive (25%), arousal (17%) and erection (17%) were the most frequent complaints. Of 22 female patients, 50% described SD; problems with drive (55%) arousal (50%), and reaching orgasm (59%) were the most frequent complaints. Total ASEX scores were correlated with age ($P < 0.07$, significant at trend level), education ($P < 0.001$), and was higher in female patients ($P < 0.02$). After controlling for the effects of age, sex, education, duration of HCV and marital status, depression levels could still significantly predict the SD ($P < 0.05$). Moreover, even after controlling the effects of all other variables, gamma glutamyl transpeptidase (GGT) levels could predict the SD status of the patients ($P < 0.05$). Our results indicate that the prevalence of SD was 35% in HCV-infected patients and the level of depression and GGT levels were predictive of patients SD status.
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Introduction

Hepatitis C virus (HCV) is one of the most important causes of acute and chronic liver disease in the world. An estimated 3% of the world's population has been infected with HCV.[1] Exposure to blood and blood products, by transfusion or parenteral drug use, remain as the major means of HCV infection acquisition.[2] Although the per-contact likelihood of sexual transmission of HCV may be very low,[3,4] the role of sexual transmission for growing pool of carriers may become an important factor for transmission of HCV through sexual intercourse.[2] However, the lack of data on the determinants of sexual transmission of HCV has limited the development of guidelines for sexual partners who may be at risk for transmitting or acquiring HCV infection.[5,6] As a result, despite the possibility of transmitting the disease, a low rate of contraception use,[7] and lower rate of condom use in their relationships[8] were found among female HCV-infected patients.

Sexuality is an important aspect of the quality of life. Although sexual transmission has been an area of research in HCV positive patients, sexual functioning of these patients receives very limited attention. On the other hand, since psychosocial influences and pathological consequences of the disease might hamper sexual functioning in HCV-infected patients, it is possible to predict sexual dysfunctions (SD) in this population. Supporting these premises in male

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patients, a high rate of erectile dysfunction (ED) was diagnosed in 39% of HCV-positive patients in comparison to 14% of control subjects.[9] Similarly, in Japan, chronic hepatitis was found to be an independent risk factor for the development of ED.[10] Screening for SD and identifying its correlates is a step towards developing better insight into overall sexuality issues in HCV patients. However, no studies dealing with all core elements of sexual functioning of male and female have been identified in the literature. The major aim of this preliminary study is to identify the point prevalence of SD in a sample of HCV-infected patients. Additionally, correlations between SD and sociodemographic, medical, biological and psychological variables are also studied.

Subjects and methods

Subjects

The present study is a part of larger project dealing with various kinds of psychosocial problems encountered in patients with hepatitis and focuses on sexual functioning of HCV-infected, chronic hepatitis patients. A total of 111 sexually active drug naive patients with chronic hepatitis C from Hepatology outpatient clinic, Department of Gastroenterology of Ankara University, School of Medicine, Ankara/Turkey were consecutively screened for the study. The diagnosis of HCV-induced chronic liver disease in each case was made on the basis of serological, clinical and histological data consisting of anti-HCV positivity, abnormal serum ALT levels, liver biopsy and symptoms of fatigue and right upper quadrant discomfort consistent with hepatitis C. Among 111 patients, 65 either meet the exclusion criteria or did not agree to participate to the study. Exclusion criteria were; age below 18 or above 65 y, medically unstable, with hospitalization or acute illness in the preceding 3 months, inability to complete self-rating scales (thus, blindness and low educational level were exclusionary criteria), any signs of cognitive impairment, interferon or psychiatric treatment in the past, the presence of diabetes, renal failure, hypothyroidism, coinfection with hepatitis B or human immunodeficiency virus, or concurrent cardiovascular disorders. Eventually, SD and its correlates were evaluated in 46 patients with HCV infection. Consents and permission to access medical records were obtained for all the participants.

Procedure

Patients included in the study underwent a structured interview to obtain sociodemographic information and information regarding their symptoms. The sociodemographic and medical variables examined were age, gender, marital status, level of education and duration of HCV infection. Patients then completed the Turkish Version of the Arizona Sexual Experiences Scale (ASEX)[11] and the Hospital Anxiety and Depression Scale (HADS).[12] Several biochemical parameters that might interfere with sexual function were also assessed in this study. These parameters included alanine transaminase (ALT), aspartate aminotransferase (AST), gamma glutamyl transpeptidase (GGT), prothrombin time (PTT), alkaline phosphatase (ALP), total bilirubin (BIL), albumin (ALB), hemoglobin (HGL) and platelet (PLT) levels. Biochemical data were obtained from the tests on the day of the interview.

Among self-rating scales for assessing sexual functioning, ASEX is used in this study. The main reason for selecting ASEX is the presence of reliability and validity studies of the Turkish version of ASEX for medical patients.[13] The ASEX is a brief 5-item scale designed to assess the core elements of sexual functioning: drive, arousal, penile erection/vaginal lubrication, ability to reach orgasm and satisfaction with orgasm. The female and male versions of ASEX differ on the gender-specific question addressing erection/lubrication. Each item is rated with a 6-point Likert system, with lower scores reflecting enhanced sexual function and higher scores reflecting impaired sexual function. A total ASEX score of 19 or greater, any one item with an individual score of either 5 or 6, or three or more items with individual scores of 4 have all been found to be highly correlated with clinician-diagnosed SD. These criteria applied for the determination of SD in this study.

Each patient's level of depression and anxiety was assessed with HADS. HADS, which consist of 14 items, seven for anxiety (HADS-anxiety) and seven for depressive symptoms (HADS-depression), is specifically designed for medical patients and validated in many cultures including Turkish.[14]

Statistical analyses

All analyses were performed with SPSS software (version 11). The frequency of sexual dysfunction was reported with bar graphics for both sexes. The *t*-test for independent-samples was used to compare the means between grouping variables. The Pearson's correlation test was used for the analysis of correlations. The patients' age, duration of HCV infection and the level of education were widely distributed in our sample. To control for the effects of these variables as well as gender and marital status, multiple regression analysis was employed for the predictive value of HADS and biological

parameters for SD. Confidence intervals were 95% (two-sided) for all analyses.

Results

Patients included in this study had received a diagnosis of HCV infection for a mean of 43.48 ± 34.09 months, with a range of 3–126 months. The mean age of patients was 46.44 ± 9.43 y (range 32–65 y); 24 (52.2%) were male; 41 (89.1%) were living with a spouse or a partner; 39 (87%) had children; 22 (43.5%) were employed and four (8.7%) were retired; 31 (67.4%) had at least 8 y of education. The mean age, duration of HCV infection, the level of educational, marital status, HADS-depression, HADS-anxiety and biochemical parameters including ALT, AST, ALP, BIL, PTT, PLT and ALB were not significantly different between male and female patients. However, HGB levels were significantly lower in female patients ($t_{(44)} = 6.30$, $P < 0.001$) and GGT levels ($t_{(44)} = 2.74$, $P < 0.01$) were significantly higher in males.

Of 46 patients, 16 (35%) complained of SD as indicated by ASEX criteria. Total ASEX scores were proportionately higher in female patients, and the gender difference for SD was significant ($t_{(44)} = 3.38$, $P < 0.02$). Analyses of correlations between demographic variables and SD revealed significant correlations with age ($r = 0.27$, $P < 0.07$, significant at trend level) and with level of education ($r = -0.64$, $P < 0.001$). For all patients, HADS-anxiety scores were not correlated with total ASEX score. However, HADS-depression scores were significantly correlated with total ASEX score ($r = 0.40$, $P < 0.005$). Total ASEX score was not correlated with ALT, AST, GGT, BIL, ALB, PTT, ALP, PLT but was correlated with HGB ($r = -0.43$, $P < 0.01$) levels.

Of 24 males, five (21%) of patients described SD, and problems with drive (25%), arousal (17%) and erection (17%) were the most frequent complaints (Figure 1). Neither HADS-depression nor HADS-anxiety scores were significantly correlated with any individual items or total ASEX score for males. Among biological parameters, only GGT levels were significantly correlated with ASEX item 1- drive ($r = 0.52$, $P < 0.04$).

Of 22 female patients, 11 (50%) described SD, and problems with drive (55%), arousal (50%), and reaching orgasm (59%) were the most frequent complaints (Figure 1). HADS-anxiety scores were not significantly correlated with any individual items or total ASEX score for female patients. However, HADS-depression scores were significantly correlated with drive ($r = 0.61$, $P < 0.003$), arousal ($r = 0.51$, $P < 0.01$), lubrication ($r = 0.43$, $P < 0.04$) and total ASEX score ($r = 0.45$, $P < 0.03$). Among biological parameters, AST, GGT levels were significantly correlated with drive, arousal, lubrication, orgasm and total ASEX score, and PLT with lubrication, orgasm and total ASEX score (r range $= -0.49$ to -0.71, $P < 0.05$ for all r's).

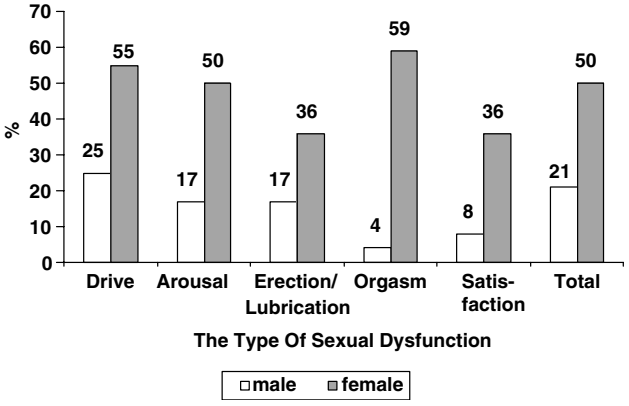


Figure 1 SD and its types in male ($n = 24$) and female ($n = 22$) HCV-infected patients. A total ASEX score of 19 or greater, any one item with an individual score of either 5 or 6, or three or more items with individual scores of 4 criteria were used for the assessment of the presence of SD. An ASEX score of 4 or greater criterion was used for the assessment of the presence of SD of individual items.[11]

As patients' age, gender, level of education, duration of HCV infection and marital status (step 1 control variables) were contributing to the total variance explaining SD, multiple regression analysis was performed to control the effects of these variables on the presence or absence of SD. At the first step, step 1 variables were entered into the equation; these control variables explained 42% of variance (40% of the variance was explained with the level of education) and significantly predicted the SD ($F_{(5, 41)} = 7.47$, $P < 0.001$). At the second step, HADS-anxiety and HADS-depression (step 2, psychological variables) results were entered into the equation using stepwise method. After excluding the effects of step 1 control variables only HADS-depression could significantly predict the SD ($t = 2.02$, $P < 0.05$). At the third step, ALT, AST, GGT, BIL, ALB, PTT, HGB and PLT (step 3, biological variables) entered into the equation using stepwise method. After excluding the effects of all step 1 and step 2 variables, GGT levels still could predict the SD status of the patients ($t = 2.27$, $P < 0.05$). Although significant correlations were found between SD and GGT, HGB and PLT levels in previous analyses, only GGT levels appeared to be an independent factor contributing to the SD in this population.

Discussion

In this study, we found that SD is present in 35% of our patients. As no control group was available in

our study, no direct comparisons could be drawn with normal population or other populations at risk. However, the frequency of SD observed in this study is much higher than the 7.7% lifetime and 5% point prevalence observed in Turkish primary care population,[15] but comparable with patients with depression,[11] patients taking antidepressants that cause SD[11,16] and end-stage renal disease patients undergoing dialysis.[17] Overall, in our population, SD was correlated with age, level of education, level of depression, and with GGT levels.

In a study conducted with male patients, chronic hepatitis was found to be an independent risk factor for the development of ED.[10] Additionally, in another study, ED was observed in 39% of HCV-positive male patients.[9] Among our male patients, 21% described SD, while 17% ED; however, drive and arousal were also affected. Although anxiety and depression levels did not predict the SD, GGT levels were significantly correlated with drive. In comparison to psychological factors, our results suggest that biological factors are more important for the development of SD in male HCV-infected patients.

Similar to general population, SD was significantly more common in female patients[11,16] and observed in 50% of our female patients. Problems with sexual drive, arousal and reaching orgasm were the most frequent complaints. Both depression and biological factors were contributing for the development of SD, biological factors being the most pronounced contributors. To our knowledge, ours' has been the only study dealing with SD in female HCV patients; therefore, no comparisons with the literature could be drawn. However, we suggest that some antidepressants such as, SSRIs, that cause SD in almost 1/3 of Turkish depressed patients [16] might be avoided in at least depressed female HCV patients.

In a study on the effects of alpha-interferon treatment on sexual functioning of male HCV-infected patients, SD was found in 22.2% of patients at baseline assessments.[18] The authors pointed out the importance of further studies to elucidate the associations between SD and biological and psychological variables. Our study provides some insight about the effects of these factors on SD. First, the level of depression was significantly correlated with SD and depression scores could predict SD even after the effects of age, sex, marital status, duration of HCV-infection and the level of education were controlled statistically. SD is common in depressed patients;[11] our results indicate that, similar to patients with primary depression, the presence of depression in HCV patients also increases the likelihood of SD. Second, blood GGT levels could predict the SD even after controlling the effects of age, sex, marital status, the level of education, duration of HCV-infection, depression, and anxiety. Additionally, PLT level was inversely correlated with female SD in our sample. As both GGT and PLT levels are highly predictive of the severity of hepatic involvement,[6] our results stress the importance of the main effect of biological factors for the development of SD in HCV-infected patients. Supporting the importance of biological factors in ED, Ferri *et al*[9] reported that plasma testosterone levels were significantly lower in patients with ED *vs* those without. Our results suggest that patients with higher GGT levels and increased depression scores are at risk for developing SD. However, much studies are needed before speculating on whether the consequences of HCV-infection itself, the decreased hepatic functioning, psychological factors and/or other factors cause the impairment in sexual functioning in HCV-infected patients.

The set of control variables (age, sex, the level of education and marital status) contributed significantly to the variance explaining the SD in this study. Among control variables, the level of education itself explained 40% of the variance contributing SD; although patients with low educational level were not included in this study, this finding might be, at least partially, related with the difficulties in understanding the ASEX items. The inverse correlation between the level education and SD also suggests the importance of education on sexual functioning in preventing and treating SD. Indirectly supporting the importance of education, it was found that, employed women with HCV infection are more likely to use contraception.[7]

There were some limitations in this study. First, our sample size was relatively small, and patients were recruited from one Hepotology Center only. Second, we have not used a structured interview for comprehensive clinical assessment of SD, depression and anxiety in our patients; rather, we relied on a self-report questionnaire for these assessments. Third, we have not studied the impacts of many factors such as endocrine and vascular abnormalities, patients' perception about the fear of transmitting the disease or family interactions that could contribute to the overall variance that might explain the SD. Fourth, age, level of education and duration of HCV infection varied widely in our sample; although we have attempted to control for the effects of these variables by means of regression analysis, the small sample size may have limited the value of our results. Fifth, our results would have been much more representative if a sex and age matched control group was used. Last but not least, our sample was more representative of educated, middle age, middle class and married patients with full insurance coverage, who accepted to participate to the study.

Our study provide some preliminary data on the frequency of SD in HCV patients and identifies depressed female patients with lower level of education at the highest level of risk for SD. Additionally, a biological factor, blood GGT levels appears to be a very significant predictor of SD for

both sexes. However, although our results indicate sexual problems in HCV patients, sexual transmission is still an issue for these patients, and if it is not contained, it will continue to spread and the death rate from hepatitis C will rise to a level far greater than that of AIDS.[19] To generate guidelines to use in clinical practice, attention by service providers and much research are needed with the aim of obtaining a good trade-off between the risk for sexual transmission and sexual functioning of the HCV-infected patients. At this point, although evidence suggests that interspousal transmission of HCV seems to be very rare,[4,20] we need further studies before reassuring HCV-positive spouses that they can maintain their normal marital life.

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