

Observational Study

Association of erectile dysfunction with depression in patients with chronic viral hepatitis

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Abstract

AIM: To investigate the prevalence of erectile dysfunction (ED) and its association with depression in patients with chronic viral hepatitis.

METHODS: This single center cross-sectional study was conducted from August 2013 through January

2014. All outpatients with chronic viral hepatitis in our liver clinic between 18 and 80 years of age were considered eligible for this study. The exclusion criteria included well-established causes of ED, such as diabetes, hypertension, hyperlipidemia, alcohol abuse, liver cirrhosis, ischemic heart disease, renal disease, neurologic disease, and malignancy. We also excluded the patients who had incompletely answered the questionnaires. ED was assessed using the validated Korean version of the International Index of Erectile Function (IIEF-5) scale. The Korean version of the self-administered Beck Depression Inventory (BDI) scale was used to assess depression in the patients. Demographic and medical data were obtained from the patients' medical records. Current or past history of psychiatric diagnosis and drug history including the use of an antiviral agent and an antidepressant were also recorded.

RESULTS: A total of 727 patients met the initial eligibility criteria. Six hundred seventeen patients were excluded because their medical records contained one or more of the previously determined exclusion criteria. The remaining 110 patients were assessed based on the BDI and IIEF-5 questionnaires. Based on the IIEF-5 scale, the prevalence of ED among patients with chronic viral hepatitis was 40%. Compared with the non-ED group, patients in the ED group were older. The proportion of patients in the ED group who had a job or who were naïve peg-interferon users was lower than that in patients in the non-ED group. Patients with ED had significantly lower scores on the IIEF-5 scale than patients without ED (11.75 ± 4.88 vs 21.33 ± 1.86 , $P = 0.000$). Patients with ED rated significantly higher scores on the BDI scale compared with patients without ED (12.59 ± 7.08 vs 5.30 ± 4.00 , $P = 0.000$). Also, the IIEF-5 scores were negatively correlated with age, employment, and BDI scores. In the multiple logistic regression analysis, age and depression were independently associated with erectile dysfunction ($P =$

0.019 and 0.000, respectively).

CONCLUSION: Patients with chronic viral hepatitis have a high prevalence of ED. Age and depression are independent factors for ED in male patients with chronic viral hepatitis.

Key words: Beck depression inventory; Chronic viral hepatitis; Depression; Erectile dysfunction; International Index of Erectile Function-5

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Core tip: The prevalence of erectile dysfunction among patients with chronic viral hepatitis is high. We assessed the prevalence of erectile dysfunction and its association with depression after excluding confounding factors. We confirmed that patients with chronic viral hepatitis have a high prevalence of erectile dysfunction, which is associated with depression.

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INTRODUCTION

Erectile dysfunction (ED) is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance^[1]. The overall frequency of ED is reportedly 32% and 53.3% among male populations in the United States and South Korea, respectively^[2,3]. Based on this high prevalence of ED, extensive investigations into the clinical and pathophysiologic mechanisms of sexual dysfunction have been carried out during the last decade^[4-6]. However, ED in patients with chronic viral hepatitis has been investigated in few limited studies, which are often not comparable because they use different surveys and patient-sampling methodologies^[7,8]. Moreover, few studies have evaluated the association between ED and depression in patients with chronic viral hepatitis. To date, none of the previous studies have investigated the relationship between ED and depression in patients with chronic viral liver disease.

The aim of this study was to evaluate the prevalence of ED in patients with chronic viral hepatitis. We also aimed to determine whether there is any correlation between ED and depression in patients with chronic viral hepatitis by using two questionnaires.

MATERIALS AND METHODS

Study design and population

This was a single center cross-sectional study of

outpatients with chronic viral hepatitis who were recruited between August 2013 and January 2014 at the Samsung Changwon Hospital, South Korea. All outpatients with chronic viral hepatitis between 18 and 80 years of age who were being treated in the liver clinic were considered eligible for this study. Many factors can cause ED. Therefore, in an effort to avoid confounding factors, we excluded patients suffering from diseases that might contribute, such as diabetes, hypertension, hyperlipidemia, alcohol abuse (including alcoholic liver disease), liver cirrhosis, ischemic heart disease, renal disease, neurologic disease, and malignancy (including hepatocellular carcinoma)^[9-13]. We also excluded the patients who had answered the two questionnaires incompletely.

Assessment of sexual dysfunction

Erectile function was assessed using the validated Korean five-item version of the International Index of Erectile Function-5 (IIEF-5). The IIEF-5 includes five items from the IIEF, and it has favorable properties for detecting the presence and severity of ED^[14]. The Korean version of the IIEF-5 has also been proven to be valid and reliable^[15]. It consists of four items focusing on erectile function, and one item focusing on intercourse satisfaction. All items were rated on a five-point scale. IIEF-5 scores are obtained by calculating the sum of the item responses, with 1 being the worst possible score and 25 being the best score. ED is usually diagnosed below a score of 21 points. However, Ahn *et al*^[15] reported the most appropriate cutoff score between ED and no ED was 17 for Korean patients (sensitivity = 91.3%, specificity = 86.3%) and ED is classified as follows: 5-9, severe ED; 10-13, moderate ED; 14-17, mild ED; and 18-25, no ED.

Assessment of depression

The Korean version of the self-administered Beck Depression Inventory (K-BDI) was used to evaluate the patients' subjective depressive mood. Its use to assess depressive mood has been validated^[16,17]. The BDI consists of 21 items, each of which is rated from 0 to 3. BDI scores range from 0 to 63. The categories of depression are usually defined as follows: < 10, normal; 10-15, mild; and ≥ 16 , moderate to severe^[18]. Therefore, in this study, the subjects were considered as having depression when the K-BDI score exceeded 10 points.

Data collection

The following data were retrospectively collected from the medical records of the patients: age, smoking status, alcohol use, employment, health insurance, religion, habitation, presence of viral hepatitis, diabetes, hypertension, hyperlipidemia, cardiovascular disease, body weight, and height. A history of any psychiatric diagnosis, such as major depressive disorder and anxiety/panic disorders was recorded. A drug history including use of antiviral agents and

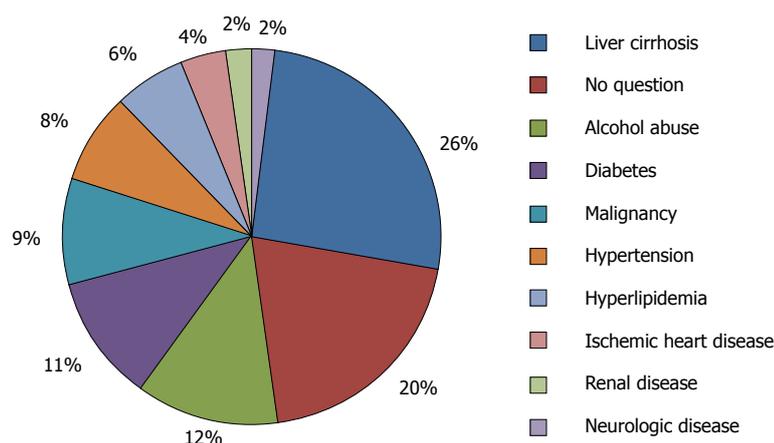


Figure 1 Patients excluded after medical analysis. We excluded patients suffering from diseases that might contribute to erectile dysfunction.

Table 1 Demographic characteristics of the patients *n* (%)

Characteristic	Non-ED (<i>n</i> = 66)	ED (<i>n</i> = 44)	<i>P</i> value
Age, yr	44.38 ± 8.90	51.36 ± 12.48	0.001
Viral etiology			
HBV	52 (78.8)	29 (65.9)	0.133 ¹
HCV	14 (21.2)	15 (34.1)	0.133 ¹
Smoking	27 (40.9)	18 (40.9)	1.000
BMI, kg/m ²	23.93 ± 2.63	24.03 ± 3.16	0.859
Employment	64 (97.0)	35 (79.5)	0.003
Health insurance ²	1 (1.5)	1 (2.3)	0.771
Religion, yes	18 (27.3)	19 (43.2)	0.084
Habitation, rural	11 (16.7)	11 (25.0)	0.284
Peg-interferon, yes	6 (9.1)	11 (25.0)	0.024

¹Among infected patients by the χ^2 test; ²Medicaid. ED: Erectile dysfunction; HBV: Hepatitis B virus; HCV: Hepatitis C virus; BMI: Body mass index.

antidepressants was also recorded. Body mass index (BMI) was calculated as kg/m².

Statistical analysis

Continuous variables are presented as mean ± SD. Differences in independent variables were analyzed by Student's *t* and by Pearson's χ^2 tests for categorical variables. Spearman's single regression analysis was used to determine the relationships between variables. Multivariate analysis using logistic regression was performed to evaluate the association of ED and other parameters. *P* < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, United States).

RESULTS

This cross sectional study initially included 727 patients who met the eligibility criteria. We excluded 617 patients according to the previously determined exclusion criteria (Figure 1). The remaining 110 patients were assessed based on the self-administered

BDI and IIEF-5 questionnaires.

Descriptive data are presented in Table 1. The mean age of the patients was 47.17 ± 10.98 years. Using the IIEF-5 scale, the prevalence of ED (IIEF-5 score ≤ 17) was found to be 40%. There was no significant difference between the ED group and the non-ED group in viral etiology, smoking, BMI, health insurance, religion, or habitation. Compared with the non-ED group, patients in the ED group were significantly older (*P* = 0.001). The proportion of patients in the ED group who had a job or who were naïve peg-interferon users was lower than that in patients in the non-ED group (both *P* < 0.05).

Patients with ED had significantly lower scores on the IIEF-5 scale than the patients without ED (11.75 ± 4.88 vs 21.33 ± 1.86, *P* = 0.000). Patients with ED reported significantly higher scores on the K-BDI scale compared with patients without ED (12.59 ± 7.08 vs 5.30 ± 4.00, *P* = 0.000).

The correlations between IIEF-5 scores and the patients' characteristics are displayed in Table 2. IIEF-5 scores were negatively correlated with age, employment, and K-BDI score (all *P* = 0.000). In the multiple logistic regression analysis, age and depression were independent factors associated with ED after adjustment for BMI, smoking, employment, health insurance, religion, habitation, viral etiology, and use of peg-interferon (both *P* < 0.05) (Table 3).

DISCUSSION

The reported prevalence of ED in patients with chronic viral hepatitis ranges from 14% to 78%^[7,8,19]. We found that 40% of the patients with chronic viral hepatitis have ED, based on the IIEF-5 scores ≤ 17. This prevalence is lower than that observed in the general Korean population (53.3%)^[3]. However, the actual difference in prevalence between patients with ED and general populations may change, because we excluded confounding factors that might contribute to ED. We found that age and depression were independently

Table 2 Correlation of International Index of Erectile Dysfunction scores with characteristics of patients with chronic viral hepatitis

Characteristic	IIEF-5 scores	
	ρ	<i>P</i> value
Age	-0.359	0.000
Viral etiology (HBV)	-0.148	0.123
Smoking	-0.021	0.825
BMI	0.089	0.356
Employment	-0.338	0.000
Health insurance	-0.013	0.894
Religion	0.165	0.085
Habitation	0.132	0.169
Peg-interferon	0.185	0.053
K-BDI scores	-0.563	0.000

BMI: Body mass index; HBV: Hepatitis B virus; K-BDI: Korean version of the Beck Depression Inventory.

associated with ED in patients with chronic viral hepatitis.

There are some explanations for the high prevalence of ED in patients with chronic viral hepatitis. One explanation involves an inflammatory-based pathway. Several complex mechanisms of HCV and other mediators of viral hepatitis that lead to inflammation, increased oxidative stress, insulin resistance, and apoptosis may be associated with the development of ED^[8,20,21]. Chronic systemic inflammation accompanied by increased C-reactive protein levels decreases nitric oxide synthesis in endothelial cells, ultimately leading to endothelial dysfunction, which may account for the association between ED and hepatitis-related liver disease^[8,22,23].

Various conditions are associated with ED^[19]. Besides strict exclusion of these conditions, we additionally analyzed other demographic conditions. In our study, age, employment, and K-BDI scores were significantly associated with ED. However, only age was correlated with ED in the logistic regression analysis. This finding is consistent with the other previously reported results^[8,19]. Interestingly, Chung *et al.*^[8] reported that in the oldest age group (> 69 years), no significant difference was observed in the frequency of prior hepatitis diagnosis between ED patients and controls. They explained that these elderly men suffered from ED due to age-related factors, which are unrelated to hepatitis, such as lower testosterone level and higher peripheral vascular resistance. Three men belonging to the oldest group were included in our study. Two had both ED and depression, and one had ED without depression. Further studies assessing the correlation between ED and depression in the oldest age group are recommended.

Depression is associated with impairments of sexual function and satisfaction^[24,25]. However, whether depression has a direct influence on ED is debatable^[26,27]. Although the prevalence of depression

Table 3 Multiple logistic regression analysis of factors for erectile dysfunction

Factor	Erectile dysfunction			
	β	SE	Exp(B)	<i>P</i> value
Age	0.064	0.027	1.066	0.019
Depression	2.511	0.544	12.322	0

All models were adjusted for body mass index, smoking, employment, health insurance, religion, habitation, viral etiology, and peg-interferon use.

is high in patients with chronic viral hepatitis^[28,29], little is known about the association between depression and ED. In this study, depression had an independent negative impact on ED in patients with chronic viral hepatitis.

ED is associated with substantially broader aspects of a man's life than just erectile functioning^[30]. It is significantly associated with a poor sexual relationship and sexual satisfaction, diminished confidence, and low self-esteem^[30]. Our study reveals that depression is associated with ED. Therefore, depression may contribute to poor outcomes in patients with chronic viral hepatitis. Although the impact of depression on adverse outcomes, such as deteriorating liver function and poor survival in patients with chronic viral hepatitis, was not examined in this study, our results suggest that it is important to develop systematic approaches to screen these patients for depression, and to plan proper treatment strategies for these patients.

There are some limitations to our study. First, the number of study participants was relatively small, therefore, the results cannot be generalized. Second, it is considered shameful to admit to the existence of ED; hence the number of patients suffering from ED could have been underestimated. In our study, 20% of the initially enrolled patients refused to answer the questionnaire. After excluding these non-responders, we categorized the participants into an ED group and non-ED group to minimize bias. Third, our study did not provide information on a causal relationship between ED and depression, due to the cross-sectional design of the study. Therefore, further large-scale randomized clinical trials are required to determine whether screening and therapeutic interventions can prevent and control ED, improve depression, and positively affect the clinical outcomes of patients with chronic viral hepatitis. Finally, several factors that we did not exclude can act as confounders and may have introduced bias.

In conclusion, patients with chronic viral hepatitis have a high prevalence of ED, which is associated with depression. In patients with chronic viral hepatitis, detection of depression and active interventions should be considered for proper management of ED.

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COMMENTS

Background

Erectile dysfunction (ED) is associated with substantially broader aspects of a man's life. But ED in patients with chronic viral hepatitis has been investigated in few and limited studies. Moreover few studies have evaluated the association of ED and depression in patients with chronic viral hepatitis.

Research frontiers

The authors evaluated the prevalence of ED and the relationships between ED and depression in patients with chronic viral hepatitis.

Innovations and breakthroughs

To minimize the effect of confounding factors that might influence ED, the authors set various conditions as exclusion criteria.

Applications

The study suggests that patients with chronic viral hepatitis have a high prevalence of ED, which is associated with depression.

Terminology

ED is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance.

Peer-review

This manuscript is a good cross-sectional study in which authors evaluated the prevalence of ED and the association with depression in patients with chronic viral hepatitis. The results are interesting. The authors emphasize that detection of depression and active interventions should be considered to properly manage ED in patients with chronic viral hepatitis.

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