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Analysis of changes in the psychological status of HCV patients after DAAs treatment

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Abstract

Background It is well known that patients with chronic hepatitis C virus (HCV) infection are experiencing both physical and psychological pressures. However, no previous studies have examined whether the psychological state of HCV patients changes after treatment with direct-acting antivirals (DAAs).

Methods A prospective cohort study was conducted using the following scales: 1. The Hamilton Depression Rating Scale; 2. The Montgomery Asberg Depression Rating Scale; 3. Global Assessment of Functioning Scale; 4. Life Event Checklist; 5. Patient Health Questionnaire-9; 6. Quick Inventory of Depressive Symptomatology; 7. The 12-item Short Form Health Survey; 8. Stigma; 9. Subjective social status. Cohort members were included if they had HCV infection and were willing to receive DAAs therapy.

Results Global Assessment of Functioning Scale score and subjective social status score were significantly different in HCV patients without DAAs treatment compared with HCV patients after treatment with DAAs ($P < 0.05$). We found no significant differences in other scales.

Conclusions The current findings suggested that there was no change in the psychological status of HCV patients after treatment with DAAs except for the patient's sense of their position.

Keywords: chronic hepatitis C, direct-acting antivirals, psychological status, subjective social status

Introduction

Hepatitis C virus (HCV) infection is a major cause of chronic liver disease with significant morbidity and mortality [1]. Chronic hepatitis C infection can progress to liver fibrosis, cirrhosis, and hepatocellular carcinoma

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(HCC), leading to an estimated annual toll of approximately 700,000 lives lost because of HCV-associated complications. The advent of all-oral direct-acting antivirals (DAAs) has brought about a transformative change in HCV therapy [2]. Since the introduction of DAAs for the treatment of chronic hepatitis C, there has been a consistent and incremental improvement in sustained virological response (SVR) rates. These rates have now surpassed 90%, even in populations that were previously challenging to treat [3]. All-oral DAA therapies have expanded treatment options, making it feasible to treat older patients and individuals with compensated cirrhosis, who are ineligible for interferon-based therapies [4].

It is widely acknowledged that individuals with chronic HCV infection frequently experience symptoms of depression, anxiety, and alexithymia, especially as they advance to the end stage of liver disease. These symptoms tend to worsen with frequent hospitalizations and changes in body image [5]. Previous studies have shown that suicidal ideation, psychological morbidity and anxiety, and depression symptoms are directly influenced by HCV-serostatus [6, 7]. Many authors have speculated that HCV replication is detected in brain tissue, but it is difficult to determine whether the neuropsychiatric symptoms are caused by the toxicity of the virus itself to the nervous system or the related emotional stress [8]. Although several studies have investigated changes in health-related quality of life after HCV eradication [9, 10], there is still no research examining whether the psychological state of HCV patients changes after DAAs treatment. We designed the current study to analyze changes in the psychological status of HCV patients after DAAs treatment.

Patients and methods

Patients

Hepatitis C virus–infected patients from Beijing You'an hospital were enrolled from December 2018, and participants were followed until December 2020. The diagnosis of HCV infection was based on medical history, clinical examination, virological examination, biochemical tests, and ultrasound findings. Eligible participants were aged 18 years or older, had HCV infection, were psychiatrically stable, were willing to receive DAAs therapy, were DAAs treatment naive, and were able to provide informed consent. Exclusion criteria included decompensated cirrhosis, inability to provide informed consent, pregnancy or breastfeeding, hypersensitivity to DAAs, presence of a previously diagnosed mental illness, alcohol abuse in the last 3 months, and other causes of liver disease other than HCV infection.

Treatment for chronic hepatitis C comprises regimens with the following DAAs: daclatasvir, simeprevir, sofosbuvir, and dasabuvir.

All procedures in this study complied with the Declaration of Helsinki (revised in 2013). The study was reviewed and approved by the Ethics Committee of the Institute of Beijing You'an Hospital of Capital Medical University. The patient's written informed consent was obtained for publication of this manuscript and images.

Psychological evaluation

All psychological assessment was carried out by an expert. All patients were given psychological tests before DAAs treatment and 1 year after DAAs treatment using the following scale: 1. The Hamilton Depression Rating Scale (HAMD); 2. The Montgomery Asberg Depression Rating Scale (MADRS); 3. Global Assessment of Functioning Scale (GAF); 4. Life Event Checklist (LEC); 5. Patient Health Questionnaire-9 (PHQ9); 6. Quick Inventory of Depressive Symptomatology (QIDS-SR16); 7. The 12-item Short Form

Health Survey (SF-12); 8. Stigma; 9. Subjective social status (SSS). The HAMD, PHQ9, QIDS-SR16, and MADRS evaluated depression severity. In HCV subjects, depression was defined by considering the HAMD, PHQ9, QIDS-SR16 and MADRS scores. The *GAF was used to* evaluate patients' social functioning, with higher scores indicating less severe illness. The LEC is a comprehensive screening instrument used to detect exposure to a range of potentially traumatic events. Post-traumatic stress disorder and subthreshold post-traumatic stress disorder subgroups exhibit a higher number of LEC events. The SF-12 is a scale for evaluating physical and mental health outcomes. Stigma is a negative emotional experience manifested by patients with mental illness. SSS is an individual's perception of their own position in the social and socioeconomic hierarchy.

Statistical analysis

Normally distributed data were expressed as mean (± standard deviation). Nonparametric data were expressed as median (interquartile range). Unpaired t tests were used for intergroup comparison of normally distributed data and the Wilcoxon test was used to compare medians for nonparametric data. All calculations were conducted using SPSS 12.0 software. *P*-values < 0.05 in two-tailed analyses were considered statistically significant.

Results

Basic characteristics of patients

A total of 113 patients met the inclusion criteria. During the follow-up period, we were unable to collect the data of four patients because they could not be contacted. Among the remaining 109 cases were 52 male patients and 57 female patients; 89 Han Chinese patients, and 20 patients with other nationalities; 49 urban registered permanent residents and 60 rural registered permanent residents. Patients' medical insurance situations were as follows: 17 patients had self-funded medical care, eight patients had public medical care, 24 patients had medical insurance, 13 patients were members of rural cooperatives, and 47 patients had unknown medical insurance status. The baseline characteristics of this population are summarized in Table 1.

Psychological analysis

The normality test was carried out for all of the measurement data. The results revealed that all data were nonparametric and expressed as median values (interquartile range). The Wilcoxon test was used to compare medians.

As shown in Table 2, GAF scores were significantly higher in HCV patients without DAAs treatment compared with HCV patients after DAAs treatment. SSS score was significantly lower among HCV patients without DAAs treatment compared with HCV patients after DAAs treatment. There were no significant differences in the other scales.

The GAF is a rating scale for evaluating the overall psychological functioning or psychiatric sickness of an individual. GAF values range from 1, which represents the hypothetically sickest individual, to 100, the hypothetically healthiest individual. The scale is divided into 10 equal intervals: 1 to 10, 11 to 20, 21 to 30, 31 to 40, 41 to 50, 51 to 60, 61 to 70, 71 to 80, 81 to 90, and 91 to 100. The defining characteristics of each 10-point interval comprised the scale. The two highest intervals, 81 to 90 and 91 to 100, represent individuals with positive mental health status. The next interval, 71 to 80, represents individuals with minimal psychopathology. Because the GAF scores of the included patients were

Table 1. Summary of baseline clinical characteristics of 109 HCV patients.

Variable	Data (n/%)
Sex, Male	52 (47.7) /57 (52.3)
Nationality, Han	89 (81.7) /20 (18.3)
Registered permanent residence, urban	49 (45.0) /60 (55.0)
Medical insurance situation	
Self-funded medical care	17 (15.6)
Public medical care	8 (7.3)
Medical insurance	24 (22.1)
Rural cooperatives	13 (11.9)
Unknown	47 (43.1)

Table 2. Changes in the psychological status of 109 HCV patients.

Test scales	Baseline data/median (IQR)	After treatment/median (IQR)	P Value
MADRS	0 (0-4)	0 (0-2)	0.789
HAMD	1 (0-2)	0 (0-3)	0.923
GAF	90 (85-95)	90 (81-93)	0.041*
LEC	1 (0-6)	1 (0-4)	0.375
PHQ9	10 (9-13)	10 (9-13)	0.979
QIDS-SR16	3 (1-4)	3 (1-4)	0.695
SF-12	39 (35-41)	39 (35-41)	0.801
Stigma	44 (32-60)	46 (24-57)	0.338
SSS	44 (36-50)	48 (40-62)	0.007*

* $P < 0.05$

all higher than 80, the difference between before and after treatment was not significant.

SSS scores reflect a person's sense of their position in the socioeconomic hierarchy, and are strongly related to health in adults. SSS predicts health outcomes above and beyond traditional objective measures of social status, such as education, income and occupation. This construct has been used frequently as a predictor for several aspects of health, including physical health, mental health, and mortality. Our results indicated that HCV patients treated with DAAs generally believed that their social status had improved slightly, which was beneficial to their mental health.

Subgroup analysis

Considering that gender and domicile may affect psychological state, we conducted subgroup analysis according to each of these two factors. The results are shown in Table 3. Gender has no effect on the difference in SSS scores before and after DAAs treatment, but because of the difference in household registration, the difference in SSS scores before and after treatment was affected. Unlike rural patients, urban patients' sense of social status did not change before and after DAAs treatment. This may be related to the high basic SSS score of urban patients. Even with HCV infection, urban patients did not think that their social status had declined.

In addition, in urban patients, patients' stigma was reduced after DAAs treatment. Stigma refers to social rejection resulting from negatively perceived characteristics; this rejection negatively impacts the identity of the stigmatized individual. After DAAs treatment, the perceived stigma of urban patients was reduced, but that of rural patients remained unchanged.

Table 3. Subgroup analysis of psychological state change.

Test scales	Male		Famale		Rural		Urban	
	P value	Z	P value	Z	P value	Z	P value	Z
MADRS	0.913	-0.109	0.674	-0.421	0.988	-0.015	0.544	-0.607
HAMD	0.962	-0.048	0.739	-0.333	0.935	-0.082	0.611	-0.509
GAF	0.192	-1.306	0.126	-1.529	0.065	-1.845	0.454	-0.749
LEC	0.242	-1.169	0.959	-0.052	0.110	-1.597	0.905	-0.119
PHQ9	0.281	-1.078	0.251	-1.147	0.347	-0.941	0.232	-1.196
QIDS-SR16	0.622	-0.493	0.991	-0.011	0.571	-0.567	0.223	-1.220
SF-12	0.879	-0.153	0.877	-0.155	0.666	-0.432	0.875	-0.157
Stigma	0.277	-1.087	0.651	-0.452	0.527	-0.633	0.035	-2.103
SSS	0.047	-1.983	0.049	-1.972	0.037	-2.090	0.149	-1.444

Discussion

Hepatitis C is a liver disease caused by the HCV, which can cause acute and chronic infections. Currently, approximately 140 million people worldwide suffer from chronic HCV infection, including 10 million people in China and 4 million people in the United States, and are at risk for cirrhosis, liver cancer, and death if untreated [11]. Currently, the treatment of HCV infection relies only on antiviral drugs [12]. Prior to 2011, the standard treatment for hepatitis C was pegylated interferon alpha (PEG-IFNα) combined with ribavirin (RBV). Cure rates for this regimen range from 70%–80% for HCV genotypes 2 and 3 and 45%–60% for genotypes 1 and 4 [13]. The development of basic and clinical research on hepatitis C over the past few years has led to the emergence of a large number of new anti-HCV drugs, including several DAAs targeting multiple molecular targets [14]. The introduction of DAAs into clinical practice represents a milestone in the treatment of HCV [15]. With DAAs treatment, the vast majority (90%–95%) of HCV-infected patients can now be successfully cured.

In addition to causing liver disease, hepatitis C also has psychological, family, and social impacts. Patients with chronic HCV infection experience a range of symptoms, including depression, fatigue and neurocognitive deficits, which affect quality of life. Mood disturbances, especially depression and fatigue, are often the most challenging symptoms faced by HCV patients [16]. Many social and emotional factors may be involved, including awareness that having a chronic disease may lead to a poor long-term prognosis, shame about being infected, fear of infecting a loved one, guilt about infection, and social stigma [17]. Although DAAs have revolutionized treatment, it remains unclear whether these psychological symptoms are likely to continue to be a major burden in HCV patients even after viral clearance.

Previous studies have reported that neuropsychological symptoms strongly influence health-related quality of life in HCV patients and there was a significant improvement of neuropsychological testing and health-related quality of life after DAAs treatment [18]. However, our research results indicated that there was no change in the depression status of HCV patients after DAAs treatment. SSS is often used as a predictor of multiple aspects of health, and our results revealed that, after DAAs treatment, HCV patients' sense of their position in the socioeconomic hierarchy improved. Regarding HCV patients with urban household registration, subjective stigma also decreased after DAAs treatment.

The study involved several limitations. First, the sample size was limited and the study was a single-center

study, which limited the reliability of the conclusions. Second, no patients with decompensated cirrhosis were included in the study; consequently, the conclusions regarding the changes in the psychological status of HCV patients after DAAs treatment cannot be extended to a more advanced stage of HCV disease. Third, we did not conduct an analysis of the influence of comorbidities and patient's addictions, which may affect patients' psychological status.

In conclusion, we found no change in the psychological status of HCV patients after DAAs treatment except for the patient's sense of their position.

Acknowledgments

We thank Benjamin Knight, MSc., from Liwen Bianji (Edanz) (www.liwenbianji.cn) for editing the English text of a draft of this manuscript.

Funding

This work was supported by grants from the National Key Research and Development Program of Ministry of Science and Technology, (2022YFC2304400), High-level public health technical talents of Beijing Municipal Health Commission (Academic Leader -02-14), Beijing Hospitals Authority's Ascent Plan (DFL20241701), Beijing Science and Technology New Star program cross-cooperation project (20230484455).

Author Contributons

Shan Tang and Yeying Liu contributed equally to this work. Shan Tang authored drafts of the paper, Yeying Liu analyzed the data, prepared tables, Zhongping Duan revised the draft. Mei Liu and Su-Jun Zheng designed the experiments and approved the final draft.

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Patient consent for publication

Not required.

Ethics approval

All procedures in this study comply with the Declaration of Helsinki (revised in 2013). The study was reviewed and approved by the Ethics Committee of the Institute of Beijing You'an Hospital of Capital Medical University. The patients' written informed consent was obtained for publication of this manuscript and images.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

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Direct-acting antiviral (DAA) molecules target HCV