REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

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DOI: 10.17235/reed.2019.6339/2019
Link: PubMed (Epub ahead of print)

Please cite this article as:
Honrubia López Raúl, Madejón Seiz Antonio, Romero Portales Miriam, García Sánchez Araceli, Castillo Grau Pilar, Erdozain Sosa José Carlos, Olveira Martín Antonio, Robles Ana, García-Samaniego Rey Javier. Quality of life study in asymptomatic patients with hepatitis C. Rev Esp Enferm Dig 2019. doi: 10.17235/reed.2019.6339/2019.

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OR 6339 inglés

Quality of life study in asymptomatic patients with hepatitis C

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Received: 23/4/2019

Accepted: 26/05/2019

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ABSTRACT

Objective and methods: an observational, longitudinal, prospective study was performed to assess changes in perceived quality of life in asymptomatic patients with hepatitis C under treatment with direct-acting antivirals. Questionnaires SF-36 and EQ-5D-5L were administered to 86 treated patients and 12 controls.

Results: there were improvements in several parameters such as physical functioning, bodily pain, general health, vitality and social functioning, particularly when the perceptions were compared before treatment and after treatment completion and following recovery.

Conclusion: these data support the hypothesis that the hepatitis C virus may worsen quality of life in asymptomatic patients.

Key words: Hepatitis C. Antiviral. Health.

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INTRODUCTION

Studies that analyze quality of life allow an assessment of perceived health during a number of disease conditions, as well as the resulting changes after treatment completion. Hepatitis C (HCV) infection presents with both hepatic (cirrhosis, cirrhotic decompensations, liver-cell carcinoma) and extrahepatic (cryoglobulinemia and porphyria cutanea tarda, among others) clinical manifestations. Thus, curing a HCV infection clearly has a great impact on perceived quality of life. However, the effect of treatment on asymptomatic patients (i.e., those who did not develop decompensated liver disease or extrahepatic manifestations), where the sole evidence of improved quality of life would be infection clearance, has not been assessed. Therefore, the goal of this project was to assess changes in perceived quality of life in asymptomatic patients with HCV treated with direct-acting antivirals (DAAs).

MATERIALS AND METHODS

This was an observational, longitudinal, prospective study to compare two groups of patients. The study was approved by the Ethics Committee in our hospital. All patients signed the informed consent and patients were consecutively enrolled while visiting the Hepatology clinic.

Patients

Asymptomatic patients (n = 86) that were due to receive treatment with DAAs (expected sustained virologic response [SVR]: > 90%) were included in the study. A survey was administered on three successive time points: before treatment (n = 86), upon treatment completion (n = 42) and at 12 weeks after treatment (n = 38).

Patients (n = 12) with F0-F1 fibrosis who received no treatment according to the current regulations issued by the Madrid Region Health Authority (2015) were used as controls. A survey was also administered in this group of patients (n = 12) over two successive follow-up visits 12 months apart.

Questionnaires

The EQ-5D-5L questionnaire was developed by EuroQol (1) and includes a descriptive portion (EQ-5D) to assess five parameters (mobility, self-care, daily activities, pain/discomfort, anxiety/depression) and a visual analogue scale (VAS). The SF-36 questionnaire assesses eight parameters (2): physical functioning, limitations due to physical issues, bodily pain, social functioning or role, mental health, limitations due to emotional issues, vitality, energy or fatigue and perceived health overall.

Statistical analysis

Qualitative variables were compared using the Chi-squared test or Fisher's exact test. Quantitative data were compared with the parametric Student's t-test or non-parametric Mann-Whitney U-test for independent samples, using the SPSS v. 21.0 package (IBM Corp; Armonk, NY. USA).

RESULTS

Sociodemographic and clinical characteristics

Of all patients included in the treatment group, 44 (51.2%) were female and 42 (48.8%) were male, with a mean age of 57.24 years and a standard deviation of 11.52 years. The most commonly used therapy was the combination of sofosbuvir and ledipasvir in 57 patients (66.3%). Ribavirin was used for the treatment of nine patients (10.8%) but only three (7.9%) of these cases completed all questionnaires. All patients that underwent treatment had a sustained virological response. Differences were only found between treated and control patients with regard to the fibrosis stage and prior therapy (Table 1).

SF-36 analysis

No statistically significant differences were found at baseline between the group who received treatment and the control arm, nor between the two visits performed for the control arm. All dimensions had improved when the treatment completion sample was compared to the treatment onset sample, although the improvement was only significant for perceived general health. When treatment onset *versus* follow-up completion samples were assessed, significant improvements were found for physical

functioning, bodily pain, general health, vitality and social functioning. In contrast, no significant differences were found between the treatment completion and follow-up completion samples (Table 2).

EQ-5D-5L analysis

No significant differences were found at baseline between the control arm and the group of patients who received treatment, nor between the two visits performed for the control arm. Among the treated patients, an increase in the proportion of subjects with no limitations was found for all the dimensions assessed when the samples at treatment onset and follow-up completion were compared (Table 3). A significant overall improvement was seen between treatment onset and follow-up completion samples. In contrast, no significant changes were seen between treatment completion and follow-up completion samples.

Stratified analysis

No significant differences were observed in any of the study parameters when the analysis was stratified into patients with (n = 15) and without (n = 22) higher education. Patients were then split into two groups, with baseline mild-moderate fibrosis (F0-F2; n = 23) and with advanced fibrosis (F3-F4; n = 15). No statistically significant differences were found between them. With regard to patients who were employed (n = 26) or unemployed (n = 12), differences were found in the perceived general health and vitality (Table 4).

DISCUSSION

This study assessed changes in perceived quality of life among asymptomatic patients (no hepatic and/or extrahepatic manifestations) with HCV on DAAs, in order to establish whether HCV may in itself be the cause of a worsening perceived quality of life, as previously suggested in some studies (3). Two previously validated questionnaires were used according to the strategy involving the simultaneous use of generic questionnaires (4). Among the specific questionnaires, the Chronic Liver Disease Questionnaire-HCV Version (CLDQ-HCV) is one of the most widely used in

hepatitis C patients (5). With regard to the EQ-5D tool, the 5L version was selected as it has been proven superior to the 3L version (6,7).

According to the SF-36 questionnaire, studies performed before the introduction of DAAs confirmed that treated patients who reached SVR had a better perceived quality of life with regard to physical, social and health-related items. However, the fact that these studies included symptomatic patients and the side effects of combined therapy with peginterferon and ribavirin, should be taken into consideration (8).

A study of 997 patients on DAAs, with a significantly better response and tolerance than interferon-based therapies (9), found a negative association between perceived quality of life and symptoms discomfort and depression using the EQ-5D questionnaires and EuroQOL scale (10). However, this study assessed quality of life at a single timepoint and did not take patient outcome following SVR into account, which is in contrast with our series. Another study that assessed 199 HCV patients on DAAs, who completed the EQ-5D-5L questionnaire at treatment onset and at 12 and 48 weeks post-treatment concluded that perceived quality of life had improved (11). Our study shows similar results, although the timepoints differ, as they included patients with comorbidities such as anxiety or depression and coinfection with human immunodeficiency virus (HIV).

A significant improvement of multiple parameters after treating asymptomatic patients was found in our study, which may indicate that infection may in itself worsen the perceived quality of life. In support of this notion, untreated patients had no changes in perceived quality of life. These results confirm those obtained by a similar study in 56 patients assessed before, during and after treatment with DAAs. This study found improvements in perceived quality of life with regard to physical functioning, physical problems, pain, general health, vitality and mental health after treatment (12). However, in our series, there were significant differences in social role and no differences in physical problems or mental health. This is likely due to the differences in the number of treated patients and survey timing. In fact, follow-up duration was a limitation in our study. Overall, it has been reported that patients with initial fibrosis stage may suffer from astenia or depression (13) and neurocognitive (14) or monoaminergic neurotransmission impairment (15).

To conclude, asymptomatic patients with HCV experience an improvement in perceived quality of life following treatment with DAAs. These data support the hypothesis that HCV may worsen quality of life in asymptomatic patients, although an effect of stigma removal and cure expectations cannot be ruled out (16).

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Table 1. Baseline characteristics of patients, both treated and untreated

Variables	*Treated (n = 86)*	*Untreated (n = 12)*	*p-value*
Age (years): mean (SD)	57.24 (11.52)	55.67 (8.88)	0.629
Gender			
Male	42 (48.8%)	6 (50%)	0.940
Female	44 (51.2%)	6 (50%)	
Marital status			
Married	50 (58.1%)	4 (33.3%)	
Divorced	11 (12.8%)	1 (8.3%)	
Single	16 (18.6%)	6 (50%)	0.18
Widowed	7 (8.1%)	1 (8.3%)	
ND	2 (2.3%)		
Education			
Primary	24 (27.9%)	2 (16.7%)	
Secondary	29 (33.7%)	6 (50%)	0.635
Higher	30 (34.9%)	4 (33.3%)	
ND	3 (3.5%)		
Employment	36 (41.9%)	4 (33.3%)	
Unemployed	46 (53.5%)	8 (66.7%)	0.583
Employed	4 (4.7%)		
ND			
Treatment			
SOF + LDV	57 (66.3%)		
OBV/PTV/ritonavir + dasabuvir	14 (16.3%)		
Rivabirin combination	9 (10.8%)		
Other	3 (3.5%)		
ND	3 (3.5%)		
Fibrosis stage			
F0-F1	3 (3.5%)	12 (100%)	
F2	41 (47.7%)		≤ 0.01
F3	20 (23.3%)		
F4	22 (25.6%)		
Prior treatment			
Yes	39 (45.4%)	2 (16.7%)	

SD: standard deviation; ND: no data; SOF: sofosbuvir; LDV: ledipasvir; OBV: ombitasvir; PTV: paritaprevir. Other: sofosbuvir + simeprevir; sofosbuvir + daclatasvir; ombitasvir/paritaprevir/ritonavir. Significant p-value: $p < 0.05$.

Table 2. Descriptive results from the SF-36 questionnaire in treated patients

Dimension	*Treatment onset (n = 86)*	*Treatment end (n = 42)*	*12 weeks of follow-up (n = 38)*	*p-value (onset vs follow-up)*
Physical functioning	90 (25)	95 (10)	95 (16.3)	*0.023*
Physical problems	25 (100)	50 (100)	75 (100)	0.175
Bodily pain	72 (41)	84 (38.3)	84 (19)	*0.004*
General health	57 (37)	72 (25)	72 (25)	*0.003*
Vitality	55 (21.3)	60 (21.3)	62.5 (25)	*0.007*
Social role	87.5 (40.6)	87.5 (37.5)	93.8 (25)	*0.041*
Emotional role	66.7 (100)	66.7 (100)	83.3 (75)	0.165
Mental health	68 (28)	72 (17)	72 (21)	*0.052*

All data are expressed as median (interquartile range) values. Significant p-value: $p < 0.05$.

Table 3. Descriptive results from the EQ-5D-5L questionnaire in treated patients

EQ-5D-5L variables		*Tx. (n = 86)*	*Tx. end (n = 41)*	*Follow-up (n = 38)*	*p-value*
Mobility					
	I have no problems walking about	77.4	80.0	86.1	0.045
	I have slight problems walking about	10.7	15.0	5.6	
	I have moderate problems walking about	7.1	5.0	8.3	
	I have severe problems walking about	4.8	0.0	0.0	
Self-care					
	I have no problems washing or dressing myself	94.0	92.5	94.4	0.61
	I have slight problems washing or dressing myself	3.6	7.5	5.6	
	I have moderate problems washing or dressing myself	2.4	0.0	0.0	
Usual activities					
	I have no problems doing my usual activities	73.8	79.5	83.3	0.66
	I have slight problems doing my usual activities	13.1	15.4	8.3	
	I have moderate problems doing my usual activities	7.1	5.1	8.3	
	I have severe problems doing my usual activities	3.6	0.0	0.0	
	I am unable to do my usual activities	2.4	0.0	0.0	
Pain/discomfort					
	I have no pain or discomfort	56.0	71.8	80.6	0.19
	I have slight pain or discomfort	25.0	20.5	11.1	
	I have moderate pain or discomfort	14.3	5.1	5.6	

	I have severe pain or discomfort	4.8	2.6	2.8	
Anxiety/depression					
	I am not anxious or depressed	58.3	67.5	77.1	0.35
	I am slightly anxious or depressed	17.9	25.0	14.3	
	I am moderately anxious or depressed	15.5	5.0	5.7	
	I am severely anxious or depressed	7.1	2.5	2.9	
	I am extremely anxious or depressed	1.2	0.0	0.0	
Health state (0-100)		72.4	78.1	82.7	0.012

Tx.: treatment. Significant p-value: $p < 0.05$. Health state (0-100) according to the EVA survey.

Table 4. Stratified analysis of general health and vitality parameters according to employment status

Dimension	*Tx. onset vs follow-up*	*p-value*	*Tx. onset vs end*	*p-value*
General health	-10.00 (23.75)		-5.00 (16.25)	
Employed (n = 23)	-15.00 (25.00)	0.070	-10.00 (19.00)	*0.006*
Unemployed (n = 12)	-2.00 (25.06)		0.00 (25.63)	
Vitality	-5.00 (20.00)		-5.00 (21.25)	
Employed (n = 23)	-10.00 (15.00)	0.080	-2.50 (25.00)	0.971
Unemployed (n = 12)	0.00 (21.25)		-5.00 (22.50)	

Tx.: treatment. All data are expressed as median (interquartile range) values. Significant p-value: $p < 0.05$.