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EVALUATION OF QUALITY OF LIFE AND PHARMACOLOGICAL EFFICIENCY OF PATIENTS WITH CHRONIC *HEPATITIS-C*

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ABSTRACT

Present study aimed to describe the quality of life and pharmacological efficiency outcomes for Armenian chronic hepatitis C patients.

We performed a prospective study, which included 275 patients with and without chronic Hepatitis C. Patients (175) with chronic Hepatitis C formed case and 200 healthy age-matched patients – control group. For the patient-reported outcomes evaluations we used one general (the 36-item short-form health survey), one specific (gastrointestinal symptom rating scale questionnaire) quality of life questionnaires and one questionnaire for evaluation of psychological status (Spielberger's tests). In case group evaluation of life quality was done twice – before and after treatment (30th day after end of treatment).

The most common type of psychological disorder was anxiety. It has also been found that 99.7% of patients had high level of reactivity and personal anxiety, making up 43.7±1.3 and 40.2±2.1 points, respectively.

The mean scores (SF-36) in case group for Physical Functioning was 70.1±0.9 points, General Health – 35.2±3.7, Vitality – 43.7±3.5 and in control group was 84.2±1.7; 52.3±4.2; 60.3±3.1, respectively.

The study results showed that the quality of life scores of patients with chronic hepatitis C were significantly lower than in age-matched controls. According to the SF-36 questionnaire, the most affected subscales were General Health and Vitality, according to the gastrointestinal symptom rating scale questionnaire – Indigestion and Constipation. The most common type of psychological disorder in case group was anxiety. Between scores of SF-36 and gastrointestinal symptom rating scale questionnaires were registered strong negative correlation. The highest increases in quality of life scores for case group after treatment were registered for "General Health" and "Vitality" domains.

KEYWORDS: *hepatitis C virus, short-form health survey, gastrointestinal symptom.*

INTRODUCTION

Hepatitis C virus (HCV) infects around 2.8% of the world's population, with estimates of 3 to 4 million new infections per year around the world [*Hanafiah K et al., 2013; Pawlotsky J et al., 2015; Pawlotsky J et al., 2018*]. For many patients who become chronically infected, HCV causes slow, progressive damage to the liver and represents one of the leading causes of cirrhosis and hepatocellular carcinoma (HCC) [*Parkin D, 2006*]. Chronic hepatitis C develops in 10% to 20% of cases leading to liver cirrhosis, and 1% to 3% of those infected can develop HCC [*Hoshida Y et al., 2014; Westbrook R, Dusheiko G, 2014; Younossi Z et al., 2014*].

It is widely known that hepatitis C virus (HCV) infection may be associated with impairment in health-related quality of life (HRQOL) [*Strauss E, Teixeira M, 2006; Ong S et al., 2008*]. Late-stage liver disease, with a high degree of fibrosis and liver dysfunction, will surely lead to impairment of HRQOL, regardless of etiology. However, many studies have shown poorer HRQOL even in the early phases of liver disease, especially in HCV patients [*Foster G et al., 1998; Teixeira M et al., 2006*].

The concept of quality of life (QOL) represents the patient's perception of the effect of the disease

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and the treatment given, upon physical, psychological and social aspects of their life [*U.S. Department, 2017*]. Patient-reported outcomes (PROs) are measures exclusively reported by the patients themselves, without the influence of the interviewer, on issues that include health-related quality of life (HRQOL) [*Younossi Z et al., 2007*].

The guidelines for the current treatment of chronic hepatitis C has rapidly evolved and continues to evolve. Hepatitis C has become a curable disease with the use of antiviral agents (>95%). Spontaneous resolution of acute HCV infection may occur in 15% to 50% of patients. Monitoring for spontaneous clearance for a minimum of 6 months before initiating treatment is therefore recommended [*Bottero J et al., 2014*].

Previously the main treatment for chronic hepatitis C virus infection was combination therapy with injectable pegylated interferon-alfa plus oral ribavirin. Because of it poorest safety profile of all the HCV antivirals, with few exceptions pegylated interferon-alfa is no longer recommended in combination regimens. Ribavirin continues to be used in combination with sofosbuvir alone or other combinations [*Myers R et al., 2015*].

Introduced in 2011 the direct-acting antiviral agents offered enhanced efficacy when combined with both PEG-IFN and ribavirin. There are three classes of approved direct-acting antiviral agents: NS3/4A protease inhibitors, NS5A inhibitors, and polymerase inhibitors (nonnucleoside inhibitors and nucleotide inhibitors). The particular combination of antivirals is determined by genotype. Several novel agents are only available as a fixed-dose combination [*Shah H et al., 2018*].

This study aimed to describe the quality of life (QoL) and pharmacological outcomes for Armenian chronic hepatitis C patients.

MATERIAL AND METHODS

Patients: We performed a prospective study, which included 275 patients with and without chronic Hepatitis C. 175 patients with chronic Hepatitis C formed case and 200 healthy age-matched patients – control group. From July 2015 until December 2017, in 24 Medical Centers we prospectively selected patients diagnosed with chronic Hepatitis C, based on medical history and laboratory test results. Inclusion criteria for the study were patients with established HCV (genotypes 1, 2 or 3). Exclusion criteria were co-infections with the hepatitis B virus or human immunodeficiency virus (HIV), hepatocellular carcinoma. The control group was selected from same Medical centers in the same period.

For case group treatment were organized with Ribavirin, with sofosbuvir alone or other combinations. Reevaluation of QOL scores in case group were done 1 month after treatment.

This study was conducted in accordance with the Declaration of Helsinki (1964). The research protocol was approved by Research Ethics Committee of National Institute of Health. All patients signed an informed consent form.

For the PRO evaluations, 3 widely used, self-administered questionnaires were used.

The 36-item Short-Form Health Survey (SF-36): The 36-item short form survey (SF-36), a self-reported measure of health status and quality of life [*Ware J, Sherbourne C, 1992*], was used to determine patient health-related quality of life. It comprises 36 items allocated across eight domains, namely: Physical Functioning, Physical Role Functioning, Emotional Role Functioning, Social Role Functioning, Mental Health, Bodily Pain, Vitality, and General Health Perceptions. The SF-36 also includes two summary scales for scoring: a physical health scale, which encompasses the domains Physical Functioning, Physical Role Functioning, Bodily Pain, and General Health Perceptions; and a mental health scale, which covers the domains Vitality, Social Role Functioning, Emotional Role Functioning, and Mental Health.

Gastrointestinal Symptom Rating Scale (GSRS) questionnaire: The GSRS is self-administered questionnaire and has 15 questions divided into 5 domains that cover the gastrointestinal system: diarrhea, constipation, abdominal pain, reflux and indigestion. The questionnaire answers are arranged according to the 7-point Likert scale, in which “1” indicates absence and “7” the higher frequency or intensity of the symptoms [*Svedlund J et al., 1988; Dimenäs E et al., 1996; Revicki D et al., 1998*].

Spielberger’s tests: The degree of situational and personal anxiety has been evaluated with the help of validated Armenian version of Spielberger’s tests [*Spielberger C et al., 1983; Mardiyan M et al. 2017*].

Spielberger’s test-questionnaire consists of 40

judgments. Twenty judgments refer to determining the situational anxiety level and the other twenty judgments refer to determining the personal anxiety level. To evaluate the anxiety level, the evaluation key is applied. Depending on the effective sensor of the respondent the degree of situational and personal anxiety is evaluated.

In practice the following scale of anxiety level evaluation is more applicable: up to 30 points – low, from 31 to 44 points – medium, 45 and higher – high.

Statistical analysis: The results are presented as percent, mean, and standard deviation. The SF-36 scores were compared with GSRS results (ISS and CSS score) using analysis of variance (ANOVA) and Pearson correlation. Differences with a $p<0.05$ were considered statistically significant. All analyses were performed using IBM_ 22.0.0 SPSS statistical package (IBM, Armonk, NY).

Results and discussion

The mean age for case group were 30.2±2.9 years and for control – 31.5±2.8.

61.3% of patients had adequate response to the disease; however, there were moderate or expressed signs of socio-psychological disorder. The most common type of psychological disorder was anxiety (40.2% in case and 9.3% in control).

According to the personal profile structure, the hypothetical scale (depression, hysteria) was dominant in case group. It is obvious that these phenomena are conditioned by the development of the neurotic type of the person at the time of disease, with the formation of an alarmingly depressive and hysterical variant, which is psychologically equivalent to anxiety and depression.

The score varies between 30 and 70 points, which indicates moderate personality disorders. 40.3% of depression patients had some symptoms of depression. The average sum was 53.7±0.9. The pattern of depression in our patients is as follows: 80.3% of anxiety and 19.7% of apathy, and 77.3% of the patients had a psychological status with depressive syndrome. In control group depressive syndrome had only 17.6% of patients.

It has also been found that 99.7% of patients had high level of reactivity and personal anxiety, making up 43.7±1.3 and 40.2±2.1 points, respectively.

The QoL measures with SF-36 questionnaire showed that patients with chronic Hepatitis C have significantly lower scores compared with controls. Based on results of study significantly lowered QoL subscales in case group were Physical Functioning, Social Role Functioning, Emotional Role Functioning, Mental Health, General Health, Vitality ($p<0.05$).

The mean scores in case group for Physical Functioning was 70.1±0.9 points, General health – 35.2±3.7, Vitality – 43.7±3.5 and in control group was 84.2±1.7; 52.3±4.2; 60.3±3.1, respectively (table 1). The highest score in control group were detected for Physical Functioning subscale (84.2±1.7) and the lowest – General Health (52.3±4.2).

The QoL measures with GSRS questionnaire showed that patients with chronic Hepatitis C have significantly lower scores compared with controls (Table 2). Based on results of study significantly higher scores were detected for all domains in case group ($p<0.05$), which indicated in impairment in health-related quality of life. Most affected domains in case group were Indigestion (12.1±0.03) and Constipation (9.1±0.03).

The results of study showed strong negative correlation between scores of SF-36 and GSRS questionnaires (-0.81).

QoL scores improvement was registered after treatment. The highest increases were registered for “General Health” and “Vitality” domains by 37.2% and 34.1%, respectively (table 3). There were no detected significant improvements for “Physical Role Functioning” and “Bodily Pain” domains ($p>0.05$).

Table 1.

QoL scores of investigated patients according SF-36 quaestionnaire

SF -36 subscales	Case group (n=175)	Control group (n=200)	P value
Physical Functioning	70.1±0.9	84.2±1.7	<0.05
Physical Role Functioning	62.4±2.4	63.2±2.4	>0.05
Bodily Pain	63.5±1.9	63.5±1.9	>0.05
General Health	35.2±3.7	52.3±4.2	<0.05
Vitality	43.7±3.5	60.3±3.1	<0.05
Social Role Functioning	65.7±1.9	75.3±2.9	<0.05
Emotional Role Functioning	60.7±0.5	70.5±0.7	<0.05
Mental Health	54.3±2.2	67.5±1.7	<0.05

TABLE 2.

QoL scores of investigated patients according GSRS quaestionnaire

GSRS domains	Case group (n=175)	Control group (n=200)	P value
Abdominal Pain	4.9±0.04	1.9±0.05	<0.05
Indigestion	12.1±0.03	6.3±0.04	<0.05
Reflux	6.8±0.04	4.8±0.05	<0.05
Diarrhea	7.9±0.04	4.9±0.04	<0.05
Constipation	9.1±0.03	4.7±0.03	<0.05

TABLE 3.

QoL scores of investigated patients according SF-36 quaestionnaire

SF -36 subscales	Case group		P value
	before treatment (n=175)	after treatment (n=172*)	
Physical Functioning	70.1±0.9	79.8±1.4	<0.05
Physical Role Functioning	62.4±2.4	67.2±2.1	>0.05
Bodily Pain	63.5±1.9	66.5±1.2	>0.05
General Health	35.2±3.7	48.3±3.2	<0.05
Vitality	43.7±3.5	58.6±2.4	<0.05
Social Role Functioning	65.7±1.9	74.1±1.8	<0.05
Emotional Role Functioning	60.7±0.5	71.3±0.7	<0.05
Mental Health	54.3±2.2	65.2±1.4	<0.05

NOTE: *QoL reevaluation was done only for 172 patients.

Strength of this study is to be one of the first studies to explore the quality of life, psychological status and QoL scores improvement after treatment of patients with chronic Hepatitis C in a developing country [*Ban SD et al., 2016*].

Conclusion

The results of the study showed that the QoL scores of Patients with Chronic Hepatitis C were significantly lower than in age-matched controls. According to the SF-36 questionnaire, the most affected subscales were "General Health" and "Vitality", according to the GSRS questionnaire - Indigestion and Constipation (9.1±0.03). The most common type of psychological disorder in case group was anxiety. Between scores of SF-36 and GSRS questionnaires were registered strong negative correlation. The highest increases after treatment were registered for "General Health" and "Vitality" domains.

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