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DYNAMICS OF QUALITY OF LIFE INDICATORS IN PATIENTS WITH CHRONIC HEPATITIS C DURING TREATMENT AND METHOD OF THEIR CORRECTION

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In addressing the issue of treatment of patients with chronic hepatitis C (CHC), scientists publish new data and discover new opportunities every day. The modern view of etiotropic therapy for patients with CHC has changed the approach to treatment. Therefore, today the effectiveness of direct antiviral drugs has been proven, which lead to the elimination of the virus, leaving unresolved the issues of further progression of liver fibrosis and improvement of quality of life.

The aim of the study was to evaluate the degree of liver fibrosis and quality of life in patients with CHC when using drugs with direct antiviral action and the method of their correction.

Materials and methods. We examined 66 patients with HCV with pre-existing grade 1 and 2 liver fibrosis before treatment. 33 patients of group 1 received etiotropic therapy with direct-acting antiviral drugs – sofosbuvir and ledipasvir, 33 patients of group II received additional methadoxine as pathogenetic treatment. The diagnosis was confirmed by polymerase chain reaction and enzyme-linked immunosorbent assay. Quality of life was assessed using the SF-36 scale.

Results. A decrease in quality indicators was observed in all patients with CHC in the form of complaints of general weakness, increased fatigue, decreased performance, mood depression, irritability, pain or heaviness in the right hypochondrium, abdominal bloating, bleeding gums, and joint pain. The greatest impairment was found in the psychological component of quality of life due to indicators of role functioning and general health of patients. Methadoxine can be recommended in the treatment of patients with CHC as a means of pathogenetic therapy, the use of which leads to a decrease in the severity of liver fibrosis and improvement of quality of life.

Keywords: chronic hepatitis C, quality of life.

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ДИНАМІКА ПОКАЗНИКІВ ЯКОСТІ ЖИТТЯ У ХВОРИХ НА ХРОНІЧНИЙ ГЕПАТИТ С ПІД ВПЛИВОМ ЛІКУВАННЯ ТА СПОСІБ ЇХ КОРЕКЦІЇ

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У вирішенні питання лікування хворих на хронічний гепатит С науковці щодня публікують нові дані та відкривають нові можливості. Сучасний погляд на етіотропну терапію хворих на хронічний гепатит С змінив підхід у лікуванні. Тому на сьогодні є доведеною ефективність застосування препаратів прямої противірусної дії, які призводять до елімінації вірусу, залишаючи невирішеними питання щодо подальшого прогресування фіброзу печінки та покращення якості життя. Проведено дослідження показників якості життя, яке показало зміни за всіма шкалами його оцінки. Найбільших змін зазнавав психічний компонент здоров'я пацієнтів. Усі хворі, які ввійшли в дослідження, отримували лікування із застосуванням препаратів прямої противірусної дії. Проте покращення показників якості життя відбувалось лише у тієї групи хворих, до терапії яких додавали метадоксин.

Ключові слова: хронічний гепатит С, якість життя.

Introduction

In recent years, scientists have made a major breakthrough in the treatment of patients with chronic hepatitis C (CHC). The use of direct-acting antivirals (DAAs) in therapy is accompanied by a sustained virologic response (SVR) [2; 5; 7; 10], i.e., it leads to the elimination of HCV in 95–100% of patients [3; 6; 9]. However, liver fibrosis (LF) does not always reverse, most often remaining at the same level or progressing [1; 4; 8; 12]. It is the functional state of the liver and the activity of fibrosis formation processes that affect the quality of life (QoL) of patients with CHC [1; 10; 11].

In our opinion, it is necessary to influence fibrosis formation in order to improve the QoL of patients with CHC.

The aim of the study was to evaluate the degree of LF and QoL in patients with chronic CHC using direct antiviral drugs and the method of their correction.

Materials and methods

Under our supervision, 66 patients with CHC were treated in the hepatocenter of the Municipal Clinical and Research Institution "The Municipal Clinical Infectious Diseases Hospital" of the City Council. On admission, they

were diagnosed with minimally severe LF (F1) and mild LF (F2). All patients were divided into two groups. Group I included 33 patients treated with DAAs – sofosbuvir 400 mg and ledipasvir 90 mg (UA/17221/01/01 of February 19, 2019, Order No. 489 of March 14, 2023), by 1 tablet once a day for 12 weeks. Group II consisted of 33 patients treated with sofosbuvir 400 mg and ledipasvir 90 mg, 1 tablet once a day for 12 weeks, and methadoxine (UA/13164/01/01 of 29/11/2017, Order No. 153 of 25/01/2022) 0.5 g twice a day for 12 weeks, and 0.5 g once a day for the next 12 weeks.

The diagnosis of CHC was confirmed by the detection of HCV RNA in the blood serum by polymerase chain reaction (PCR) and specific (aHCV, aHCVNS3, aHCVNS4, aHCVNS5, aHCV-IgM) antibodies by enzyme-linked immunosorbent assay (ELISA). The degree of LF was determined by elastography (FibroScan). The Short Form Medical Outcomes Study (SF-36) questionnaire was used to assess the QoL of patients.

The survey results were presented in the form of scores on 8 scales, compiled in such a way that a higher score indicated a higher level of QoL. The first scale – Physical Functioning (PF) reflects the degree to which the physical condition limits the performance of physical activities (self-care, walking, climbing stairs, weight bearing, etc.). The second scale, Role Physical (RP), indicates the impact of the physical condition on daily role activities (work, daily duties). The third scale is "pain intensity" (Bodily Pain – BP), which assessed the impact of pain on the patient's ability to engage in daily activities, including housework and outdoors. The fourth scale, General Health (GH), allows patients to assess their current health status and treatment prospects. The fifth scale is Vitality (VT), a patient's self-assessment of himself or herself. The sixth scale, Social Functioning (SF), determines the degree to which the patient's physical or emotional state limits social activity (communication). The seventh scale is Role Emotional (RE), which assesses the degree to which the emotional state interferes with work or other daily activities, including large time costs, reduced workload, reduced quality, etc. The eighth scale is Mental Health (MH), which characterizes mood, depression, anxiety, and the overall level of positive emotions.

All indicators were combined into two components – "Physical Component of Health" (PH) and "mental component of health" (MH_1). PH included the following components: physical functioning, role functioning due to physical condition, pain intensity, and general health. MH_1 consisted of the following scales: mental health, role functioning due to emotional state, social functioning, and life activity.

The degree of LF was studied at the time of the patient's visit to the hepatology center and after 24 weeks of follow-up. QoL was assessed at presentation, 12 weeks and 24 weeks. Statistical data processing was performed using Microsoft Office 2012, to identify statistical differences between the degree of LF at presentation and after 24 weeks, as well as between the degree of LF and QoL indicators, the Mann-Whitney U test was used (H0): No statistically significant differences between the results of groups 1 and 2; H1: Differences between the results of groups 1 and 2 are statistically significant).

The study implemented measures to ensure the safety and rights of patients, human dignity and ethical standards in accordance with the principles of the Declaration of Helsinki, the European Convention on Human Rights and the current laws of Ukraine. The study was approved by the Bioethics Commission of the Odesa National Medical University of the Ministry of Health of Ukraine (protocol No. 4 dated April 10, 2013).

Informed consent was obtained from each patient after a thorough explanation of the nature and scope of the study. After obtaining the patient's consent to use the data from the medical records, all necessary measures were taken to ensure anonymity and confidentiality.

Results and their discussion

During the initial survey, patients had the following complaints general weakness – in 19 (57.58%) patients of group I and 21 patients of group II (63.64%), increased fatigue – 17 (51.52%) and 19 (57.58%) patients, decreased work capacity – 12 (36.36%) and 13 (39.39%) patients – 37.88%, depressed mood – 11 patients (33.33%) and 12 patients (36.36%), irritability – 8 (24.24%) and 9 (27.27%) patients, pain or heaviness in the right hypochondrium – in 19 (57.58%) and 20 (60.61%) patients, abdominal bloating – in 7 (21.21%) and 7 (21.21%) patients, periodic nosebleeds and bleeding gums – in 6 (18.18%) and 6 (18.18%) patients, joint pain – in 4 (12.12%) and 5 (15.15%) patients, respectively.

During elastography, signs of minimally expressed LF (F1) were diagnosed in 18 (54.54%) patients of group I and 17 (51.51%) patients of group II. Mildly expressed LF (F2) was determined in 15 (45.45%) patients of group I and 16 (48.48%) patients of group II.

Patients with LF grade F1 complained of: general weakness (16 patients – 24.24%), increased fatigue (12 patients – 36.36%), decreased performance (7 patients – 10.61%), mood depression (6 patients – 9.91%), irritability (3 patients – 4.55%), pain or heaviness in the right hypochondrium (14 patients – 21.21%). The number of patients with complaints in the mild LF was higher than in patients with minimally expressed LF. Thus, 24 patients with F2 (72.73%) complained of generalized weakness, 24 patients (72.73%) of increased fatigue, 18 patients (54.55%) of decreased work capacity, 17 patients (51.52%) of mood depression, 14 patients (42.42%) of irritability, 25 patients (75.76%) with pain or heaviness in the right hypochondrium, 14 patients (42.42%) with abdominal bloating, 12 patients (36.36%) with recurrent nosebleeds and bleeding gums, 9 patients (27.27%) with joint pain.

Also, abdominal palpation revealed an increase in liver size by an average of (1.33±0.11) cm in patients with F1 and by (2.12±0.14) cm in patients with F2.

When patients came to the hepatology center, a decrease in all QoL indicators of patients with CHC was noted. When interviewing patients with CHC before treatment, certain changes in the RP and GH scores were found. The results obtained were lower than in healthy individuals, indicating a negative impact of the emotional state and general health of patients on everyday life. Thus, the RP score was 1.6 folds lower than the physiological values, and the GH score was 1.9 folds lower (Table 1).

Table 1

QoL indicators in patients with CHC (M±m)

Group / Indicator	Healthy (n=32)	Patients with CHC	
		I group (n=33)	II group (n=33)
PF, points	96.17±4.41	77.42±17.15*	78.85±17.03*
RP, points	85.8±15.4	54.4±16.8*	54.24±14.22**
RE, points	97.8±8.23	58.63±27.32*	56.58±22.67*
VT, points	83.7±9.15	64.39±10.78*	67.72±11.08*
MH, points	77.07±5.74	65.45±14.13*	65.82±11.66*
SF, points	91.47±3.49	70.30±13.49*	65.0±12.56*
BP, points	95.73±9.43	62.78±16.79*	59.18±14.46*
GH, points	73.67±10.08	39.55±2.69*	41.97±3.39*
PH,%	87.85±9.23	63.54±16.62*	66.31±15.52*
$MH_{1,\%}$	89.64±8.91	65.81±16.43*	60.03±14.49*

Notes:

1. * – difference is significant compared to healthy individuals ($p<0.01$)
2. ** – difference is significant compared to healthy individuals ($p<0.05$)

We reassessed the QoL indicators 12 and 24 weeks after the start of treatment. Thus, after 12 weeks, patients in group I showed a 1.3-fold increase in QoL, which indicated general health, alone. In group II, changes in QoL were more significant. For example, there was a 1.7-fold increase in PF, MH, and PH, and a 1.6-fold increase in RE, BP, and MH_1 ($p<0.01$).

After 24 weeks in group I, PF was even lower than at week 12 of treatment, and when assessing PF in group II, it was at the physiological level.

The role functioning of patients with CHC, due to their physical condition, also underwent changes during the observation period. After 24 weeks, RP in group I continued to decline and was 1.4 folds lower than in healthy subjects and patients of group II ($p<0.01$). In group II, normalization of RP was simultaneously observed ($p<0.01$).

The index of role functioning due to the emotional state after 24 weeks was 1.2 folds lower than in healthy individuals in group I from the beginning of treatment ($p<0.01$). This indicator increased only in patients of group II by 1.3 folds compared with the index at the time of admission ($p<0.01$).

The indicator that assessed the fullness of life with energy (VT) after 24 weeks increased only in group I – 1.4-folds ($p<0.01$).

Indicators of MH, SF and PH after 24 weeks in group I were the same as on admission, and in group II MH, SF and PH were the same as in healthy individuals.

MH_1 in group I after 24 weeks remained lower than in healthy individuals. In group II, the index of the psychological component of health was 1.6 folds higher than on admission ($p<0.01$).

During the control elastography after 24 weeks, changes in the activity of fibrosis formation in the liver were observed. At the same time, in group I, fibrotic changes did not reverse. Progression of LF occurred in 3 patients of group I. Thus, F1 was established in 17 (51.00%) patients, and F2 – in 13 (39.00%) patients. Also, in 2 (6.0%) patients, LF progressed from mild to moderate (F3), and in 1 (3.0%) to severe. In group II, on the contrary, the progression of fibrotic changes in the liver of patients with CHC stopped. When assessing the severity of LF in patients of group II, the results were as follows: no signs of LF (F0) were diagnosed in 3 (9.09%) patients, minimally expressed LF (F1) – in 23 (69.00%) patients (18.00% more than on admission), and mild LF (F2) – in 7 (21.00%) patients (27.00% less than at presentation). Thus, in 3 patients who were diagnosed with minimally expressed LF during the first examination, there were no signs of LF after 24 weeks. And in 9 (27.00%) patients who had mild signs of LF at the time on admission, LF became minimally expressed. During the statistical processing of the results, there were no statistically significant differences between the degree of LF in patients of group I on admission and after 24 weeks (H0). Whereas the differences between the results of LF assessment in group II on admission and after 24 weeks were statistically significant (H1 – $p\leq0.05$), and statistically significant differences were found between the results in group I and group II after 24 weeks (H1 – $p\leq0.01$).

At the subjective examination after 24 weeks, a significant decrease in the number of complaints was also observed in patients treated with methadoxine.

Thus, only 2 (6.06%) patients complained of generalized weakness and 1 (3.03%) patient complained of increased fatigue and decreased performance.

During palpation, a decrease in liver size was observed in patients treated with methadoxine, since it was in this group that an increase in patients with F0 and F1 was observed. Thus, in group I, the liver size decreased by an average of 0.5 cm, while in group II, 22 (66.67%) patients had a decrease in liver size by an average of 1 cm, and 11 (33.33%) patients had their liver size normalized by palpation.

Conclusions

1. A decrease in QoL was observed in all patients with CHC in the form of complaints of generalized weakness, increased fatigue, decreased performance, mood depression, irritability, pain or heaviness in the right hypochondrium, abdominal bloating, bleeding gums, and joint pain.
2. The greatest violations were found in the psychological component of QoL, due to indicators of role functioning and general health of patients.

3. Methadoxine can be recommended in the treatment of patients with CHC as a means of pathogenetic therapy, the use of which leads to a decrease in the severity of LF and improvement of QoL.

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