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*Full Length Research Article*

# Impact of interferon free therapy on the quality of life of the patients with virus C chronic hepatitis

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**The infection with hepatitis C virus (HCV) is a major cause of chronic liver diseases, with approximately 71,000,000 chronically infected persons worldwide. Medical care for patients with a liver disease associated with HCV has advanced considerably due to a consolidated understanding of the physiopathology of the disease, as well as due to the evolution of the diagnosis procedures and to the improvement of therapy and prevention. The combined therapy with pegINF and Ribavirina is limited both by effectiveness and by tolerability, due to the adverse reactions that appear along with the increase of the number of therapy weeks, thereby affecting the quality of life and the prognosis of the liver disease. The study aims at evaluating the quality of life of patients with chronic viral hepatitis C under interferon free treatment (Viekirax – Exviera). We have undertaken a prospective study on a group of 54 patients, where of 30 patients treated with interferon free regimens and 24 patients (control group) represented by patients who were completely evaluated but were not included in the treatment because they did not meet the eligibility criteria according to the protocol. The quality of life during therapy was evaluated by using the SF-LDQOL questionnaire in its abbreviated version, which allows for evaluating the main components of the quality of life related to health, "symptoms of liver disease", "consequences of liver disease", and "problems related to the disease". Following the analysis and the interpretation of the questionnaire used, we found that the patients who did not receive the treatment presented more frequently a psychosocial unbalance (social activities), psychoemotional (the stigmata of the liver disease, life hope, sadness) and loss of interest for the sexual activity. In the case of patients treated with interferon free regimens we found an improvement of the quality of life for the whole duration of the therapy, this being correlated, especially, with drug interactions that were limited or easily manageable and had minimal adverse effects. During the study, these patients presented an increase of the psychoemotional, psychosocial balance, and the sexual activity was not influenced. As far as the quality of life is concerned, the interferon free therapy proves is effectiveness and imposes as first option therapy, especially in patients with psychoemotional unbalances.**

**Keywords:** Hepatitis C virus; Interferon-free regimen; Liver cirrhosis; Health related quality of life.

## INTRODUCTION

The hepatitis C virus (HCV)is most widely spread in the United States, with approximately three million chronically infected persons in the non-institutionalized population (http://www.cdc.gov/hepatitis/HCV/HCVfaq.htm). This disease causes approximately 17,000 new infections and 15,000 deaths every year (http://www.cdc.gov/hepatitis/HCV/HCVfaq.htm). In the event that the disease is left to evolve naturally, approximately 27% of the persons with chronic HCV infection will develop cirrhosis (The American Association for the Study of Liver Diseases) and, out of these, approximately 25% will evolve to the terminal stage of the disease or hepatocellular carcinoma (Klevens et al., 2012).

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For the past years, the treatment of HCV infection has undergone a major revolution, by the introduction of direct action antivirals (DAA), which are agents that interfere with various stages of the replicative cycle of a virus, which replaced the standard therapy (peg INF and ribavirina), which acts on various non-specific ways to stimulate the antiviral immune response. DAA's lead to viral eradication in more than 90% of the patients treated (Kohli et al., 2014; European Association for Study of L. EASL Recommendations on Treatment of Hepatitis C, 2015).

In 2011, there were launched two DAA's of the first generation, from the class of NS3 protease inhibitors (Boceprevir and Telaprevir), and subsequently the second and the third generation, which constituted a major step in the treatment of patients infected with HCV genotype 1. Beside the fact that they are significantly more effective, they offer important additional benefits,including a tolerability profile that makes them adequate also forpatients previously excluded from treatment (Lens et al., 2014), a simplified management due to the short duration of the treatment, and the oral way of administration.

Due to its high costs of the treatment, the access of patients to these therapies is limited, requiring a rigorous selection and blocking the large scale use of the drugs (Craxi et al., 2016).

The year 2013 announced an unprecedented therapeutic victory with a few new DAA's with various viral targets, including NS3 protease inhibitors, nucleoside / nucleotideanaloguesandRNA-dependent non-nucleoside inhibitorsof polymerase and NS5A inhibitors, some of which were already approved by EMA and/or FDA in 2013 (sofosbuvir and simeprevir) and in 2014 (daclatasvir, Viekira Pak (ritonavir with paritaprevir plus dasabuvir), Harvoni (ledipasvir + sofosbuvir), in 2015.All these new DAA's have proved to be amazingly effective (90% - 100% SVR), safe and well tolerated, while all oral interferon free combinations cure and even determine the eradication of HCV infection (Stanciu and Trifan, 2015; Ward, 2014).

In the specialized literature, the quality of life is associated with the "subjective state of well-being", "happiness or satisfaction with life". The model of "health related quality of life" (HRQL) can be defined as the ensemble of elements related to the impact of health and medical care on the quality of life. In 1948, the World Health Organization defined health as being not only the absence of a disease or of an infirmity, but the presence of a state of physical, mental, and social well-being (Moleavin and Keresztes, 2012; Darii, 2018).

The data in the literature reveal that the health related quality of life represents an integral index that refers to the impact of the disease and of the treatment on the patient in the latter's own perception. Therefore, its concepts include multiple aspects, having the role to identify the health needs of persons suffering from various diseases, such as: physical state, psychological state, social state, spiritual state, symptoms, work, and the functional role, social interactions, psychological state, the side effects of the treatment and the financial costs of the disease (Darii, 2018; Karner-Huțuleac, 2013).

## MATERIAL AND METHOD

To carry out this study, we used a prospective observation project. 54 patients were selected and evaluated according to the protocol for establishing the eligibility criteria in view of initiating the interferon free therapy. The study period was January 2018 – July 2018 and it included 30 patients treated with interferon free regimens (Viekirax – Exviera) and 24 patients (control group) who did not meet the eligibility criteria for various reasons (comorbidities, concomitant medication, grade of hepatic fibrosis). All patients signed the informed consent for the treatment and, respectively, for their participation in the study.

The quality of life before and after the end of therapy was evaluated by use of the SFLDQOL combined multidimensional questionnaire (abbreviated form) which includes: SF-36 generic questionnaire for the evaluation of the quality of life, and LDQOL –a specific instrumentfor appreciating the quality of life of patients with chronic liver diseases (Karner-Huțuleac, 2013).

The SF-36 questionnaire (Medical Outcome Study), in its abbreviated form,conceived as an indicator of the health state used in population studies, clinical trials, methodological studies in the general population (Darii, 2018), the advantages of which are the short time of completion, which justify its use in clinical trials or in the medical practice. It consists of 11 items that envisage: vitality, pain, emotional reactions, social isolation, physical mobility, physical activity, life and relations with others.

Applying the LDQOLquestionnaire is an effective method, which facilitates the works of physicians within the evaluation of the quality of life and eventually leads to the design and implementation of a targeted plan for the management of the chronic hepatic disease, indispensable for the medical practice (Karner-Huțuleac, 2013).

The SF-LDQOL questionnaire, in its short version, is easier to use in practice and it has a high level of sensitivity and specificity to appreciate the quality of life of the patients with chronic hepatic ailments. By SF-LDQOL estimation one can evaluate the maincomponents of the health related quality of life, namely "the symptoms of the liver disease", "the consequences of the liver disease", and "the disease related issues". With regard to this last aspectwe should mention that the items and scales proposed in this questionnaire are easy to apply in practice and they can be applied to all age groups, both before and after the therapy (Karner-Huțuleac, 2013).

**Table 1.** Demographic characteristics patient groups

| Characteristics | Control group (0, n = 24) | Study group (1,n=30) |
|---|---|---|
| Men : Women | 9 : 15 | 12:18 |
| Original environment<br>Urban : rural | 20:4 | 22: 8 |
| Average age of patients | 45,15±3,81<br>(20-59 years) | 43,12±4,1<br>(18-61 years) |
| Average duration of the disease (years) | 8,2 ±5,3 | 8,9± 4,07 |
| Associated comorbidities | 24 | 0 |

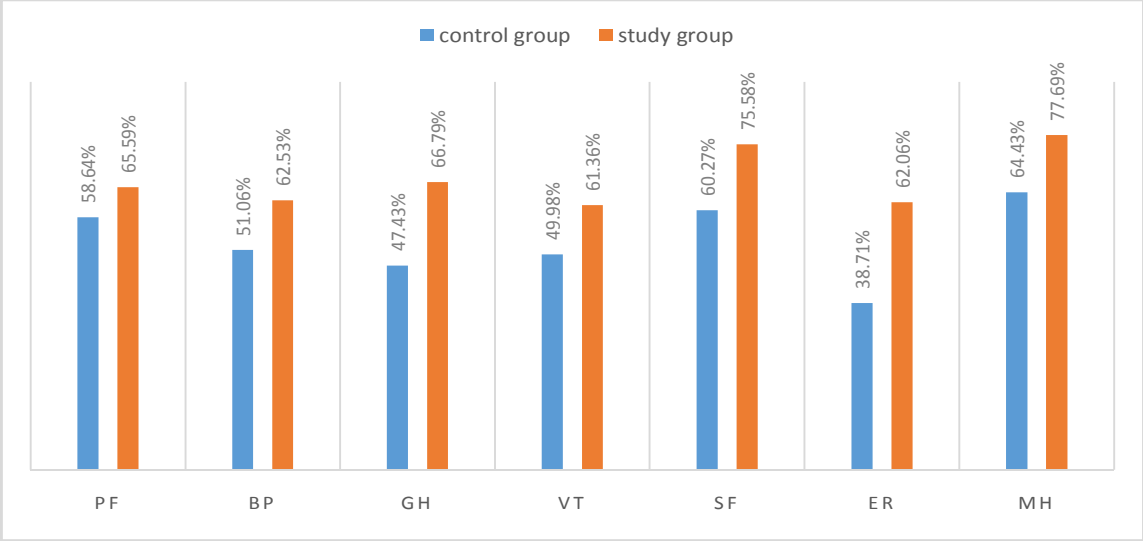


**Figure 1**. Graphic representation of the variations of the scale SF-36 before initiating the antiviral therapy on the subgroups studied

**Abbreviations:** PF – physical function; BP – somatic pain; GH – general health; VT – vitality; SF – social function; ER – emotional role; MH – mental health

## RESULTS

Out of the total group studied, consisting of 54 patients, there were made up two distinct subgroups ofpatients, who filled out the questionnaires concerning their quality of life, and the results were subsequently compared.

Group 0: control group (24 patients) who were evaluated completely according to the protocol, but were excluded from treatment because they did not meet the eligibility criteria.

Group 1: study group (30 patients) who met theeligibility criteria for the treatment and initiated the interferon free therapy (Viekirax and Exviera) for 12 weeks.

We envisaged to study the impact of applying – or not – the antiviral therapy on the quality of life of the patients with liver diseases, as well as evaluating the quality of life before and after applying the interferon free therapy.

Before initiating the interferon free antiviraltherapyfor both subgroups studied, the scores of SF-36 questionnaires showed some modifications related especially to the following dimensions:physical function (PF), somatic pain (BP), general health (GH), vitality (VT), social function (SF), emotional role (ER), mental health (MH), with predominance of an altered general state of health, social function, emotions, and mental health in the patients from the study groups as compared to the control group.

The general state of health, investigated by aid of the SF-36 score, is appreciated by the respondents as follows: (blue – group 0 (control group); yellow – group 1 (study group); grey – column) (satisfactory – good – unsatisfactory). (Figure 2)

As one can see from the graph, it was obtained a significant improvement at the level of all items studied in the scale SF-36, for the patients of the study group 1 at

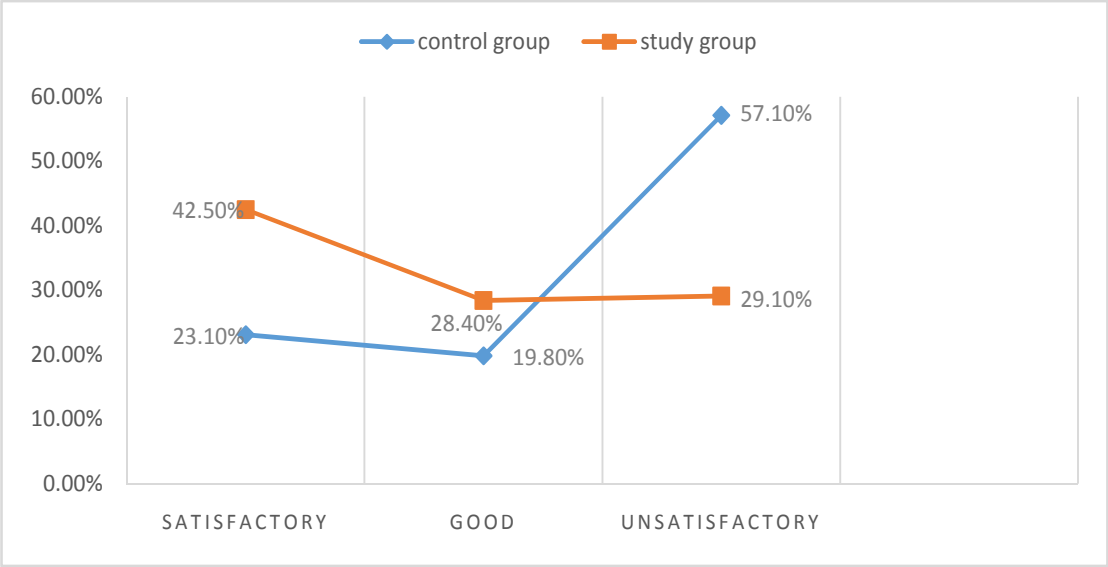


**Figure 2.**

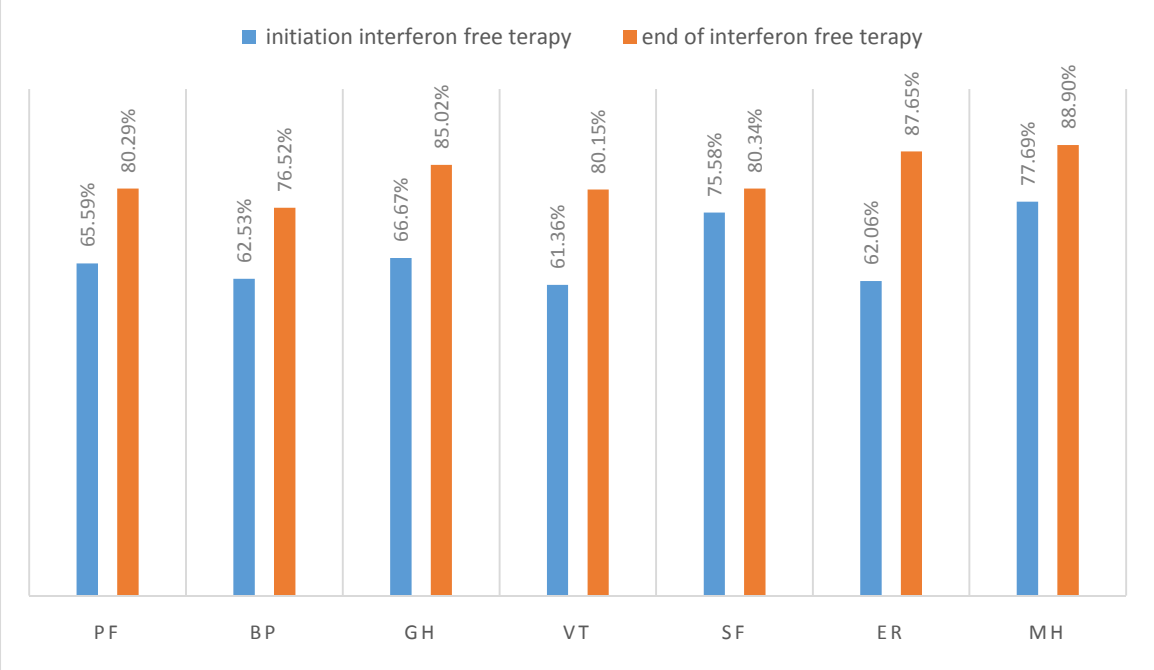


**Figure 3.** Graphic representation of the variations of the scale SF-36 at the end of interferon free treatment for the study group 1 as compared to the therapy initiation period.

Abbreviations: PF – physical function; BP – somatic pain; GH – general health; VT – vitality; SF – social function; ER – emotional role; MH – mental health

the end of the interferon freetherapy, thanks especially to the effectiveness and tolerability of the new therapy, to the minor side effects recorded, simplification of the administration, short duration of the therapy, which led in the end to an increase of the quality of life, preponderantly expressed by the increase of the level of emotional and global status.

| | Study group 1 | | Group 0 (observational/control) |
|---|---|---|---|
| | **Before the interferon free therapy** | **At the end of the interferon free therapy** | |
| 1. Symptoms related to the liver disease | 62.80% ±6.63 | 86.80 % ± 3.45 | 60.00% ±6.62 |
| 2. Consequences of the liver disease | 60.02% ± 12.77 | 73.00% ± 6.40 | 55.90% ± 3.20 |
| 3. Concentration and Memory | 64.90% ± 10.33 | 87.92 % ± 3.33 | 61.00% ± 13.38 |
| 4. Problems caused by the disease | 61.70% ± 15.66 | 86.80 % ± 3.40 | 57.50 % ± 3.35 |
| 5. Sleep | 63.00% ± 14.55 | 82.50 % ± 3.87 | 56.00% ± 7.72 |
| 6. Isolation | 65.00% ± 12.06 | 87.00 % ± 3.43 | 58.00 % ±12.06 |
| 7. Hope | 63.50 % ± 14.52 | 84.50 % ± 3.12 | 53.50 % ± 4.69 |
| 8. Stigmata of the liver disease | 76.10 % ± 6.28 | 79.00 % ± 2.43 | 56.50 % ± 3.87 |
| 9. Sexual function/problems | 75.12 % ± 6.28 | 76.12 % ± 6.28 | 69.40 % ± 13.62 |

The results obtained demonstrate that these increases are statistically correlated to a significant extent with the effectiveness of the interferon free therapy, which contributes essentially to the improvement of the well-being of patients with chronic liver diseases. One should note that the percentage of improvement of the scales “stigmata of liver disease” and“problems regarding the sexual interest” did not show a significant improvement in the sense of a marked increase of the values thereof, due to the fact that ¼ of the patients declare the presence of sexual dysfunctions.

## CONCLUSIONS

- The results obtained show that the quality of life of the patients treated with the new interferon free regiments undergo significant modifications in the sense of the appreciations thereof, we found an improvement of the relationships at the social, family, and occupational levels.
- Statistically, based on investigation, the patients in the group 1 reveal an improvement in 7 fields/items of the questionnaire SF-LDQOL, recorded in the two phases – before and after the interferon free therapy, this result summing up the percentages of improvement of the values of the scales “symptoms of the liver disease” (from 62.80% up to 86.80%), “the consequences of the liver disease” (from 60.02% up to 73%), “concentration and memory” (from 64.9% up to 87.92%), “problems caused by the disease” (from 61.70% up to 86,80%), “sleep” (from 63% up to 83,50%), “isolation” (from 65% up to 87%), “hope” (from 63.50% to 84.50%).
- Despite the success of theinterferon free antiviral therapy, the “stigmata of liver disease”, as well as “sexual problems” affect the patients’ quality of life.
- There is an important psychological impact of the diagnosis on the quality of life and the presence of complications determines a high degree of anxiety.
- The interferon free antiviral therapy has an enormous positive impact on the quality of life as compared to that of the untreated patients.
- The results of the study evidence the necessity of evaluating the mental health and the social support of patients with chronic liver disease.
- The interferon free regimens prove their superiority in the treatment and eradication of the HVC infection and they were imposed as first option therapy in patients with psychoemotional unbalances, thereby proving the necessity of increasing the access thereto.

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