Research Article

Quality of Life as an Integrative Indicator of Health Status in Patients with Chronic Hepatitis C and Concomitant Diabetes Mellitus Type II

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Abstract

The main indicators of quality of life in patients with chronic hepatitis C with concomitant diabetes mellitus type II were studied on the basis of SF-36. A sharp decrease in physical and mental health was observed in patients with combined comorbidity in comparison with the group of patients without concomitant diabetes mellitus type II. Improvement of the patients’ quality of life by all parameters was detected under the influence of alpha-lipoic acid and lactulose use in addition to antiviral therapy.

Keywords
chronic hepatitis C; diabetes mellitus; quality of life; treatment

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Problem statement and analysis of the recent research

The issue of viral hepatitis (VH) is one of the most urgent and unresolved issues in medical science and health care [1, 7, 8]. This is evidenced by the rapid spreading, more frequent monitoring of this pathology in young patients, high risk of hepatic cirrhosis (HC) and hepatocellular carcinoma development. Studies of recent decades have shown that HCV infection is not only a cause of hepatic disorders but is also a systemic pathological process, generalized infection resulting in many organs and systems affection [2, 3, 7]. Unlike hepatitis B, hepatitis C incidence is associated with increased incidence of diabetes mellitus (DM) type II: there is some link (or links) between the presence of hepatitis C virus and the onset of DM type II. Hepatitis C virus (HCV) (in particular, genotypes 3a and lb) in the body is known to increase cells insulin resistance directly interfering with insulin-signaling cascade [5, 10, 11]. Insulinemia in its turn leads to increased replication of HCV in vitro [12]. The study of the mechanisms of both liver and body as a whole damage in case of this associated pathology is an extremely important aspect of modern medicine. Chronic diseases in patients manifest not only in significant expenditure but also in the negative impact on lifestyle [2, 9]. Therefore, it is important for the doctor to determine how the disease affects the person, including all aspects of life. These types of studies focused directly on a patient are known as the study of quality of life (QOL).

Quality of life (QOL) is a concept encompassing many aspects of human life and describes the ability of an individual to function in a society according to his or her status and to enjoy it. Over the last years the study of health related quality of life (HRQL) has developed as a separate medical science with its research methods, evaluation criteria, domain of usage, etc. It is based on the definition of QOL by the WHO as individual correlation of the position in the community in the context of culture and value system of the society with the goals of the individual, his or her plans, abilities and the degree of general unsettled state [6, 9], that is the person’s perception of his or her position in life including physical, mental and social well-being, independence, quality of the environment where he or she lives, the degree of satisfaction. Indicator of QOL related to health generally reflects the degree of person’s adaptation to the disease and ability to perform usual functions corresponding to the socio-economic status [6, 9].

The study of 642 patients with chronic hepatitis C (CHC) confirmed that individuals with hepatitis C had lower quality of life than the control group [4, 6]. In addition, patients with a sustained response to monotherapy with interferon were found to experience a significant improvement in quality of life. Over the last years the study of health related quality of life (HRQL) has developed as a separate medical science with its research methods, evaluation criteria, domain of usage, etc. It is based on the definition of QOL by the WHO as individual correlation of the position in the community in the context of culture and value system of the society with the goals of the individual, his or her plans, abilities and the degree of general unsettled state [6, 9], that is the person’s perception of his or her position in life including physical, mental and social well-being, independence, quality of the environment where he or she lives, the degree of satisfaction. Indicator of QOL related to health generally reflects the degree of person’s adaptation to the disease and ability to perform usual functions corresponding to the socio-economic status [6, 9].

The study of 642 patients with chronic hepatitis C (CHC) confirmed that individuals with hepatitis C had lower quality of life than the control group [4, 6]. In addition, patients with a sustained response to monotherapy with interferon were found to experience a significant improvement in quality of life. Evaluating the quality of life of patients with CHC without cirrhosis before the treatment Foster and colleagues [13] found that patients with CHC had significantly lower quality of life in all eight areas of SF-36. Even if clinical signs of liver damage are absent, the very presence of HCV infection or even just the patient’s awareness on his disease decreases the quality of life due to both its physical and mental compo-
104 patients with CHC (84 patients with CHC associated with DM type II and 20 patients without comorbidity as a comparison group) at the age of 21 to 65 were included into the research. They underwent examination, treatment and observation at the clinical base of the Department of Infectious Diseases at Ivano-Frankivsk National Medical University in the Department #1 at the Regional Clinical Infectious Diseases Hospital in Ivano-Frankivsk. The patients were divided as follows: 84 patients with CHC on the background of concomitant DM type II were treated with antiviral therapy (AVT) with pegylated interferon alpha-2b and alpha-2a and ribavirin during 48 weeks. These patients were divided into 4 groups depending on the treatment. 20 patients (Group I) received only AVT. 21 patients (Group II) received alpha lipoic acid (ALA) in addition to AVT. 23 patients (Group III) received lactulose in addition to AVT. 20 patients (Group IV) received ALA and lactulose according to the proposed regimen along with AVT. All patients were with genotype 1b.

Russian version of the international SF-36 questionnaire was used to determine the QOL indicators. This version was developed by the researchers at the International Center for Quality of Life Studies, (ICQLS, Saint-Petersburg, 1998). The results of the research showed its high consistency with the QOL characteristics conducted in other countries. Thus, Ukraine has the experience in adaptation of the international version of SF-36 questionnaire which may be used to study the QOL of healthy individuals of all categories of patients, to evaluate the effectiveness of comprehensive treatment or individual drug action. The use of SF-36 questionnaire provides an opportunity to obtain integrated quantitative evaluation of QOL of patients with CHC and completes conducted comprehensive researches. In order to measure QOL the SF-36 questionnaire determined the following criteria: Physical Functioning (PF), Role-Physical Functioning (RP), Bodily Pain (BP) and its impact on the ability to be engaged in daily activities, General Health (GH) as a subjective respondent’s assessment of his general health at the present time, Vitality (VT) as a subjective respondent’s assessment of his vitality, Social Functioning (SF), the role of emotional problems in physical dysfunction (Role-Emotional – RE), Mental Health (MH) as a subjective mood assessment.

QOL criteria are used to determine the effectiveness of treatment in health programs, to determine the benefits of treatment approach [6, 9].

Questionnaires were formed to determine the quality of life. They were completed by patients before the treatment, after 2 and 6 months of the treatment and at the end of the therapy.

All patients were included into the research after signing an informed consent.

Statistical processing of the research results was conducted on a PC using a standard package Statistica 5. Mean values (M), mean error (m), significance of differences according to Student’s t-test were assessed. Pearson correlation coefficient was used to assess interrelation between the studied characteristics.

1. Materials and methods

2. Results of the research and their discussion

Studying the effect of DM type II on the quality of life of patients with CHC before the treatment, we detected the following changes in the main indicators of SF-36 questionnaire (Table 1). PF indicator in the patients with concomitant DM type II was 1.3 times lower than in patients with CHC without comorbidities (53.27±1.91 versus 71.25±3.42, p<0.001) and 1.6 times lower than in the control group (p<0.001). PF indicator in patients with CHC without comorbidity was 1.2 times lower than in healthy individuals (p>0.05).

Physical abilities restriction led to the decrease in everyday activity of patients in both groups according to PF indicator. However, PF indicator in patients of the comparison group was not significantly different from that in the control group (51.25±9.15 points versus 65.9±5.54, p>0.05).

PF indicator in patients with concomitant DM type II constituted 27.81 ± 4.27 scores and was 1.8 times lower than in the comparison group (p<0.001) and 2.4 times lower compared to the control group (p<0.01) (see Table 1).

Pain syndrome in terms of BP indicator was not significantly different compared to the control in both studied groups (p>0.05) but was 1.3 times lower in the main group compared to the comparison group (p<0.001). The overall assessment of patients’ health as satisfactory was decreased in both groups in comparison with healthy individuals and constituted 47.70±3.85 scores in the patients without concomitant DM type II and 37.40±2.37 scores in the patients of the main group (p<0.001). Moreover, GH index was 1.3 times lower in the main group than in the comparison group (p<0.05).

VT indicator decreased in both groups with no significant difference between the groups (p>0.05). Social activity of patients with CHC and concomitant DM type II (according to SF indicator) decreased by 1.3 times in comparison with the control group and comparison group (p<0.001, p<0.05) due to the presence of more significant clinical symptoms (general...
weakness, fatigability, nausea, discomfort and pain in the right hypochondrium). Social activity of the patients in the comparison group did not decrease and constituted 65.38±5.23 scores compared to 69.9±4.68 points in the control group (p>0.05).

Patients of both study groups had significantly lower indices of mental status. Restriction of daily activities due to emotional problems was more significant in patients with CHC combined with DM type II – RE indicator was 2.9 times lower than in patients without comorbidity (23.90±3.33 scores versus 69.98±7.22 scores, p<0.001) and 2.2 times lower than in healthy individuals (p<0.001). RE indicator in the patients of comparison group was almost identical to that in healthy individuals. “Mental health” (MH) indicator was reduced by 1.12 times in comparison with that before the treatment (p<0.05) while MH indicator in the patients of the main group decreased by 1.3 times in comparison with the control group (p<0.001) and 1.2 times compared to the comparison group (p<0.05).

Thus, the presence of associated CHC pathology and DM type II significantly reduces the quality of life of patients and the planned prescription of antiviral therapy (AVT) also reduces the emotional and mental part of patients’ normal social activity and directly affects the physical health sensation. Therefore, the use of medication contributing to the maintenance of normal physical and mental functioning of patients with CHC with concomitant diabetes type II, namely α-lipoic acid and lactulose is reasonable.

The influence of the proposed treatment regimen on the quality of life of the patients is shown in Table 2. Normalization of quality of life 2 months after the beginning of treatment in the patients of group I who underwent only AVT occurred only according to 1 criterion (BP) which approximated to the indicator of the control group (59.60±1.57 scores versus 53.35±4.99 scores and 62.20±5.03 scores, p>0.05).

6 months after the beginning of treatment in this group, normalization of quality of life occurred in terms of 4 indicators of SF-36 questionnaire: RE indicator increased by 2.5 times, BP indicator increased by 1.1 times, SF indicator increased by 1.5 times and MH indicator increased by 1.3 times. At the end of treatment another indicator, namely RF (p>0.05) returned to normal. That is, the use of AVT helped to reduce the patients’ perception of their health as such that limited ordinary physical activity, patients’ social activity, reduced the intensity of pain. Deterioration of the mental health component (due to worsening of mood, the constant presence of anxiety and improved patients’ mental health) and patients’ physical activity was detected in this group within 2 months of treatment with AVT. The improvement in this indicator occurred after 6 months of treatment.

Normalization of quality of life occurred after 2 months of treatment in terms of 2 indicators (SF, BP, p>0.05) in patients of group II who were treated with alpha-lipoic acid on the background of AVT. SF indicator increased by 1.3 times after 6 months of treatment in comparison with that before the treatment, RE indicator increased by 2.06 times (p<0.001) and MH indicator increased by 1.2 times (p<0.001). Improvement in QOL in terms of already 5 indicator of SF-36 questionnaire (RF, BP, SF, RE and MH) (p>0.05) was detected at the end of treatment in patients of group II. Thus, the use of ALA along with AVT promoted the decrease in the sense of impact of physical and emotional problems on restriction of daily activities.

Analyzing the dynamics of the quality of life indicators in the patients of group III who were prescribed lactulose
## Table 2. Dynamics of quality of life indicators in the patients with CHC and concomitant diabetes mellitus type II under the influence of treatment, M±m

<table>
<thead>
<tr>
<th>Study groups</th>
<th>PF</th>
<th>RF</th>
<th>BP</th>
<th>GH</th>
<th>VT</th>
<th>SF</th>
<th>RE</th>
<th>MH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy (n=20)</td>
<td>83.8±6.17</td>
<td>65.9±5.54</td>
<td>62.2±5.03</td>
<td>73.2±5.82</td>
<td>68.0±4.96</td>
<td>69.9±4.69</td>
<td>51.4±4.49</td>
<td>60.4±3.86</td>
</tr>
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<td>I</td>
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</tr>
<tr>
<td>Before the treatment (n=20)</td>
<td>48.75±1.66</td>
<td>25.00±8.89</td>
<td>53.35±4.99</td>
<td>36.50±4.70</td>
<td>31.15±5.38</td>
<td>52.50±4.01</td>
<td>24.98±6.34</td>
<td>44.80±4.05</td>
</tr>
<tr>
<td>2 months of treatment</td>
<td>36.00±1.69</td>
<td>15.00±2.81</td>
<td>59.60±1.57</td>
<td>33.33±1.72</td>
<td>33.00±1.38</td>
<td>50.63±0.63</td>
<td>34.97±1.67</td>
<td>36.00±0.82</td>
</tr>
<tr>
<td>6 months of treatment</td>
<td>65.50±1.49</td>
<td>62.50±2.87</td>
<td>58.30±3.29</td>
<td>54.50±0.57</td>
<td>56.50±1.54</td>
<td>77.25±3.27</td>
<td>64.94±1.67</td>
<td>58.80±1.23</td>
</tr>
<tr>
<td>12 months of treatment</td>
<td>55.50±5.27</td>
<td>57.50±6.81</td>
<td>69.40±4.69</td>
<td>54.90±3.31</td>
<td>52.00±3.49</td>
<td>73.75±3.94</td>
<td>53.31±7.01</td>
<td>58.80±2.50</td>
</tr>
<tr>
<td>II</td>
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<tr>
<td>Before the treatment (n=21)</td>
<td>55.95±5.57</td>
<td>26.19±7.21</td>
<td>53.43±6.57</td>
<td>38.48±4.46</td>
<td>31.95±4.42</td>
<td>51.79±3.48</td>
<td>23.79±5.70</td>
<td>44.19±3.54</td>
</tr>
<tr>
<td>2 months of treatment</td>
<td>60.71±3.85</td>
<td>40.48±7.61</td>
<td>68.86±4.58</td>
<td>49.10±3.25</td>
<td>45.48±2.95</td>
<td>67.26±3.81</td>
<td>42.81±3.36</td>
<td>49.78±3.00</td>
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<tr>
<td>6 months of treatment</td>
<td>58.33±3.91</td>
<td>44.05±6.43</td>
<td>81.43±2.63</td>
<td>51.52±1.82</td>
<td>45.48±1.98</td>
<td>70.39±2.86</td>
<td>49.17±5.45</td>
<td>53.90±3.14</td>
</tr>
<tr>
<td>12 months of treatment</td>
<td>62.62±3.44</td>
<td>64.29±5.05</td>
<td>70.14±5.80</td>
<td>44.14±5.14</td>
<td>41.90±4.86</td>
<td>66.67±3.60</td>
<td>61.09±9.91</td>
<td>48.76±4.42</td>
</tr>
<tr>
<td>III</td>
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<tr>
<td>Before the treatment (n=22)</td>
<td>56.52±3.92</td>
<td>26.09±9.36</td>
<td>54.00±4.17</td>
<td>36.65±4.39</td>
<td>31.13±4.43</td>
<td>51.14±5.26</td>
<td>23.17±6.77</td>
<td>45.22±4.29</td>
</tr>
<tr>
<td>2 months of treatment</td>
<td>33.91±0.44</td>
<td>20.65±2.02</td>
<td>61.65±1.65</td>
<td>33.70±1.81</td>
<td>34.57±1.47</td>
<td>50.54±0.54</td>
<td>34.89±1.59</td>
<td>36.52±0.77</td>
</tr>
<tr>
<td>6 months of treatment</td>
<td>66.74±1.46</td>
<td>64.13±2.64</td>
<td>64.13±2.64</td>
<td>74.17±4.88</td>
<td>54.17±0.53</td>
<td>75.87±3.46</td>
<td>65.15±1.45</td>
<td>60.87±1.22</td>
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<tr>
<td>12 months of treatment</td>
<td>58.04±5.05</td>
<td>58.70±6.21</td>
<td>71.30±4.55</td>
<td>56.48±3.05</td>
<td>53.70±3.34</td>
<td>73.91±3.68</td>
<td>56.50±6.77</td>
<td>59.48±2.24</td>
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<tr>
<td>IV</td>
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<tr>
<td>Before the treatment (n=20)</td>
<td>51.25±2.05</td>
<td>25.00±8.89</td>
<td>53.35±4.61</td>
<td>38.05±5.79</td>
<td>31.90±4.18</td>
<td>51.25±5.66</td>
<td>23.32±8.41</td>
<td>44.00±4.21</td>
</tr>
<tr>
<td>2 months of treatment</td>
<td>72.00±1.38</td>
<td>75.00±4.44</td>
<td>98.50±1.50</td>
<td>62.00±1.03</td>
<td>58.00±0.92</td>
<td>85.00±1.15</td>
<td>59.94±3.06</td>
<td>58.40±1.10</td>
</tr>
<tr>
<td>6 months of treatment</td>
<td>66.25±3.48</td>
<td>63.75±7.13</td>
<td>93.50±2.58</td>
<td>56.25±2.10</td>
<td>53.50±2.33</td>
<td>81.88±3.57</td>
<td>71.64±6.06</td>
<td>64.00±3.31</td>
</tr>
<tr>
<td>12 months of treatment</td>
<td>73.50±4.20</td>
<td>77.50±5.71</td>
<td>86.35±4.66</td>
<td>66.10±5.18</td>
<td>58.25±5.56</td>
<td>89.29±5.69</td>
<td>96.66±2.30</td>
<td>63.60±5.18</td>
</tr>
</tbody>
</table>

Notes.

- **p<0.001***; **p<0.01**; **p<0.05*** – a significant difference between the indicator before the treatment of patients with CHC and concomitant DM and the indicator in each study group after the treatment;
- **p<0.001***; **p<0.01**; **p<0.05*** – significant difference between the indicator in each study group after the treatment and healthy individuals;
- **p<0.001***; **p<0.01**; **p<0.05*** – significant difference between the indicator in each study group after the treatment and the same indicators in the patients of Group I.

In addition to AVT, the positive tendency towards QOL normalization was observed only after 6 months of treatment. At the end of the treatment QOL normalization in group III occurred in terms of 5 indicators of SF-36 questionnaire (RF, BP, SF, RE and MH) that increased by 2.4 times in terms of RF, (p<0.001), by 1.3 times in terms of BP, (p<0.05), by 1.4 times in terms of SF, (p<0.001), by 2.4 times in terms of RE, (p<0.001) and by 1.3 times in terms of MH, (p<0.01). In addition, a decrease in mental health indicator (MH) and physical activity indicator (RF) (p<0.001) was observed in this group of patients after 2 months of treatment in comparison with the indicators before the treatment. This may indicate
negative reaction to AVT in these patients.

Using ALA and lactulose along with AVT in group IV, the normalization of QOL of patients in terms of all SF-36 questionnaire indicators was observed during the observation period with a significant difference between the groups (see Table 2). At the end of treatment PF indicator in this group of patients was 1.3 times higher than in groups I and III (p<0.05), 1.2 times than in group II (p>0.05). RF indicator in patients of group IV was 1.3 times higher than in groups I and III (p<0.05). Pain indicator BP was higher in patients of group IV compared to groups I, II, and III by 1.2 times on average at the end of treatment (p<0.05). GH indicator in the patients of group IV was 1.4 times higher in comparison with group II (p<0.01). VT indicator in group IV increased by 1.4 times (p<0.05). Social activity (SF) of the patients in group IV was 1.2 times higher compared to study groups I and III and 1.3 times higher in comparison with group II (p<0.05). RE indicator in the patients of group IV was 1.9 times higher than in group I (p<0.001), 1.6 times higher than in group II (p<0.001) and 1.8 higher than in group III (p<0.001). MH indicator in the patients of group IV was 1.1 times higher compared to study groups I and III and 1.3 times higher than in group II.

Summarizing, a conclusion may be drawn that conducted therapy significantly improved both the physical condition and mental status of the patients. Moreover, the conducted research demonstrated significant improvement of QOL in patients treated with comprehensive therapy with the inclusion of alpha-lipoic acid and lactulose, with almost complete physical and social rehabilitation during the period of treatment.

4. Prospects for further research

The research is promising in terms of further study of QOL in patients with CHC with the use of new direct-acting antiviral drugs and their combined use with alpha-lipoic acid and lactulose.

3. Conclusions

1. The results of QOL analysis using SF-36 questionnaire demonstrated that a sharp decrease in all QOL indicators was observed patients with CHC and concomitant DM type II.

2. Normalization of quality of life in patients of group I after AVT occurred according to 4 indicators of SF-36 questionnaire (RE, BP, SF and MH). Normalization of quality of life in patients of group II and III who received AVT in complex with alpha-lipoic acid and lactulose occurred according to 5 indicators of SF-36 questionnaire (RF, BP, SF, RE and MH). The normalization of QOL according to all indicators of SF-36 questionnaire was observed throughout the observation period and the significant difference between the groups in patients of group IV who were treated with AVT in combination with alpha-lipoic acid and lactulose.

3. The inclusion of assessment of patients’ quality of life according to SF-36 questionnaire is important to assess the severity of chronic hepatitis C and treatment efficacy.

References


Received: 24 October 2016
Revised: 18 November 2016
Accepted: 21 November 2016