

Gender and age differences of compliance in liver transplant recipients

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Academic editor: Tatyana Pokrovskaya ♦ Received 18 January 2019 ♦ Accepted 15 February 2019 ♦ Published 27 March 2019

Citation: Kosmacheva ED, Babich AE (2019) Gender and age differences of compliance in liver transplant recipients. Research Results in Pharmacology 5(1): 31–35. <https://doi.org/10.3897/rrpharmacology.5.33173>

Abstract

Introduction: The aim of the paper was to evaluate the compliance in patients who have undergone orthotopic liver transplantation (OLT).

Materials and methods: A voluntary anonymous survey was conducted among liver transplant recipients. The control group included patients with chronic non-infectious diseases requiring persistent treatment. The questionnaire “The level of Compliance” designed by R.V. Kadyrov was used.

Results and discussion: The following compliance levels were identified in liver transplant recipients: the general level – 95.8 ± 9.4 ; the social level – 30.4 ± 4.2 ; the emotional level – 33.3 ± 3.7 ; the behavioral level – 32.0 ± 3.8 . The compliance levels of the control group were significantly lower compared to the values of group 1, respectively: the general level – by 9%, the social level – by 5.6%, the emotional level – by 10.3% and the behavioral level – by 11.9%. The general compliance level of the recipients under 50 years old reached 93.5 ± 6.8 ; the social compliance level – 28.9 ± 3.9 ; the emotional compliance level – 33.6 ± 2.9 and the behavioral compliance level – 31.0 ± 2.2 .

Conclusions: Liver transplant patients have higher levels of general, behavioral and emotional compliance compared to patients with chronic diseases. Neither gender nor age differences were identified in any types of compliance.

Keywords

liver transplant recipients, compliance, gender and age differences.

Introduction

The compliance to therapy according to the definition of the World Health Organization is defined as an extent to which a patient follows treatment recommendations, including timely medications intake, diet, changes in the lifestyle and regular visits to a doctor (World Health Organization – WHO 2001).

A low level of compliance is a worldwide problem as patients' compliance to treatment recommendations significantly affects the outcome of almost all diseases. The compliance to treatment of diseases with high risk of disability and mortality has been actively studied over the past decades. In the register and observational studies of patients with cardiovascular, broncho-pulmonary, endocrinological, gastroenterological, rheumatological

diseases, the low levels of compliance to vital drugs were recorded (Dobrovolskaya et al. 2018, Krivoshapova et al. 2018, Machilskaya 2016, Mashkunova et al. 2018, Mayorova and Khrushcheva 2018, Olevskaya et al. 2018).

Due to the dramatically high medical and social costs of transplant care and the subsequent vital immunosuppressive therapy, the compliance of transplant recipients is of great interest to both practicing doctors and researchers – healthcare providers.

The compliance to an effective immunosuppressive regimen was defined in the early works of S. De Geest et al. (De Geest et al. 1999) as a vital behaviour to prevent the post-transplant rejection. The researchers found that non-compliance to drug treatment led to an increase in late acute transplant rejection in 3% of cases in patients who had undergone heart transplantation (De Geest et al. 1998). In kidney transplant recipients, non-compliance to drug therapy is associated with a prognosis worsening, which may result in an acute and chronic transplant rejection, functional depression leading to a dialysis or mortality (De Geest et al. 1995, Nevins et al. 2001, Shoskes et al. 1997). The return to dialysis after transplant rejection increases the risk of mortality by 78% compared to the patients on dialysis from the waiting list of (Rao et al. 2007). The studies of compliance in liver transplant recipients were conducted in a number of foreign clinical centers (Berlakovich et al. 2000, Drent et al. 2005, O'Carroll et al. 2006, Schweizer et al. 1990, Stillely et al. 2010). The majority of the studies involved a small number of patients and evaluated compliance by different methods, which makes it difficult to compare the results. Having analyzed the scientific literature of both Medline database and the largest Russian electronic library of scientific publications (e-library) over the last 15 years, no study has been found of the compliance in liver transplant recipients in Russian transplant centers.

The **aim** of the paper was to evaluate the compliance in patients who underwent OLT in the “Scientific and Research Institute – S.V. Ochapovsky Regional Clinical Hospital One”.

Materials and methods

A voluntary anonymous survey was conducted among liver transplant recipients (group 1) operated on at the state budgetary healthcare institution – “Scientific and Research Institute – S.V. Ochapovsky Regional Clinical Hospital One” of the Ministry of Healthcare of Krasnodar region. The study was approved by the local ethics committee. The questionnaire “The Level of Compliance” designed by R.V. Kadyrov was used in the research (Kadyrov et al. 2014).

The questionnaire consists of the two parts with 66 statements each – for healthy people and for those with chronic diseases. The control group (group 2) involved patients with chronic noncommunicable diseases requiring persistent treatment. Three types of compliance behavior – social, behavioral and emotional – were as-

sessed. The following indicators of compliance behavior were used: subtle – from 0 to 15 score points; moderate – from 16 to 29 score points, and significant – from 30 to 40 score points. The overall compliance level is represented by the sum of the score points of all compliance behavior indicators and is interpreted as follows: a low compliance level – from 0 to 40 score points, an average compliance level – from 41 to 80 score points, and a high compliance level – from 81 to 120 score points.

Statistical processing of the results was carried out using Statistica 10 software package. The data are presented as $M \pm \sigma$. The results of the study were processed by nonparametric methods of statistical analysis using the Mann-Whitney test for independent samples and the Wilcoxon test for dependent groups. Differences were considered significant at a significance level of $p < 0.05$.

Results and discussion

The study involved 86 patients who underwent OLT in “Scientific and Research Institute – S.V. Ochapovsky Regional Clinical Hospital № 1” (main group 1) and 56 patients with chronic diseases (control group 2). Three questionnaires from group 2 were rejected as they were not completed in full. Thus, 139 questionnaires were included in the statistical analysis. The main causes of liver failure that required transplantation were viral hepatitis (60.5%), primary biliary cirrhosis (16.3%), autoimmune (9.3%) and toxic hepatitis (9.3%).

The mean age of the recipients was 50.3 ± 8.6 years, with the proportion of men being 54.7%. The following compliance levels were identified in group 1: the general level reached 95.8 ± 9.4 ; the social level – 30.4 ± 4.2 ; the emotional level – 33.3 ± 3.7 and the behavioral level – 32.0 ± 3.8 . In group 2, the general compliance level was 87.6 ± 10.9 ; the social level – 28.8 ± 4.8 ; the emotional level – 30.2 ± 3.4 and the behavioral level – 28.6 ± 3.9 . Compared to control group 2, group 1 had the higher compliance levels, as follows: the general level – by 9% ($p=0.01$), the social level – by 5.6% ($p=0.22$), the emotional level – by 10.3% ($p=0.01$) and the behavioral level – by 11.9% ($p=0.005$). The absolute average scores and the distribution of behavioral, emotional and social compliance levels in both groups are shown in Figure 2.

In the transplantation context, the idea of compliance is multifaceted. It may include compliance to drug therapy, which involves not only taking immunosuppressants, but also a number of clinical and pharmacological groups of drugs prescribed to recipients, among the most frequent ones being antiviral drugs, antimicrobials, antifungal agents, anti-lipidemic drugs, insulin, oral hypoglycemic agents, and antihypertensive drugs. All these drugs are used to prevent or to treat both complications of immunosuppressive therapy and other factors that have a negative effect on transplant and recipient's survival. Thus, according to the abovementioned, patients were not informed of which medication the survey questions were related to.

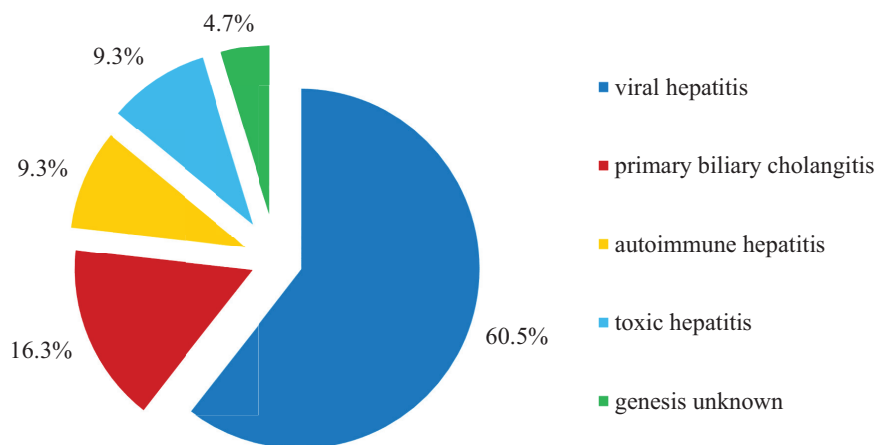


Figure 1. Distribution of diseases requiring orthotopic liver transplantation

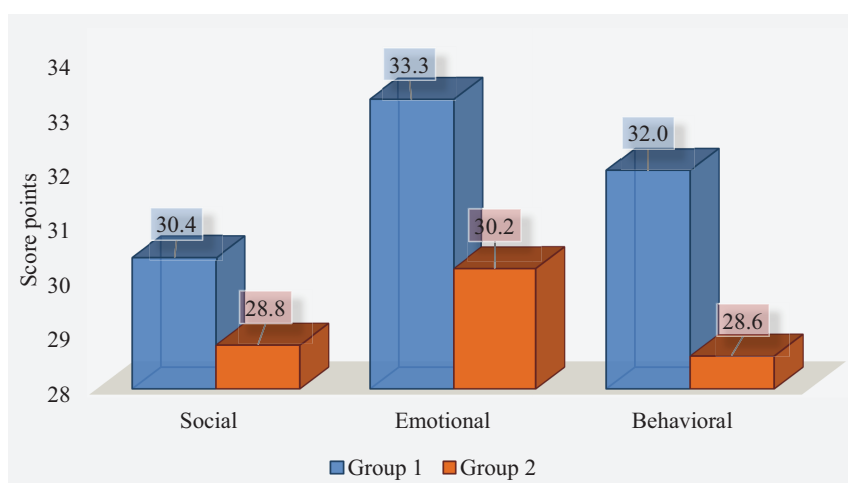


Figure 2. Distribution of compliance types in recipients (group 1) and patients with chronic diseases (group 2). Note: * – $p < 0.05$

The present study used a questionnaire by R.V. Kadyrov “The Level of Compliance” (Kadyrov et al. 2014), which allows, unlike screening questionnaires, for example, by Morisky et al. (Morisky et al. 1986), to study the various components of compliance (emotional, social, behavioral).

The gender analysis of liver transplant recipients’ compliance in women and men showed the following results, respectively: the general compliance level was 97.5 ± 1.96 and 94.3 ± 1.86 ($p = 0.25$), the social level was 30.7 ± 0.92 and 30.1 ± 0.73 ($p = 0.60$); the emotional level was 34.1 ± 0.82 and 32.7 ± 0.82 ($p = 0.23$) and the behavioral level was 32.7 ± 0.86 and 31.5 ± 0.72 ($p = 0.32$). The general compliance level in transplant recipients under 50 years old was 93.5 ± 6.8 ; the social level – 28.9 ± 3.9 ; the emotional level – 33.6 ± 2.9 and the behavioral level – 31.0 ± 2.2 . The comparison of liver recipients aged over and under 50 showed no significant differences. The following compliance levels were identified in patients over 50: the general compliance level reached 95.7 ± 9.4 ($p = 0.85$); the social level – 30.1 ± 4.2 ($p = 0.76$); the emotional level – 33.5 ± 3.7 ($p = 0.30$) and the behavioral level – 32.1 ± 3.8 ($p = 0.21$).

It was determined that the liver transplant recipients had higher levels of general, behavioral and emotional compliance compared to the patients with chronic diseases. Neither gender nor age differences in any types of compliances were identified. The great majority of the respondents showed the general compliance level within 80 to 120 score point (on average exceeding 90 score point). This fact reflects a high level of compliance to therapy and is consistent with the research by Berlakovich G.A. et al. (Berlakovich et al. 2000), which reports about 3% of cases of patients’ non-compliance to clinical prescriptions. The authors relied on computerized observation protocols, but the idea of non-compliance was not clearly defined (Berlakovich et al. 2000).

The facts of high compliance in liver transplant recipients contrast with a number of foreign studies carried out over the past years. One of the first studies evaluating the prevalence of transplant recipients’ non-compliance to therapy was accomplished by Schweizer et al. in 1990 (Schweizer et al. 1990), with the immunosuppression steroid regimens dominating. Three out of thirteen adult liver transplant recipients had 23% level of non-com-

pliance to drug therapy, two of them died. One patient suffered from rejection episodes which occurred due to the low compliance, which was evaluated by the level of cyclosporine in the blood. The study conducted by O'Carroll et al. (O'Carroll et al. 2006) reported about 24% of the non-compliance cases in liver transplant recipients. The low compliance rate to immunosuppressive therapy reached 15%, according to the retrospective examination of the recipients in Scotland (Stilley et al. 2010). According to Burra P. et al., the rate of non-compliance to immunosuppressive therapy among adult liver transplant patients ranges from 15 to 40% (Burra et al. 2011).

Thus, in a number of transplant centers the opposite results were obtained. It can be explained by heterogeneity in the priorities for usage of different immunosuppressive regimens to prevent liver rejection. It is well-known that side effects from drugs are the risk factors causing low level of compliance (Drent et al. 2005, O'Carroll et al. 2006, Rovelli et al. 1989, Schweizer et al. 1990).

The side effects from the inhibitor of calcineurin, cyclosporine and glucocorticoids are most pronounced. Over the last several years, the administration of non-steroid treatment regimens in many transplant centers has resulted in a decreased frequency of undesirable side effects and an improved subjective tolerance to treatment. Thus, patients are less concerned about the possible future issues with hormone therapy administration, which contributes to better compliance to the recommended therapy. It can be assumed that the dramatic differences among the results of compliance evaluation in studies completed in different years are primarily caused by the significant progress in immunosuppressive regimens prescribed to liver transplant recipients, as they now almost completely exclude usage of glucocorticoids.

Another important aspect of compliance evaluation, influencing the results and complicating the literature data comparison, is lack of an objective and accurate measurement method. Many authors who research compliance in transplant recipients emphasize that nowadays there are both direct and indirect methods of assessment, but there is no gold standard for measuring compliance to drug therapy; each method has its strengths and weaknesses (Dobels et al. 2005, Hathaway et al. 1999, Laederach-Hofmann and Bunzel 2000).

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The multidirectionality in assessing the results of compliance, revealed by a number of authors in different years, has led to the conclusion that only a multimodal approach based on several measurement methods is more sensitive and acceptable than usage of a single indicator (Drent et al. 2009, Quittner et al. 2008).

Consequently, further studies are to obtain facts by relying not only on survey methods, which are subjective to some extent, but also on quantitative and objective methods of compliance assessment, such as determination of the concentration of drugs in the systemic blood, the count of tablets used, consideration of pharmacotherapy schemes applied, etc. Apart from that, in order to specify the disease prognosis in liver transplant recipients, it is necessary to break down compliance to drugs and general lifestyle recommendations. Non-compliance to immunosuppressive therapy increases the risk of transplant rejection and its potential loss, while non-compliance to general lifestyle recommendations (for example, avoiding alcohol and smoking after transplantation) may lead to other complications, such as de novo tumour and an increase in the healthcare costs.

Conclusions

1. Liver transplant recipients have higher statistically significant ($p < 0.005-0.01$) levels of general, behavioral and emotional compliance compared to those in patients with chronic diseases.
2. There are no significant differences in the level of social compliance between the groups of liver transplant recipients and the group of patients with chronic diseases.
3. The emotional and social compliance levels in liver transplant patients were the most and the least pronounced, respectively.
4. Neither significant gender nor age differences in any types of compliance in the group of liver transplant recipients were identified.

Conflict of interests

The authors have no conflict of interest to declare.

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