Research Article

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Health-related quality of life, depression, and anxiety in patients with autoimmune hepatitis

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Background & Aims: Improving health related quality of life (HrQoL) in patients with chronic diseases such as autoimmune hepatitis (AIH) should be a major treatment goal. However, little is known on the HrQoL in patients with AIH, and the topic is not given attention in current practice guidelines. We therefore conducted a single center study evaluating HrQoL in 103 consecutive outpatients with AIH.

Methods: Patient-reported HrQoL data were analysed in relation to clinical disease parameters and compared to representative data of the German population as well as control patients.

Results: Based on patient-reported data, a major depressive syndrome (10.8%) was found to be five times more frequent in AIH patients compared to the general population (p <0.001). The rate of severe symptoms of anxiety was also found to be significantly increased compared to the general population (p = 0.006). In seven of the eleven patients who scored for a major depressive syndrome a psychiatric comorbidity had not been diagnosed before. Major factors associated with depression and anxiety were concerns with regard to the progression of the liver disease.

Conclusions: This study identified – for the first time – a high rate of previously unrecognized severe symptoms of depression and anxiety in patients with AIH. Of importance for daily clinical practice, the factors associated with these symptoms may in part be amenable to targeted counselling and adequate treatment of the disease, thereby offering the chance to improve the care and HrQoL of AIH-patients.

Introduction

Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease with an excellent response to immunosuppressive treatment [1]. Although the short to medium term prognosis is good, the long term outcome of patients may be impaired by an increased rate of liver-related mortality as well as treatment-related side effects, such as the development of malignancy [2,3]. Current practice guidelines focus on the biochemical and histological remission as the primary goal of treatment, since these could correlate with the long term prognosis [1].

However, the perception of important treatment endpoints may differ between patients and physicians. Factors such as physical and mental functioning as well as social and economic circumstances influence the quality of life for patients. Understanding and improving health-related quality of life (HrQoL) has therefore emerged as a major issue in patient-centred care. In the past years, there have been several studies on HrQoL in patients with chronic liver diseases, including patients with HCV and HBV infection as well as non-alcoholic steatohepatitis and cholestatic liver diseases [4–11]. HrQoL, especially the physical component of HrQoL in chronic liver disease has been shown to be reduced in patients with advanced stage of fibrosis and cirrhosis, irrespective of the underlying disease [8–10,12]. In primary biliary cirrhosis (PBC), fatigue and pruritus are major determinants of HrQoL [4–6,13].

Currently, there is no detailed analysis of HrQoL specifically addressing patients with AIH and the issue of HrQoL has not received attention in the most recent American and British practice guidelines [1,14]. While treating patients with AIH, the

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Abbreviations: AIH, autoimmune hepatitis; HrQoL, health-related quality of life; SF-12, 12-item short form health survey; PHQ-9, 9-item pepression module from the patient health questionnaire; MDS, major depressive syndrome according to PHQ-9 coding algorithm; ODS, other depressive syndrome according to PHQ-9 coding algorithm; GAD-7, 7-item generalized anxiety disorder screener.

impression was that the overall wellbeing of our patients was often impaired despite excellent treatment responses and a favourable disease prognosis [15]. We therefore conducted a study on HrQoL in consecutive AIH patients attending our specialized outpatient clinic. In addition to assessing the physical and mental components of HrQoL, we measured symptoms of anxiety and depression as major determinants of mental disorders. Specific concerns hypothesized to relate to AIH were investigated asking additional *ad hoc*-questions. Our findings demonstrated a high rate of severe symptoms of anxiety and depression in patients with AIH, which was not increased in patients with cirrhosis or elevated markers of inflammatory activity. Concerns regarding the prognosis of the disease were highly associated with these symptoms. Appropriate counselling and treatment of the disease should therefore include addressing these concerns in order to improve HrQoL in AIH-patients.

Patients and methods

Patients

This study included consecutive patients with AIH attending the outpatient clinic of the 1st Department of Medicine, University Medical Center Hamburg-Eppendorf from April 2008 to July 2009. 103 patients gave their consent to participate in the study, representing 75% of all AIH patients seen in the outpatient department during the study period. AIH was diagnosed according to accepted criteria [1] and positive response to immunosuppressive treatment. Viral hepatitis was excluded using serology. All but three patients received immunosuppressive treatment and only one patient presented with an acute flare of the disease with serum aminotransferase levels above five times the upper limit of normal. Liver cirrhosis was present in 27% of patients, while none had decompensated cirrhosis. Clinical data was retrospectively retrieved from patient charts whereas HrQoL data was assessed prospectively via patient-reported outcome measures. Patient characteristics are given in Table 1.

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the appropriate institutional review committee. All patients gave written informed consent.

Methods

In 2008–2009, patients received the questionnaires at the time of the outpatient visit. HrQoL was assessed by the 12-item Short Form Health Survey (SF-12) [16,17]. SF-12 data obtained in this study was compared to a representative age and gender matched sample from the German general population (N = 7.124) [16], as well as to published data from patients with arthritis (N = 695) [16]. Depressive symptoms were identified using the nine item depression module of the patient health questionnaire (PHQ-9) [18–20], which assesses symptom severity and offers a categorical algorithm to identify major – or other depressive syndromes according to DSM-IV. Data obtained in this study was compared to unpublished representative data of the German general population (age and gender matched, N = 1.939) in 2007 and to published data of patients with inflammatory rheumatic diseases (N = 164) in 2001 [21]. Symptoms of anxiety were assessed using the Generalized Anxiety Disorder Screener (GAD-7) [22,23]. GAD-7 data obtained in this study was compared to published data of the German general population (age and gender matched, N = 3.720) [23]. In addition, eight *ad hoc*-questions were added to the questionnaire to identify AIH-specific concerns. These questions were asked at the end of the questionnaire to prevent a bias on depression and anxiety related answers.

Statistical analysis

t tests were used to determine if AIH-patients with cirrhosis significantly differed from AIH-patients without cirrhosis in their physical component score (PCS) or their mental component score (MCS) of the SF-12, and to compare PCS- and MCS-scores of AIH-patients with the general population and other patient groups. *Chi*^{2}-tests were applied to identify significant differences between AIH-patients and the general population with respect to the frequency of other depressive syndrome, major depressive syndrome, and moderate and severe anxiety symptom levels. Principle component analysis was used to determine the factors representing the common content of the *ad hoc*-questions. Multiple regression analyses (backward technique) were used to identify relevant predictors for the criteria depression severity and severity of anxiety symptoms in AIH-patients. The variable immunosuppressive treatment for regression analyses was defined as medication with azathioprine or 2nd or 3rd-line treatment excluding prednisolone in order to detect an effect of steroids on HrQoL. The adjusted determination coefficient R^2 is reported as a measure of variance of the criterion explained by the regression model. For multiple regression analyses with the criterion depression severity, complete clinical as well as questionnaire data including all variables was available for 75 (of 103) AIH-patients, for regression analysis with the criterion severity of anxiety symptoms complete data was available for 74 AIH-patients. No missing data imputation methods were used.

Table 1. Demographic and selected clinical and laboratory features of subjects studied.

	AIH patients (n = 103)
Clinical features	
Age (mean and range)	50 (17-82) yr
Women	71%
Liver cirrhosis*	27%
Treatment	
With prednisolone	51/95 (54%)§
Any immunosuppression without prednisolone	41/95 (43%)§
Liver tests$	
ALT (median and range)	29 (9-307) IU/L
IgG	12.2 (6.5-25.5) g/dl
Total bilirubin	0.5 (0.2-2.5) mg/dl
Complete biochemical remission#	77%
Co-morbidities	
Malignancy	7%
Other autoimmune diseases	23%
Psychiatric/neurologic	14%
Cardiovascular and others	36%
Family status	
Married	50%
Single	30%
Divorced/separated	10%
Widowed	7%
Education	
High school	38%
College/university	32%

*Liver histology revealed concomitant steatosis and steatohepatitis in one patient each.
§Out of 95 patients with complete data on medication dosage (three patients without immunosuppressive treatment).
$Normal range: ALT: <35 IU/L (women), <50 IU/L (men); IgG: <16 g/L; total bilirubin: <1.2 mg/dl.
#According to the updated definition of complete biochemical remission (AASLD practice guideline 2010).

Results

Physical and mental wellbeing in patients with autoimmune hepatitis

77% of patients were in complete biochemical remission at the time of the first evaluation of HrQoL as depicted by the median