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World J Gastroenterol 2007 June 7; 13(21): 3003-3008
World Journal of Gastroenterology ISSN 1007-9327

RAPID COMMUNICATION

Assessment of health-related quality of life in Chinese patients with minimal hepatic encephalopathy

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Received: 2007-03-26 Accepted: 2007-04-18

Abstract

AIM: To evaluate the health-related quality of life (HRQOL) based on the Chinese version of SF-36 and Chronic Liver Disease Questionnaire (CLDQ) in subjects with chronic hepatitis B, liver cirrhosis, including patients with minimal hepatic encephalopathy (MHE).

METHODS: The SF-36 and CLDQ were administered to 160 healthy volunteers, 20 subjects with chronic hepatitis B and 106 patients with cirrhosis (33 cases exhibited MHE). HRQOL scores were compared among the different study groups. The SF-36 includes eight health concepts: physical functioning, role-physical, body pain, general health, vitality, social functioning, role-emotion, and mental health. Six domains of CLDQ were assessed: abdominal symptoms, fatigue, systemic symptoms, activity, emotional function and worry.

RESULTS: Compared with healthy controls (96.9 ± 4.5, 86.6 ± 18.4, 90.1 ± 12.5, 89.0 ± 5.7, 87.5 ± 4.3, 95.8 ± 7.1, 88.5 ± 15.9, 88.7 ± 5.2 in SF-36 and 6.7 ± 0.5, 6.1 ± 0.6, 6.3 ± 0.6, 6.5 ± 0.5, 6.3 ± 0.5, 6.8 ± 0.4 in CLDQ), patients with chronic hepatitis B (86.3 ± 11.0, 68.8 ± 21.3, 78.9 ± 14.4, 60.8 ± 10.5, 70.8 ± 8.6, 76.1 ± 12.6, 50.0 ± 22.9, 72.2 ± 10.6 and 5.5 ± 1.0, 4.5 ± 1.0, 5.2 ± 1.1, 5.3 ± 0.9, 4.8 ± 0.9, 4.9 ± 1.0) and cirrhosis (52.8 ± 17.4, 32.8 ± 27.9, 61.6 ± 18.9, 30.2 ± 18.3, 47.9 ± 20.1, 54.0 ± 19.2, 28.9 ± 26.1, 51.1 ± 17.8 and 4.7 ± 1.2, 3.9 ± 1.2, 4.7 ± 1.2, 4.7 ± 1.3, 4.7 ± 1.0, 4.4 ± 1.1) had lower HRQOL on all scales of the SF-36 and CLDQ ($P < 0.01$ for all). Increasing severity of liver cirrhosis (based on the Child-Pugh score/presence or absence of MHE) was associated with a decrease in most components of SF-36 and CLDQ, especially SF-36.

CONCLUSION: The Chinese version of SF-36 along with CLDQ is a valid and reliable method for testing MHE in patients with liver cirrhosis. Cirrhosis and MHE are associated with decreased HRQOL.

Key words: Minimal hepatic encephalopathy; Liver cirrhosis; Health-related quality of life; Chronic hepatitis B; Chinese

Bao ZJ, Qiu DK, Ma X, Fan ZP, Zhang GS, Huang YQ, Yu XF, Zeng MD. Assessment of health-related quality of life in Chinese patients with minimal hepatic encephalopathy. *World J Gastroenterol* 2007; 13(21): 3003-3008

http://www.wjgnet.com/1007-9327/13/3003.asp

INTRODUCTION

Minimal hepatic encephalopathy (MHE) is defined as a condition in which patients with liver cirrhosis show several quantifiable neuropsychological defects in the presence of a normal neurological examination[1-3]. In the past two decades, there has been an increasing realization that the traditional assessment of medical outcomes following medical interventions is unsatisfactory. Therefore, health-related quality of life (HRQOL) has gained importance as an outcome measure in clinical and epidemiological studies[4,5].

Generic and specific instruments have been used to measure HRQOL. Generic instruments, such as the widely used Medical Outcomes Study 36-Item Short Form Health Survey (SF-36)[6], provide a global assessment of a given disease and allow comparisons with the general population and other diseases. Generic instruments do not assess disease-specific symptoms, such as pruritus in liver disease, and probably are less responsive to small, yet clinically important, changes. To assess specific aspects of a disease and provide a more responsive instrument for clinical studies, disease-specific instruments have been developed. The disease-specific HRQOL instrument evaluated for different stages of liver diseases is the Chronic Liver Disease Questionnaire (CLDQ)[7].

With the growing interest in monitoring the state of an illness by means of HRQOL instruments, the question arises as to which biological, psychological, and sociodemographic factors may influence HRQOL in

patients with chronic liver diseases. Only a few studies have assessed biological and psychosocial predictors of HRQOL measured by both a generic and a disease-specific HRQOL instrument in a cohort of patients with different causes and severities of liver disease. Therefore, in the present study we used the Chinese version of the SF-36 as a generic instrument and the CLDQ as a disease-specific instrument. The purpose of our study was to identify the most relevant domains of HRQOL impairment in patients with various chronic liver diseases; and to assess predictors of disease severity in patients with various chronic liver diseases, and especially MHE.

MATERIALS AND METHODS

This study was approved by the hospital ethics committee. Education level of all the objects was not less than 9 years.

Patients

All patients gave an informed consent to participation after a full explanation of the study protocol. The diagnosis of chronic hepatitis B and cirrhosis was made according to the criteria revised in 2000 National Symposium in China[8]. The diagnosis of chronic HBV was based on the presence of hepatitis B surface antigen for at least 6 mo, elevated serum alanine aminotransferase (ALT) levels, HBeAg or anti-HBe positive test, and presence or absence of serum HBV DNA as detected by the hybridization method. The diagnosis of cirrhosis was based on clinical finding, laboratory tests, imaging studies, and liver histological examination.

Exclusion criteria were overt hepatic encephalopathy (HE) or a history of overt HE or neurological or mental diseases; alcohol-related liver disease or history of recent (< 4 wk) alcohol intake; history of recent (< 4 wk) use of drugs affecting psychometric performances like sedatives or other psychotropic drugs and antiviral treatment for chronic hepatitis B; a history of liver transplantation or shunt surgery or transjugular intrahepatic portosystemic shunt for portal hypertension; a history of recent (< 4 wk) gastrointestinal bleeding and electrolyte imbalance; severe medical problems such as congestive heart failure, pulmonary disease, cerebrovascular diseases and diabetes mellitus that could influence HRQOL measurement; and inability to perform neuropsychological tests and correct filling of the questionnaires because of poor vision.

The enrollment period extended from December 2003 to February 2006 and the study was conducted at the Renji Hospital and Huadong Hospital. Twenty adult patients with a diagnosis of hepatitis B and 106 patients with cirrhosis confirmed by clinical findings, laboratory tests, imaging studies and liver histological (10 patients) were invited to take part in the study. The Child-Pugh's scores were used to assess the severity of liver cirrhosis.

Comparison groups

One hundred and sixty healthy volunteers who presented for their yearly physical examination and had no specific complaints or illness requiring treatment served as the controls. These individuals also completed the neuropsychological assessment, and SF-36 and CLDQ questionnaires.

Neuropsychological assessment

Number Connection Test-A (NCT-A): This test is a derivative of the Trail Making Test and measures cognitive motor abilities. In the NCT-A, subjects have to connect numbers printed on paper consecutively from 1 to 25, as quickly as possible. Errors are not enumerated, but patients are instructed to return to the preceding correct number and then carry on. The test score is the time the patient needs to perform the test, including the time needed to correct the errors. A low score indicates a good performance.

Symbol digit test (SDT): This is a subtest of the Wechsler Adult Intelligence Scale (WAIS) and measures motor speed and accuracy. The patient is given a list of symbols associated with digits from 1 to 9 and is asked to fill in blanks with numbers that correspond to each symbol. The test score is the total number of correct sequential matching of numbers to symbols in a 90-second interval. A high score indicates a good performance.

After an explanation of each psychometric test, an abbreviated demonstration test was administered to ensure that the patient understood the test properly. Age dependent normal values of NCT-A and DST were determined from the 160 healthy volunteers. Normal values were expressed as mean ± 2 standard deviations[9].

Neurophysiological assessment

Electroencephalogram (EEG): The EEG was recorded while the patient lay comfortably in a quiet room using standardized techniques (Harmanie, Stellate Co., Canada). The EEG was considered abnormal if the background frequency showed alpha rhythm abnormity, slowing (< 8 Hz) or disappearing or obvious asymmetry, or appearance of theta waves when compared with the background frequency of normal adults of the same age. All the records were evaluated manually by a single observer to avoid interobserver error.

Diagnosis of MHE

MHE was diagnosed when patients had an abnormal score on at least one of the two psychometric tests (NCT-A and DST), or if the EEG was abnormal[10-13].

Assessment of daily function

The SF-36 is a reliable and valid instrument to measure all domains of health status by means of 36 items[6]. It measures 4 domains in the area of physical health (Physical Functioning, Role limitation-physical, Bodily Pain, and General Health) and 4 domains in the area of mental health (Role Limitation-Emotional, Vitality, Mental Health, and Social Functioning). Responses to the questions in each domain are added to provide 8 scores between 0 and 100, with higher scores reflecting better HRQOL. The component summary scores of the SF-36 were used as generic measures of HRQOL.

The CLDQ is designed to assess all relevant domains of HRQOL in patients with chronic liver disease and has

been recently validated in Chinese-speaking patients[7]. With 29 items on a 7-point Likert scale ranging from 1 (all the time) to 7 (none of the time), 6 subscale scores (abdominal symptoms, fatigue, systemic symptoms, activity, emotional functioning, worry) and a CLDQ overall score can be calculated. By dividing each domain score, CLDQ results can be presented on a scale of 1-7, with 1 indicating the worst and 7 indicating the best HRQOL. Scores of the subscales of the CLDQ were used as specific measures of HRQOL.

Patients were asked to complete the questionnaires of the Chinese version during regular outpatient visits or during a hospital stay, while healthy volunteers completed the questionnaires during their annual physical examinations. Physicians were trained to give instructions when needed, collect the questionnaires, and record clinical data using standardized forms. The SF-36 and CLDQ scores obtained in patients were compared with the scores in 160 healthy individuals recruited from two hospitals in Shanghai.

Statistical analysis

All data were analyzed using SPSS (version 10.0; SPSS, Inc., Chicago, IL). Data derived from descriptive statistical analysis are presented in the form of percentages for categorical variables and mean ± SD for continuous data. Categorical data were compared using chi-square test, and continuous data, Student's *t* test or, if appropriate, nonparametric tests. Stepwise multiple regression analysis was used to study the influence of independent variables on the CLDQ and SF-36 domains while controlling the effect of other variables. A P value < 0.05 was considered statistically significant.

RESULTS

Education level of all the objects was not less than a 9 years old. All 126 patients and 160 healthy subjects completed the two questionnaires. The demographic and clinical data are shown in Table 1. The various causes of cirrhosis were chronic hepatitis B (70 cases), chronic hepatitis C (6 cases), schistosomiasis (11 cases), autoimmune liver disease including primary biliary cirrhosis, autoimmune hepatitis, and primary sclerosing cholangitis (19 cases).

The results of HRQOL in different study groups are shown in Table 2. Reliability refers to the precision or reproducibility of a measure, and validity refers to an instrument's ability to truly measure what it intends to measure[14]. To assess test reliability, 23 subjects completed the questionnaire twice; the interval between the tests was 2 d. Pearson's item-scale correlation coefficients of SF-36 for the results of the two tests ranged from 0.71 to 0.92, and CLDQ from 0.78 to 0.88 (Table 2). Cronbach's alpha was computed to assess SF-36 and CLDQ internal-consistency reliability[15], for all eight scales of SF-36 and six domains of CLDQ. The alpha value exceeded 0.70 (from 0.71 to 0.94) for all the test results with the exception of social-functioning (0.67) in the SF-36 questionnaire (Table 2).

Thirty-three (31.1%) of the 106 patients with cirrhosis had at least one abnormal test result. These 33 patients were considered to have MHE, whereas the remaining 73 patients were not considered to have MHE.

Table 1 Demographic and clinical data of different study groups

	Control subjects (n = 160)	Chronic hepatitis B (n = 20)	Cirrhosis (n = 106)
Age	44.8 ± 7.1	43.2 ± 6.3	45.4 ± 7.2
Gender M/F	115/45	6/14	73/33
Educational level, yr	11.7 ± 2.5	12.3 ± 2.7	11.3 ± 2.3
Child-Pugh class	-	-	A 28/B 64/C 14
MHE (+/-)	-	-	33/73
ALT (U/L)	25.4 ± 8.0	89.4 ± 32.5	48.2 ± 23.6

Compared with healthy controls, patients with chronic hepatitis B and cirrhosis had lower HRQOL on all scales of the SF-36 and CLDQ questionnaires (P < 0.01 for all). Increasing severity of liver cirrhosis (based on the Child-Pugh score/presence or absence of MHE) was associated with a decrease in most components both SF-36 and CLDQ (Table 2). However, patients with Child-Pugh B and C had similar HRQOL score on both SF-36 and CLDQ (P > 0.05), with the exception of role-physical and vitality on SF-36. There was a significant difference between patients with and without MHE on SF-36 score (P < 0.01), but no significant difference (P > 0.05) on CLDQ score except for abdominal symptoms.

DISCUSSION

In 1946, the World Health Organization (WHO) defined health as "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity"[16]. This definition represents a departure from defining health solely in terms of death and disease. Testa and Simonson defined HRQOL as the "physical, psychological and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, expectations and perceptions"[17]. HRQOL cannot be observed and measured directly, the assessment of HRQOL depended on the subjects response to the questionnaires.

Two basic approaches characterize the measurement of HRQOL: generic instruments and specific instruments[18]. Although developed recently relative to other generic measures, the SF-36 is currently the most widely used health status measure, particularly in the gastroenterology literature. Major advantages of generic instruments include dealing with a variety of areas and use in any population, regardless of the underlying condition. Because generic instruments apply to a variety of populations, they allow for broad comparisons of the relative impact of various health care programs. Generic profiles may, however, be unresponsive to changes in specific conditions. In this study, we chose CLDQ, which is a disease-specific scale developed by Younossi and colleagues to measure HRQOL in patients with chronic liver disease. The CLDQ focuses the respondent on the previous 2 wk period, and are in a question format with seven-category response scales. These scales have been used in several countries,

Table 2 Comparison of health related quality of life in different study groups as assessed by the SF-36 and CLDQ questionnaires

Domains	Control (n = 160)	Chronic hepatitis B (n = 20)	Cirrhosis (n = 106)			Cirrhosis (n = 106)		Pearson item-scale correlations (n = 23)	Internal reliability coefficients (Cronbach's α) (n = 106)
			Child-Pugh A (n = 28)	Child-Pugh B (n = 64)	Child-Pugh C (n = 14)	Non-MHE (n = 73)	MHE (n = 33)		
SF-36									
PF	96.9 ± 4.5	86.3 ± 11.0[a]	63.0 ± 15.8[a]	50.4 ± 17.0[a,b]	43.6 ± 13.4[a,b]	59.9 ± 14.2[a]	37.1 ± 13.1[a,d]	0. 92	0.85
RP	86.6 ± 18.4	68.8 ± 21.3[a]	50.9 ± 24.0[a]	28.9 ± 26.1[a,b]	10.7 ± 18.9[a,b,e]	40.8 ± 27.5[a]	15.2 ± 19.7[a,d]	0.83	0.86
BP	90.1 ± 12.5	78.9 ± 14.4[a]	71.0 ± 13.6[a]	58.0 ± 19.7[a,b]	59.5 ± 18.3[a,b]	66.8 ± 16.5[a]	50.2 ± 18.9[a,d]	0.72	0.80
GH	89.0 ± 5.7	60.8 ± 10.5[a]	46.1 ± 16.5[a]	25.9 ± 15.7[a,b]	18.2 ± 13.1[a,b]	34.8 ± 18.8[a]	20.0 ± 12.3[a,d]	0.78	0.73
VT	87.5 ± 4.3	70.8 ± 8.6[a]	61.1 ± 17.4[a]	45.5 ± 19.4[a,b]	32.1 ± 11.6[a,b,e]	55.1 ± 19.1[a]	31.8 ± 11.0[a,d]	0.82	0.71
SF	95.8 ± 7.1	76.1 ± 12.6[a]	67.1 ± 18.0[a]	50.3 ± 17.1[a,b]	44.4 ± 18.5[a,b]	61.5 ± 16.7[a]	37.4 ± 13.0[a,d]	0.71	0.67
RE	88.5 ± 15.9	50.0 ± 22.9[a]	51.2 ± 21.2[a]	22.4 ± 23.8[a,b]	14.3 ± 17.1[a,b]	35.2 ± 26.0[a]	15.2 ± 20.6[a,d]	0.90	0.86
MH	88.7 ± 5.2	72.2 ± 10.6[a]	64.4 ± 11.6[a]	48.3 ± 17.5[a,b]	37.1 ± 13.1[a,b]	56.0 ± 17.5[a]	40.2 ± 13.2[a,d]	0.82	0.78
CLDQ									
AS	6.7 ± 0.5	5.5 ± 1.0[a]	5.2 ± 1.1[a]	4.5 ± 1.2[a,b]	4.1 ± 1.1[a,b]	4.9 ± 1.2[a]	4.1 ± 1.0[a,d]	0.81	0.87
FA	6.1 ± 0.6	4.5 ± 1.0[a]	4.3 ± 1.2[a]	3.8 ± 1.2[a,c]	3.5 ± 1.1[a,b]	4.0 ± 1.2[a]	3.6 ± 1.2[a]	0.83	0.94
SS	6.3 ± 0.6	5.2 ± 1.1[a]	5.2 ± 1.2[a]	4.7 ± 1.3[a]	4.4 ± 1.2[a,c]	4.9 ± 1.3[a]	4.6 ± 1.1[a]	0.87	0.81
AC	6.5 ± 0.5	5.3 ± 0.9[a]	5.0 ± 1.2[a]	4.7 ± 1.3[a]	4.4 ± 1.3[a]	4.9 ± 1.3[a]	4.5 ± 1.2[a]	0.88	0.75
EF	6.3 ± 0.5	4.8 ± 0.9[a]	4.8 ± 1.0[a]	4.7 ± 1.0[a]	4.6 ± 1.0[a]	4.8 ± 1.0[a]	4.6 ± 1.1[a]	0.82	0.89
WO	6.8 ± 0.4	4.9 ± 1.0[a]	4.8 ± 1.0[a]	4.3 ± 1.1[a,c]	4.2 ± 1.1[a]	4.5 ± 1.1[a]	4.2 ± 1.0[a]	0.78	0.88

PF: physical functioning; RP: role-physical; BP: body pain; GH: general health; VT: vitality; SF: social functioning; RE: role-emotion; MH: mental health; AS: abdominal symptoms; FA: fatigue; SS: systemic symptoms; AC: activity; EF: emotional function; WO: worry. [a]$P < 0.01$ *vs* control group; [b]$P < 0.01$, [c]$P < 0.05$ *vs* Child-Pugh A; [e]$P < 0.05$ *vs* Child-Pugh B; [d]$P < 0.01$ *vs* non-MHE.

and their validity, reproducibility, reliability and sensibility have been confirmed[15,19-22].

Chronic hepatitis B and liver cirrhosis are two of the most common diseases in China. It has been observed that 30%-84% patients with cirrhosis have MHE[23-26]. Patients with MHE have no recognizable clinical symptoms of hepatic encephalopathy but do have mild cognitive and psychomotor deficits[12,27-29]. There is a significant reduction in many of the domains related to HRQOL in patients with MHE[30]. Early diagnosis and treatment of MHE is extremely important, because of the high prevalence of liver diseases in China. We found that HRQOL in patients with chronic liver disease is much lower than that of healthy people. The SF-36 and CLDQ have both recently been proposed as useful additions to the clinical armamentarium when investigating HRQOL. Severely ill individuals can find answering detailed questions quite demanding and, therefore, the SF-36 and CLDQ were a logical and appropriate development for use in such situations. The CLDQ contains questions that may be important in patients with hepatic encephalopathy; however, items important in patients with variceal bleed or ascites are lacking. Both SF-36 and CLDQ are short and easy to administer, and correlate with the severity of liver disease as defined by Child-Pugh classification. However, patients with Child's B and C disease had similar HRQOL scores on both the CLDQ and the SF-36, possibly indicating that neither focuses sufficiently on issues of particular concern to patients with the most significant hepatic decompensation. Our data shows that as the liver disease becomes more severe, patients' HRQOL as measured by the SF-36 and the CLDQ deteriorates. This supports the construct validity of the instrument as a cross sectional measure of HRQOL for chronic liver disease. Although scale scores for CLDQ also deteriorate with disease severity, this was not true for all scales. Only the abdominal symptoms scales of CLDQ did capture this change in MHE patients.

The questionnaires are cheap and convenient, can be used in developing countries, and are complementary to the clinical data. More complicated tests would increase the patients' fatigue and mental burden and affect their performance efficiency[31]. These tests do not take much time to complete. The neuropsychological assessment (SDT and NCT) and questionnaires (SF-36 and CLDQ) could be completed within 60 min in the outpatient clinics and on the patients bedside.

There is only limited data on HRQOL in patients with MHE. Most studies in these patients have used generic instruments, mainly the SF-36. The results obtained in the present study demonstrate that the Physical, Psychological and Social domain scores on both the SF-36 and the CLDQ remain relatively stable in the absence of any therapeutic intervention (based on repeat assessment after a 2 d interval in a proportion of subjects with cirrhosis and in the control group).

It is possible that recruiting patients from just two hospitals may have resulted in a selection bias, although our study sample included patients with a wide spectrum of disease severity (non-cirrhotics to Child's C cirrhosis). However, given the nature of the quality of life concerns, a major difference across populations seems unlikely. Finally, we did not investigate the ability of these questionnaires to detect important changes over time, even if that change is small. We are addressing these issues in ongoing studies on patients with MHE.

In summary, the SF-36 and CLDQ appear to be responsive to clinically meaningful change in the Physical, Psychological and Environmental domains. We conclude that patients with MHE have impairment in their daily functioning as assessed by the SF-36 and the CLDQ. In addition to existing biochemical and physiological parameters, the use of HRQOL instruments (both generic and disease-specific) will enhance our ability to measure

comprehensively the delivery of health care to patients with chronic liver disease[32].

COMMENTS

Background

Owing to the high prevalence in liver cirrhosis, clinicians and researchers in increasing numbers are beginning to recognize minimal hepatic encephalopathy (MHE). The importance of MHE is related to several factors: the neuropsychological defects may result in a reduction in the ability to carry out daily activities, may confer an increased risk for road traffic accidents and accidents at the workplace, it could lead to a deterioration in the quality of life, and it could be a marker for clinical hepatic encephalopathy in the future. The rapid economic development in China has resulted in improvement in the quality of life, and traditional indicators such as mortality and objective clinical parameters are no longer sufficient to assess the effect of illness and the outcome of treatment. There is an increasing demand for a valid and acceptable health-related quality of life (HRQOL) measure for Chinese people.

Research frontiers

Generic and specific instruments are used to measuring HRQOL. Although many HRQOL measures have been developed in Western countries, few are applicable to the people in China. The major obstacle is the cultural and language differences between the populations of China and Western countries. The purpose of this study is to evaluate the HRQOL based on SF-36 and Chronic Liver Disease Questionnaire (CLDQ) in subjects with chronic hepatitis B and liver cirrhosis, especially with regard to the status of MHE. Therefore, we used the Chinese version of the SF-36 as a generic instrument and the CLDQ as a disease-specific instrument in a well-characterized sample of patients.

Related publications

The present study is one of a series of studies we have performed which cover the diagnosis, treatment, HRQOL and follow-up assessment of patients with MHE. We have cited several articles from other investigators that provide additional information related to MHE and HRQOL.

Innovations and breakthroughs

Despite the importance of HRQOL, few workers have assessed quality of life and its determinants in patients with chronic liver disease. We evaluated the impact of chronic liver disease on HRQOL, looked for differences in HRQOL by severity of liver disease, and attempted to identify clinical variables with disproportionate effects on HRQOL. Our findings indicate that the Chinese version of SF-36 along with CLDQ are valid and reliable methods for measuring HRQOL in patients with liver cirrhosis. We observed that cirrhosis and MHE are associated with a decrease in the HRQOL.

Applications

HRQOL is important for measuring the clinical impact of chronic disease. Physiologic measures provide useful information to the clinicians, but are of limited interest to patients since they often correlate poorly with functional capacity and well-being, areas in which patients have the most interest. For example, two patients with similar severity of clinical disease often have dramatically different responses to HRQOL. Furthermore, the questionnaires are cheap and convenient, can be applied in developing countries, and provide information that is complementary to the clinical data.

Terminology

The term "subclinical hepatic encephalopathy" is well recognized but has been replaced by the term "minimal HE" because of the potential misleading consequence of the word "subclinical." Subclinical may suggest a different pathogenesis of the problem and may imply a lack of clinical importance to this diagnosis. We used the term "health-related quality of life" because there are various aspects of life that are generally not considered as "health," including income, freedom, and quality of the environment. Clinicians and researchers focus on HRQOL, although when a patient is ill, almost all aspects of life become health related.

Peer review

The present study is a well performed analysis looking at the quality of life in patients with hepatitis B and cirrhosis, with and without MHE. We recommend that future studies should assess PHES (psychometric hepatic encephalopathy score) to determine and quantify the presence of MHE. PHES is a battery of five tests (number connection test A and B, digit symbol test, line tracing test and serial dotting test) that is currently considered as the "gold standard" for the determination of MHE. The purpose of this recommendation is that the same test is used in all studies. This would allow clinicians and researchers to compare data obtained in different parts of the world, which up to now has not been possible. This would accelerate the progress in the understanding of MHE, a condition which cannot be ignored any longer.

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