The Comparison of WHOQOL-BREF with Disease Specific Heath Related Quality of Life Questionnaire in Irritable Bowel Syndrome

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Abstract- Irritable Bowel Syndrome (IBS) is one of the most common gastrointestinal disorders particularly affecting the quality of life (QOL). Evaluating QOL in IBS patients is a valuable method of defining a psychobiological pattern of disease. Various disease specific and general instruments are now available to measure health-related QOL (HRQOL) in IBS patients. Though, no comparison has been made between these tools especially in non-western countries. We aimed to compare QOL measures between two specific and general QOL questionnaires in a sample of Iranian IBS patients. A total of 250 IBS patients were diagnosed based on Rome III criteria (mean age 29.6 ± 9.6 years). HRQOL was assessed using disease specific quality of life for IBS (IBS-QOL) and generic World Health Organization Quality of Life-BREF (WHOQOL-BREF) questionnaires. Patients also completed Speilberger`s "State/Trait Anxiety Inventory" and "Beck Depression Inventory-II" for the evaluation of anxiety and depression symptoms. The severity of symptoms was independently associated with HRQOL in patients using WHOQOL-BREF and IBS-QOL (r = -0.48 and -0.39 respectively, $P < 0.001$). In linear regression analysis, a strong correlation was observed between the HRQOL scores of IBS-QOL and the WHOQOL-BREF questionnaires (standard β = 0.86 (95%CI: 1.15 - 1.44), P value < 0.001). Controlling for anxiety and depression symptoms did not influence the strength of observed correlation. The WHOQOL-BREF is a psychometrically sound, rapid and convenient instrument whose HRQOL measure is as valid and accurate as the disease-specific IBS-QOL questionnaire. It seems reasonable to use the WHOQOL-BREF alongside the IBS-QOL.
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Acta Med Iran 2015;53(11):717-724.

Keywords: Irritable Bowel Syndrome; Primary Health Care; Quality of Life; Questionnaires

Introduction

Irritable bowel syndrome (IBS) is a functional disorder of intestine. It is one of the most prevalent causes of recurrent abdominal pain, making patients seek medical advice and go to gastroenterology clinics (1). The prevalence is estimated up to 22% in the general population (2-4). IBS incurs significant financial and psychological burden (5-8). It has a complex and not vividly cleared pathophysiology consisting of abnormal intestinal motility, excessive irritability of abdominal viscera and psychosocial disorders and components. Interactive mechanism between emotional areas of the brain, afferent sensory perceptions and intestinal motor responses also play an important role (9,10).

A recent systematic review suggests that about half of IBS patients have at least one concomitant somatic disorder which are associated with more severe symptoms and increased rate of psychopathologies such as anxiety, depression or somatization (11,12). It is shown that existing psychiatric disorders may lead to an accentuation of symptoms in patients with IBS and stressful life events also alter intestinal motility (13-15). Actually up to 94% of patients with IBS suffer from psychiatric co-morbidities (11,16).

Timely diagnosis and treatment of these conditions might be helpful in the management of IBS patients (17-19).

It seems that IBS has a great impact on quality of life (QOL) and patients with IBS have poorer QOL than the general population (20-22). Some researches show that QOL in IBS patients might be comparable to or even poorer than other troublesome diseases like

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gastroesophageal reflux disease, renal insufficiency and chronic obstructive pulmonary disease (23). It is now known that the severity of symptoms in patients with IBS is associated with QOL (24,25). The QOL of IBS patients depends not only on the symptoms of the disease itself, but also on the associated psychological conditions (12,26,27).

Therefore, the routine health-related QOL (HRQOL) assessment must be an integral part of the management process and is recommended by the latest American College of Gastroenterology statement on the management of IBS (28).

Disease-specific and general HRQOL instruments have been used in IBS patients (29-31). The most widely used specific questionnaire for HRQOL assessment in IBS patients is the IBS quality of life inventory (IBS-QOL). Only a few studies have compared these two categories (31-33), nevertheless some experts believe that disease-specific questionnaires are more potent and accurate in assessing HRQOL in IBS patients (34).

Hence, a small reduction in the demand imposed on clinical staff and patients may result in better use of HRQOL assessment in a clinical setting (35). The World Health Organization QOL-BREF (WHOQOL-BREF), developed by World Health Organization is such a promising measure for assessing QOL in general (36). The WHOQOL-BREF has not been used in IBS patients and its efficacy has not been evaluated in comparison with the disease-specific IBS-QOL inventory. The aim of this study was to examine the competence of the WHOQOL-BREF with respect to the validated IBS-QOL instrument in Iranian IBS patients.

Materials and Methods

Patients selection

A total of 250 consecutively selected IBS patients, older than 14 years, recruited from outpatient gastroenterology clinic of a general hospital. The recruitment process was performed between November 2012 and September 2013. Written informed consent was obtained from all patients. IBS was diagnosed according to Rome-III criteria by a board certified gastroenterologist (37). Imaging or endoscopic studies were performed by the same gastroenterologist to rule out any organic diseases only if there was a clinical indication. The study design was approved by ethics committee of Tehran University of Medical Sciences.

We excluded patients from the study using these exclusion criteria: 1) existing organic gastrointestinal disease; 2) previous abdominal surgery or hospital admission because of abdominal pain; 3) symptom accentuation with dairy products; 4) abnormal laboratory profile including anti-tissue transglutaminase antibodies, stool exam, urinalysis, thyroid and liver function tests; 5) abnormal imaging or endoscopic study, and 6) alarm signs defined as weight loss, dysphagia, anemia, new onset symptoms at fifty years or above, nocturnal diarrhea, bloody stool and family history of cancer.

Socioeconomic features

These features such as age, sex, domicile, marital status and educational status were recorded during the initial interview. Educational status in patients without diploma was labeled as "low" and in patients with diploma degree or above as "high".

Domicile was categorized into urban and rural based on the area of residence during the past two years. Afterward, each patient was delivered four different questionnaires for evaluation of HRQOL, anxiety, and depression.

Symptom severity

Severity assessment was made using the self-reported symptom severity questionnaire. It has a single query "How bad is the discomfort?" referring to the previous four weeks.

The meaning of discomfort was explained to the patients to help them assessing severity better; abdominal pain and/or IBS associated bowel symptoms were the most common interpretation of patients. Patients responded to the question considering their daily life during the previous month by choosing one of the three choices: Can be overlooked if I do not think about it; cannot be overlooked, but does not influence my lifestyle; and influences my lifestyle. Responses were considered mild, moderate, and severe respectively.

Health-related QOL

Disease-specific QOL inventory for IBS (IBS-QOL) is specially designed to assess QOL in individuals with IBS (38,39). The total score was calculated by summation of subscale scores and then converted to a final score of zero to 100 (40). Obviously, higher total scores indicate better QOL.

The HRQOL was also measured by the World Health Organization QOL-BREF (WHOQOL-BREF)

questionnaire which thoroughly assesses four different domains of QOL including physical, psychological, social and environmental aspects (36). The time frame used to evaluate HRQOL was four weeks.

Anxiety and depression symptoms

Anxiety and depression symptoms were also assessed in our set of patients as the main related psychiatric comorbidities. Beck Depression Inventory II (BDI-II) (41) was used to specify symptoms of depression in participants. The scores were interpreted as follows: 0- 13 indicative of minimal depression; 14-19 indicative of a mild level of depression; 20- 28 labeled as moderate depression and 29- 63 showing more severe forms of depression (42).

For measuring symptoms of anxiety in participants, Spielberger`s State/Trait Anxiety Inventory (STAI) was used (43); the higher total scores (both categories) indicates a higher level of anxiety symptoms. Total of state and trait anxiety scores were used as the indicator of anxiety symptom ranging from 40 to 160. Validated Persian version of all previously mentioned questionnaires were used in this study (44-46). For illiterate patients a clinical psychologist helped them to fulfill the questionnaires.

Statistical analysis

Normal distribution of the continuous variables was evaluated by the Kolmogorov-Smirnov test. Analysis of variances (ANOVA) was performed to examine the association between HRQOL, anxiety and depression symptoms with different severity status. Then we determined the correlation between these variables using Spearman nonparametric correlation coefficient.

The relationship between the IBS-QOL measure with the WHOQOL-BREF, anxiety, depression, and self-reported symptom severity was analyzed by multivariate linear regression analysis and standardized beta was calculated. The second set of analysis involved correlation and partial correlations in assessing the independent association between the IBS-QOL and the WHOQOL-BREF, controlling for personality variables (anxiety, depression, self-reported severity).

The level of significance was set to 0.05 for all analyzes. All statistical calculations and analyzes were performed by an expert medical statistician using SPSS statistical software Ver. 21.0 (SPSS Inc., Chicago, Illinois, USA).

Results

Total of 300 consecutive IBS patients were visited in an outpatient gastroenterology clinic, of which 250 patients (16-51 years) with the mean age of 29.6 years were recruited in the study. Normal distribution was seen in age, depression scores, anxiety scores and QOL (Z = 1.2, 1.3, 1.4 and 1.2 respectively; $P > 0.05$).

General characteristics including age, sex, educational status, marital status, domicile and IBS subtype along with self-reported measures of symptom severity, anxiety, depression and HRQOL were acquired by appropriate questionnaires are showed in Table 1. Of 250 patients, mild, moderate and severe symptoms were reported in 132 (52.8%), 91 (36.4%) and 27 (10.8%) patients, respectively.

Table 2 shows all questionnaire results based on different severities reported by patients and also the association between severity status with QOL scores, anxiety and depression inventory measures. QOL scores, anxiety and depression measures were significantly different between patients with different symptom severities ($P = 0.001$).

Symptom severity was inversely related to HRQOL using both disease specific IBS-QOL inventory and general WHOQOL-BREF questionnaire (ρ = -0.49 and -0.38 respectively, all $P < 0.001$). Anxiety and depression scores were obtained by BDI-II and STAI were also significantly correlated with severity (ρ = 0.41 and 0.51 respectively, $P = 0.01$).

The magnitude of the associations among IBS-QOL and WHOQOL-BREF measures are reflected in Pearson's correlation (r = 0.82, $P < 0.001$). We further conducted a partial correlation analysis to identify whether this significant zero-order correlation was independent of variables such as anxiety, depression and self-reported severity that might influence the perception of HRQOL (47). Given the analysis result, the association between the IBS-QOL score and the WHOQOL-BREF score remained significant at the 0.001 level but slightly decreased in strength (r = 0.76) which is well above our acceptable substantial correlation (r = 0.4).

Multivariate regression analysis showed that IBS-QOL measure is properly and accurately predictable by WHOQOL-BREF questionnaire, the result of which is shown in table 3 (standard β = 0.86 (95%CI: 1.15 - 1.44), $P < 0.001$).

Figure 1 shows the scatter plot diagram for relationship between IBS-QOL and WHOQOL-BREF questionnaire results (r2 = 0.67, $P < 0.001$).

Table 1. Demographic characteristics and self- reported quality of life measures of the studied population

Demographics	Number (%)	Mean ± Standard Deviation
Age (year)		29.6 ± 9.6
Gender		
Female	135 (54)	
Male	115 (46)	
Education Status		
Low (under diploma)	169 (67.6)	
High (diploma and above)	81 (32.4)	
Domicile		
Urban	227 (90.8)	
Rural	23 (9.2)	
Marital Status		
Married	198 (79.2)	
Not married	52 (20.8)	
IBS Subtypes		
IBS-D	69 (27.6)	
IBS-C	82 (32.8)	
IBMS-M	99 (39.6)	
Self-reported Measures		
Symptom severity		
Mild	132 (52.8)	
Moderate	91 (36.4)	
Severe	27 (10.8)	
WHOQOL-BREF		
Physical Domain		23.67 ± 5.22
Psychological Domain		19.36 ± 3.72
Social Domain		10.68 ± 2.51
Environmental Domain		27.74 ± 5.04
Total		85.69 ± 16.1
IBSQOL score		79.32 ± 24.5
State/Trait Anxiety Inventory score		92.25 ± 19.02
Beck Depression Inventory II score		15.91 ± 6.65

IBS: Irritable Bowel Syndrome; IBS-D: IBS Diarrhea dominant; IBS-C: IBS Constipation dominant; IBS-M: IBS Mixed type; WHOQOL-BREF: World Health Organization`s Quality of Life Brief Questionnaire; IBSQOL: Irritable Bowel Syndrome Quality of Life Inventory

Table 2. Correlation between severity status and health-related quality of life, anxiety and depression symptoms

	Comparing means				Nonparametric correlation	
	Mild	**Moderate**	**Severe**	***P* value (ANOVA)**	**Spearman coefficient (ρ)**	***P*. value**
IBSQOL score	87 ± 24.43	74.08 ± 24.46	59.41 ± 13.73	0.001	-0.49	<0.001
WHOQOL_BREF					-0.38	
Physical	25 ± 5.64	22.88 ± 4.35	19.85 ± 2.98	0.001		
Psychological	20.88 ± 3.6	18.15 ± 3.18	16 ± 1.84	0.001		
Social	11.42 ± 2.29	10.03 ± 2.42	9.22 ± 2.68	0.001		
Environmental	29.17 ± 5.26	26.6 ± 4.11	24.59 ± 4.53	0.001		
Total	92.28 ± 16.45	80.42 ± 12.45	71.26 ± 7	0.001		<0.001
BDI-II score	13.26 ± 5.6	16.6 ± 4.35	26.56 ± 6.72	0.001	0.41	0.01
STAI score	85.2 ± 16.79	97.65 ± 17.72	108.48 ± 18.14	0.001	0.51	0.01

IBSQOL: Irritable Bowel Syndrome Quality of Life Inventory; WHOQOL-BREF: World Health Organization`s Quality of Life Brief Questionnaire; BDI-II: Beck Depression Inventory-II; STAI: State/Trait Anxiety Inventory

Table 3. Correlation between IBSQOL scores and the studied variables

	Standardized β	95% Confidence Interval for β	*P*. value
WHOQOL-BREF score	0.86	(1.15) - (1.44)	<0.001
Beck Depression Inventory-II score	0.07	(-0.04) - (0.62)	0.08
State/Trait Anxiety Inventory score	0.03	(-0.09) - (0.16)	0.16
Symptom severity	-0.04	(-4.78) - (1.94)	0.40

IBSQOL: Irritable Bowel Syndrome Quality of Life Inventory; WHOQOL-BREF: World Health Organization`s Quality of Life Brief Questionnaire
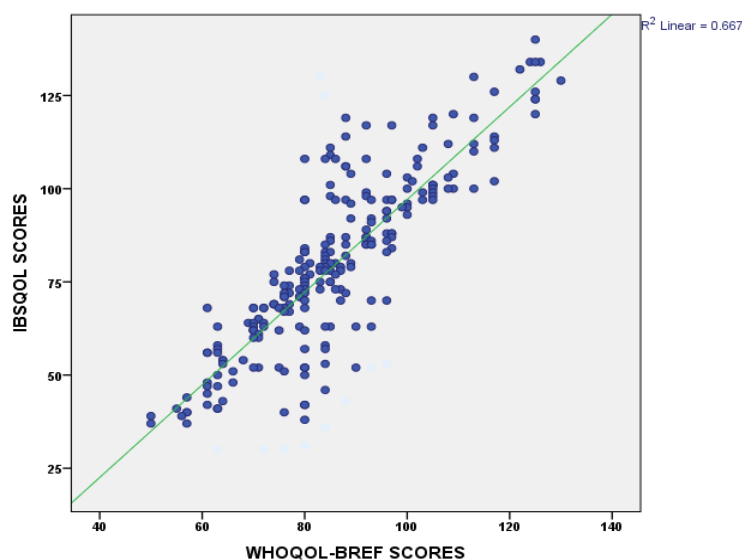
Figure 1. The correlation of IBSQOL and WHOQOL-BREF

IBSQOL=Irritable Bowel Syndrome Quality of Life questionnaire; WHOQOL-BREF=WHO Quality of Life Brief questionnaire

Discussion

IBS is the most common gastrointestinal disorder which imposes a great direct and indirect burden on the community. Patients with IBS report even more activity limitation than patients with another chronic disease such as diabetes, heart disease, stroke and nearly equal to that of cancer. Measuring HRQOL in this widespread disabling disease should be an integral part of management and follow-up of involved patients.

Applying WHOQOL-BREF in our study revealed the liaison between poor QOL and self-reported symptom severity which was consistent with the results of the IBS-QOL. These findings were parallel with the study of Kanasawa *et al*., (48). Other studies as well have related severity of symptoms with QOL measures (24,25). The current study did not show statistically significant relation between QOL and age, sex, marital status, educational status, domicile, anxiety and depression symptoms. Tough Monnikes in 2011 conducted a study showing that QOL is affected by sex and psychological conditions as well as symptom

severity (6).

Indeed, IBS itself may not necessarily be the cause of poorer QOL in IBS patients and some studies have reported that even more than 50% of IBS patients claim other factors like related anxiety as the major cause of diminished QOL (33). The basic construction of generic and disease-specific QOL instruments may be charged. Disease-specific measures assume that specific condition is the primary cause. So originally they underestimate the role of associated conditions on QOL. Contrarily, generic instruments basically involve functional domains deemphasizing the specific condition. Diseases like IBS, which frequently accompany with other medical conditions, highlight this debate even more.

The present major goal was to inspect the qualities of the general WHOQOL-BREF as a measure of overall HRQOL in patients with IBS. As such measure, the questionnaire should be easy to use, simple to understand by patients and interpret by physicians, quick in developing meaningful data unflawed by confounding variables that might affect the perception of QOL and

particularly comply with the previously established measures of QOL in IBS.

Regarding patient friendliness, the WHOQOL-BREF has been developed cross-culturally and consists of not very detailed questions which take no more than 5 minutes to complete, compared to other tests such as SF-36 (10–15 minutes) and the IBS-QOL (15 minutes). Moreover, intricate mathematics is not required to clarify its QOL profile. Therefore, the WHOQOL-BREF has an advantage over other QOL tools that are more challenging to interpret (23). The WHOQOL-BREF also facilitates judgment of self-perceived health (question 2) which is a sensitive measure of medical comorbidity (49).

With respect to compliance with previously proved QOL measures, our set of data showed strong and statistically significant correlation between the WHOQOL-BREF and the IBS-QOL. Some studies have compared other general questionnaires to disease-specific ones for evaluation of HRQOL in IBS patients (31-33). Lackner et al. in 2006 showed that general CDC HRQOL-4 instrument is as good as the IBS-QOL (33). Park et al. also studied generic SF-36 and the IBS-QOL in Korean patients, reporting the same HRQOL measure by both (31). To our knowledge no such comparison was performed before using the WHOQOL-BREF in IBS patients. This study shows that the IBS-QOL scores can be derived precisely out of WHOQOL-BREF measure of HRQOL.

Another important feature of a good HRQOL instrument is its independence of other potentially confounding factors which is somehow largely neglected in psychometric validation studies of QOL measures (50). The problem arises when you cannot certainly say that any significant zero order association revealed is not the effect of a third variable. Actually personality attributes such as anxiety and depression have been found to affect HRQOL (13,47). In the present study, controlling for anxiety, depression and self-reported severity did not significantly decrease the strength of correlations observed between the WHOQOL-BREF and the IBS-QOL.

It might look dubious that the two questionnaires studied here share same aspects but do not cover same areas of QOL. It must be stated that authors do know that other short HRQOL tools also exists, though the purpose of this study was to show the properties of WHOQOL-BREF in the assessment of HRQOL in IBS patients and the authenticity of IBS-QOL as the standard disease-specific QOL assessment tool in this disease is not debatable. Fortunately, WHOQOL-BREF is a tool encompassing both health and non-health domains which are of great value in evaluating QOL in IBS patients suffering from various aspects of QOL impairments.

Strengths and limitations

According to practical barriers that prevent physicians from implementing routine QOL assessment, shifting focus from assessing QOL to its clinical predictors (e.g. anxiety, hopelessness) as mentioned in some studies (51), would not be any more straightforward and extracting those measure does not clearly reflect HRQOL. The principal strength of this study was to apply an easy to use and calculate QOL instrument which elicit HRQOL measure as well as previous widely accepted IBS-QOL; while being unaffected by other confounding factors involved.

One should keep in mind that there are some limitations in this study. We just recruited IBS patients who were referred to the outpatient gastroenterology clinic and patients with any major complication or hospital admission were excluded. Thus, the results of this study are not generalizable to all IBS patients, particularly patients with severe disease requiring hospitalization for better control. Another limitation arises regarding the recall period used in our survey. While one month may be acceptable for some general aspects of the WHOQOL-BRIEF without quick changes such as money, transportation and security; it may not be suitable for some health items with more fluctuations.

The cross-sectional design of the study limited our estimation of QOL changes or improvement after proper treatment. Another prospective survey might be needed to evaluate the functionality of the WHOQOL-BREF in this important scope. Yet conducting a study to compare the content validity of the two tests might also help to better clarify the observed results.

As routine HRQOL assessment in IBS patients is now recommended in clinical guidelines, implementing sensitive, simple and valid measures might be a good strategy. The WHOQOL-BREF is a psychometrically sound, rapid and convenient instrument providing physicians a handy tool to use alongside the IBS-QOL.

Acknowledgement

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