

Effect of Irritable Bowel Syndrome on Sleep Quality and Quality of Life of Inflammatory Bowel Disease in Clinical Remission

Abstract

Background: Inflammatory bowel disease (IBD) as a chronic and debilitating disease is affected by sleep disturbance which increases the risk of malignancy. Sleep disturbance is more common in irritable bowel syndrome (IBS) and few reported studies have assessed its role in IBD. We evaluated the effect of IBS on sleep quality and quality of life (QOL) of IBD patients in clinical remission. **Methods:** In a cross-sectional study, 115 IBD patients in clinical remission aged from 14 to 70 years referred to gastroenterology outpatient departments and private gastroenterology offices from 2007 to 2016. Patients considered in four groups (with/without IBS). The Revised "Rome III criteria" used for diagnosing IBS. Pittsburgh Sleep Quality Index questionnaire and the health-related QOL questionnaire used for evaluating sleep quality and QOL. **Results:** About 85 (73.9%) cases had ulcerative colitis (UC) and 30 (26.1%) cases had Crohn's disease (CD). Forty (34.8%) cases had IBD + IBS. Poor sleep quality in UC + IBS (OR: 0.018, $P = 0.003$) and UC (OR: 0.016, $P = 0.002$) was less than CD. Diseases extent in left side colitis (OR: 0.064, $P = 0.016$) were less than with pancolitis. Sleep quality affected by quality of life (IBDQ) ($P = 0.048$). Mean quality of life (IBDQ) in patients who had poor sleep was 11% less than those with good sleep. **Conclusions:** The syndrome of IBS affects the sleep quality of IBD in clinical remission, especially in CD. Its additive effect with IBD may worsen symptoms that correlated with sleep disturbance, such as pain, psychological and physical condition, and QOL.

Keywords: Inflammatory bowel diseases, irritable bowel syndrome, quality of life, sleep

Introduction

Inflammatory bowel disease (IBD) as a chronic and debilitating disease is affected by sleep disturbance. Importance of sleep in the regulation of many physiological functions has recently confirmed.^[1] On average, every adult person needs eight hours of night's sleep.^[2] Based on the statistical reports from the center for disease control and prevention, about 70 million American are suffering from chronic sleep disorders.^[3] Various studies have shown that the chronic sleep disorder may cause cardiovascular diseases, diabetes mellitus, and obesity.^[4] Also, that increases the risk of infectious diseases and overactivation of immunological system.^[5] Relation between the sleep disorder and chronic inflammatory diseases as asthma, systemic lupus erythematosus, rheumatoid arthritis, and IBD has reported by many studies.^[2,6-8] Besides, sleep restriction in animal models increases the release of inflammatory cytokines as for example TNF- α , IL-6, and also C-reactive

protein which are taken as activity markers in IBD.^[9] Sleep disorder can lead to fatigue in inflammatory diseases and is probably a cause of fatigue in patients with IBD. It is notable that fatigue is one of the common complaints of patients with IBD, which negatively and remarkably affects their health-related quality of life (HRQOL).^[10]

IBDs which consists of Crohn's disease (CD) and ulcerative colitis (UC) are multifactorial chronic disorders resulting from inappropriate immunological inflammatory response of body to intestinal microbes in a genetically susceptible patients.^[11,12] Morphological alterations and immunological responses are limited to colon in UC and the inflammation with a variable length is limited to the mucosa. Inflammation in CD may affect any part of the gastrointestinal system which maybe widespread and its lesions may penetrate through the intestinal wall. Diarrhea, abdominal pain, gastrointestinal bleeding, weight loss, malnutrition, and fatigability are most important symptoms

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Ali Zargar,
Somayeh Ahmadi
Gooraji¹,
Bahareh
Keshavarzi¹,
Ali Akbar Haji
Aghamohammadi²

Department of Internal
Medicine, Velayat Hospital,
Qazvin University of Medical
Sciences, Qazvin, Iran, ¹Velayat
Clinical Research Development
Unit, Velayat Hospital, Qazvin
University of Medical Sciences,
Qazvin, Iran, ²Department of
Internal Medicine, Metabolic
Diseases Research Center,
Qazvin University of Medical
Sciences, Qazvin, Iran

Address for correspondence:

Dr. Ali Akbar Haji
Aghamohammadi,
Velayat Clinical Research
Development Unit, Velayat
Hospital, 22 Bahman
Blvd, Qazvin, Iran.
E-mail: ahmohammadi@qums.ac.ir

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related to IBD which can affect different aspects of patients' psychological status, thereby imposing limitations in their life style.^[13] Global prevalence of UC is about 0.5–5.21 and for CD is about 0.1–16 individuals per 100,000 people.^[14] IBDs are chronic inflammatory disorders of the gastrointestinal system that affect more than 1 million people in the United States and 7 million worldwide.^[15] It seems that the pathogenesis of IBD is complicated and several environmental factors besides the genetic mutations and defects in immunological system contribute to this disease which can affect the HRQOL of such patients to some extent. Studies have shown that stress is taken as an important risk factor in the pathogenesis of IBD. Patients with IBD are more suffering from psychological impairments such as depression and anxiety as compared to normal population.^[16] Despite this, some of the environmental factors which may play role in the pathogenesis of IBD are less to deal with, and sleep disorder is one of them.^[17,18]

Recent investigations have shown that 50% of patients with inactive IBD suffer from a low sleep quality and this estimate is higher in patients with active disease.^[17,18] Besides, the HRQOL of patients with IBD is less than healthy population. Both diseases of UC and CD affect the HRQOL to some extent.^[19,20] On the other hand, sleep disturbance is more common in irritable bowel syndrome (IBS).^[21] Many studies have reported a significant relation between the sleep quality and HRQOL^[22-25] but the role of IBS in the quality of life and quality of sleep of IBD patients is less attended and discussed. In this study, we evaluated the effect of IBS on sleep quality and quality of life of IBD patients in clinical remission. Besides, the relation between sleep quality and quality of life was evaluated by studied disease groups in order to assess the effect of IBS on its relation.

Methods

In the cross-sectional study, 115 patients with IBD diagnosed by clinical, endoscopic, histologic, and if needed imaging were entered to the study. Patients referred to gastroenterology outpatient department of Qazvin University and private gastroenterologists' consultation offices were included from April 2007 to March 2016 and recruited in Des 2016 for completing the questionnaires provided if they had a stable clinical condition for the past 6 months. IBD patients were divided into two groups, with and without IBS. A revised "Rome III criteria" were used for diagnosing IBS. For UC, the clinical remission is defined as cessation of bleeding and normal stool frequency^[26] and for CD is defined as of Crohn's Disease Activity Index of less than 150.^[27]

Exclusion criteria were as follows: if there was any other chronic disease affecting the quality of life, drug abuse or/and any drug with positive or negative effect on sleep, and psychiatric disease.

Evaluation of sleep quality in patients suffering from inflammatory bowel disease

To evaluate the patients' sleep quality, the Pittsburgh Sleep Quality Index – a standard questionnaire – was used. Its validity and reliability has been reported by the global researchers in articles. This questionnaire was first translated to Persian by the researchers and then its validity and reliability was confirmed with a Cronbach's alpha from 0.78% to 82%.^[28] This questionnaire is used to evaluate the sleep quality and consists of questions in seven components including subjective sleep quality, sleep duration, sleep latency, habitual sleep efficacy, sleep disturbances, use of sleeping medications, and daytime dysfunction over the last month. Items of this questionnaire are scoring from 0 to 3, and the higher score indicates the worse sleep quality (score >5). Questionnaires were being questioned and filled by a trained questioner from the patients. In some studies on evaluation of sleep quality, the cut point is not exactly stated by value of 5. In our study, regarding dispersion in sleep quality score of patients with IBD with and without associated IBS, Roc curve (receiver operating characteristic) was used to detect the accuracy rate of test. Area under the Roc curve was obtained as 70% which is acceptable. Besides, its related sensitivity and specificity rates were 75% and 60%, respectively, which are obtained as per cut point 6.

Evaluation of health-related quality of life

To evaluate the HRQOL, two standard questioners of IBDQ and SF-36 were used which evaluate the domains of quality of life and physical and mental health, respectively.

The questionnaire of IBDQ consists of 32 questions which are categorized in 4 domains: (a) intestinal symptoms (10 questions), (b) systemic symptoms [consisting of sleep disorder and fatigue (5 questions)], (c) emotional function [including depression and anxiety and anger (12 questions)], and (d) social function [capability to participate in social activity and affairs (5 questions)]. For each question, seven answers are considered in which score 1 denotes the worst and score 7 denotes the best condition. Total score for each individual varies from 32 to 224, and the higher the score, the better the condition. Reliability and validity of IBDQ in Persian language was investigated in 2015 by Maleki *et al.*^[29]

The SF-36 is one of the most used generic HRQOL questionnaires in medical research which assesses the functional status, well-being, and general perception of health. SF-36 questionnaire consists of 36 items and 8 domains, physical function, social function, role function emotional function, psychological health and vitality; body pain and global health are evaluated. Additionally, SF-36 also provides two general measures from the functions, that is, physical component summary which measures the domain of physical health and the mental component

summary which evaluates the psychosocial health. Scores in each of these domains vary from 0 to 100 and the higher score denotes for a better quality of life. Reliability and validity of this questionnaire in Iranian population has been confirmed.^[30] Questionnaires were being questioned by a trained questioner and in some sections filled by a gastroenterologist.

In addition to above questionnaires, patients' demographic and clinical and management details were also collected.

Statistical analysis

Normality of data was evaluated using Shapiro–Wilk test, Kolmogorov–Smirnov test, and also *Q–Q* plot. Normality of data and homogeneity of variance among groups are confirmed. Analysis was done by the use of statistical tests such as Chi-square, analysis of variance, and logistic regression by the software of SPSS software for Windows, version 22.0 (SPSS, Chicago, IL, USA). Significant level was considered at level of 0.05.

Results

Data from 115 patients were analyzed of whom 58 (50.4%) cases were male and 57 (49.6%) cases were female. The mean age was 38.6 ± 12.2 with a range from 14 to 70 years. Eighty-five (73.9%) patients had UC disease and 30 (26.1%) had CD disease (colitis). From a total of IBD patients, 40 (34.8%) cases had IBS. In IBD patients with IBS, 29 (25.2%) cases had UC + IBS and 11 (9.6%) cases had CD + IBS. Besides, in IBD patients without IBS,

56 (48.7%) cases had UC and 19 (16.5%) cases had CD. Factors of age ($P = 0.862$) and sex ($P = 0.226$) were not significant among four groups (CD, UC, CD + IBS, UC + IBS). Patients' demographics are summarized by sleep quality in Table 1.

On evaluating the effect of IBS on sleep quality of IBD patients, their quality of life (IBD-Q) and their general quality of life (SF-36), significant results were obtained related to sleep quality ($P = 0.000$) and the quality of life of IBD patients (IBDQ) ($P = 0.000$). CD patients (with poor sleep frequency of 84.2%) and patients with CD + IBS (poor sleep frequency of 87.5%) had the poorer sleep quality. UC patients (good sleep frequency of 73.6%) had the better sleep quality. Besides, the mean quality of life of IBD patients (IBDQ) with IBS was less than those without IBS [Table 2].

In a multivariate logistic regression analysis, the effect of patients "characteristics and quality of life on sleep quality" was evaluated. Results showed that factors of disease group, disease extent, and quality of life of IBD (IBDQ) significantly affected the sleep quality. Significant results of multivariate logistic regression are summarized in Table 3. Odds of a poor sleep quality in both patients with UC + IBS (OR = 0.018, $P = 0.003$) and UC (OR = 0.016, $P = 0.002$) was significantly 98% less than odds of CD patients. Poor sleep quality in patients with CD + IBS (OR = 2.19, $P = 0.591$) was twofold more than CD patients without IBS, but this result is not significant.

Table 1: Inflammatory bowel disease patients' characteristics (n=115) and their relation with sleep quality level

Variable	Category	Sleep quality, n (%)		P
		Good (score <6)	Poor (score >6)	
Gender	Male	26 (51)	25 (49)	0.311
	Female	34 (60.7)	22 (39.3)	
Marital status	Married	49 (55.1)	40 (44.9)	0.774
	Single	10 (58.8)	7 (41.2)	
Job	Government job	7 (35)	13 (65)	0.145
	Private job	10 (66.7)	5 (33.3)	
	House wife	26 (65)	14 (35)	
	Retired and other	10 (62.5)	6 (37.5)	
	Self-employed	7 (43.8)	9 (56.2)	
Educational level	Under diploma	23 (71.9)	9 (28.1)	0.068
	Diploma and upper	19 (61.3)	12 (38.7)	
	University and upper	16 (44.4)	20 (55.6)	
EIM	No	27 (50.9)	26 (49.1)	0.289
	Yes	33 (61.1)	21 (38.9)	
Disease extent	Distal colitis	33 (68.8)	15 (31.2)	0.042*
	Left side colitis	11 (39.3)	17 (60.7)	
	Pancolitis	15 (60)	10 (40)	
Treatment type	ASA	40 (50.6)	39 (49.4)	0.294
	Corton	3 (75)	1 (25)	
	AZA	7 (58.3)	5 (41.7)	
	Renicet	3 (100)	0 (0)	

*Significant at level of 0.05. EIM=Extra-intestinal manifestations, ASA: Acetylsalicylic acid, AZA: Azathioprine

Table 2: Comparison of sleep quality and Inflammatory bowel disease patients' quality of life, SF-36 among four groups

Variable	Level	Disease groups				P
		UC + IBS	CD + IBS	UC	CD	
Sleep quality	Poor, n (%)	10 (37)	7 (87.5)	14 (26.4)	16 (84.2)	0.0001*
	Good, n (%)	17 (63)	1 (12.5)	39 (73.6)	3 (15.8)	
IBDQ	-	62.6±17.2	54.4±11.2	78.5±15.5	72.4±9.9	0.0001*
Mean±SD						
SF-36	-	42.9±10.2	41.8±7.2	46.1±10.4	44.57±9.08	0.395
Mean±SD						

*Significant at level of 0.05. SD=Standard deviation, IBS=Irritable bowel syndrome, UC=Ulcerative colitis, CD=Crohn's disease

Table 3: Predicting effect of factors affected the sleep quality level (poor vs. good) of inflammatory bowel disease patients with irritable bowel syndrome using logistic regression

Variable	Coefficient (β)	SE	P	OR	CI 95% for OR
Disease groups			0.011*		
UC + IBS	-4.024	1.356	0.003*	0.018	0.001-0.255
CD + IBS	0.787	1.465	0.591	2.198	0.193-25.02
UC	-4.126	1.305	0.002*	0.016	0.001-0.208
CD (colitis)	Ref [#]	-	-	-	-
IBD quality of life	-0.114	0.041	0.048*	0.892	0.823-0.967
Disease extension			0.035*		
Distal colitis	1.752	1.104	0.113	5.763	0.662-50.16
Left side colitis	-2.75	1.140	0.016*	0.064	0.023-0.193
Pancolitis	Ref [#]	-	-	-	-

[#]Reference group, *significant at level of 0.05. SE=Standard error, IBS=Irritable bowel syndrome, CI=Confidence interval, UC=Ulcerative colitis, CD=Crohn's disease, OR=Odds ratio

In another result obtained from the logistic regression, poor sleep quality in patients with left side colitis was about 93% less than those with pancolitis (OR = 0.064, P = 0.016). Besides, the quality of life of IBD patients (IBDQ) with poor sleep quality was 11% less than those with good sleep quality (OR = 0.89, P = 0.048) which is statistically significant.

Discussion

In this study, we evaluated the effect of IBS on sleep quality and quality of life of IBD patients in clinical remission. Results of our study showed that UC patients with or without IBS had a better sleep quality and quality of life. Besides, patients with CD + IBS had the lowest mean quality of life as was their sleep quality. IBS itself may affect the quality of life of IBD patients without considering their sleep quality. On evaluating the relation of sleep quality to the quality of life of IBD patients with or without IBS, it can also be understood that the use of IBDQ questionnaire may be more beneficial. It can also more imply on the effect of IBS on quality of life of IBD patients and their sleep quality, especially in CD + IBS patients. Results of our study also indicated that poor sleep

quality in patients with left side colitis was less than those with pancolitis.

Recently, many studies have investigated the relation between gastrointestinal physiology and inflammation with sleep and have reported a significant correlation between them.^[2] Many studies have shown that changes in the sleep pattern can lead to leukocytosis and rise of natural killer cells with the resultant rise in inflammatory cytokine production as for example TNF-α and IL-6. It is interesting to know that the cytokines playing role in the regulation of sleep and awakens are also involved in the pathogenesis of IBD.^[6,32] Therefore, sleep disorder and IBD can result in a reinforcing loop to the extent that sleep disorder results in deterioration of IBD symptoms and IBD results in sleep disorder vice versa. Many studies have shown that patients suffering from IBD and IBS have a lower sleep quality and a higher sleep disorder as compared to the control group.^[17,33]

Results from the study conducted by Ranjbaran *et al.*^[31] showed that the sleep disorder affects patients with CD (78%) more than those with UC (48%), which is in accordance to our results and confirmed the same. Evaluation of patient's quality of life by the use of IBDQ tests showed a significant relation between the disease groups, but this result was not obtained by SF-36 tests. Many studies have shown that IBD and IBS reduce the HRQOL to a considerable extent in these patients.^[34-36] Results of this study showed that similar to many other studies,^[34,37] there is no prominent difference in the quality of life between patients with CD or UC. Present study showed that the mean quality of life (IBDQ) in patients with IBD + IBS is lower than that of patients without IBS as compared with CD patients. In accordance to our results, study by Blagden *et al.*^[38] showed that quality of life of patients suffering from IBS is remarkably lower than that of patients with IBD. In the other words, IBS affects the quality of life through social and emotional aspects of patients more than the IBD does. With respect to these explanations, it can be inferred that in evaluating the relation of sleep with quality of life of IBD patients with IBS, the use of IBDQ questionnaire can be more beneficial as implied the role of IBS on the quality of life and sleep quality of such patients, especially in patients with CD.

Also, different results regarding the relation between the sleep disorders of IBD with its activity state have been reported. Ranjbaran *et al.*^[31] in their study found that the level of sleep disorder has no significant relation with disease activity. Many other studies have shown that the sleep disorder in patients with CD has a significant relation with the disease activity and had no relation with inactive disease.^[39] In the present study, only factors of the disease groups, disease extent and quality of life, have significantly affected sleep quality.

Conclusions

It can finally be concluded that the syndrome of IBS affects the sleep quality of IBD patients in clinical remission, especially in CD patients. Besides, IBS can also affect the relation between the sleep quality and the quality of life of IBD patients. Therefore, as the role of sleep disturbance in worsening of IBS symptoms (both intestinal and nonintestinal once) including pain, mood, and poorer IBS-related QOL is definite, its additive effect with IBD may worsen disease status, psychological and physical condition.

As the entities like sleep and quality of life may be affected by many factors, therefore perhaps further variables in order to evaluate the quality of life and quality of sleep in these patients (as, e.g., the measurement of cytokines, molecular details, and psychological assessment of patients) may be needed, which are the limitations of our study that are recommended to be considered as much as possible in future studies.

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Conflicts of interest

There are no conflicts of interest.

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