



Nonadherence to Medication in Inflammatory Bowel Disease: Rate and Reasons

Mohammad Reza Ghadir¹, Mohammad Bagheri², Homayoon Vahedi^{3*}, Nasser Ebrahimi Daryani⁴, Reza Malekzadeh⁴, Ahmad Hormati⁵, Shadi Kolahdoozan⁶, Meghedi Chaharmahali⁶

1. Associate Professor, Qom Gastroenterology and Hepatology Research Center, Shahid Beheshti Hospital, Qom University of Medical Sciences, Qom, Iran
2. Assistant Professor, Digestive disease Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
3. Associate Professor, Digestive disease Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
4. Professor, Digestive disease Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
5. Assistant Professor, Qom Gastroenterology and Hepatology Research Center, Shahid Beheshti Hospital, Qom University of Medical Sciences, Qom, Iran
6. Researcher, Digestive disease Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

* Corresponding Author:

Homayoon Vahedi, MD
Digestive disease Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
Telefax: +98 21 82415400
Email: vahedi@ams.ac.ir
Received: 08 Oct. 2015
Accepted: 01 Feb. 2016

ABSTRACT

BACKGROUND

This study is the first study to evaluate the nonadherence rate and reasons of same patient with inflammatory bowel disease (IBD) in Iran.

METHODS

During 9 months, 500 patients with IBD were enrolled in the study. Patients were interviewed about their nonadherence behaviors. Factor analysis was used to analyze the collected answers.

RESULTS

The overall rate of nonadherence was 33.3% (27.6% intentional nonadherence and 5.7% unintentional nonadherence). 33.6% of the patients had at least one relapse after discontinuing treatment. The most frequent reason for intentional nonadherence was discontinuing the treatment after recovering from symptoms (42.7%). The most frequent reason for unintentional nonadherence was forgetfulness (5.2%). 19.8% of the patients did not visit their gastroenterologist on time and they purchased drugs from the drugstore. These patients reported that their clinics were too far and difficult to access. There was no significant relationship between nonadherence and demographic variables.

CONCLUSION

Multiple reasons are suggested as factors of medication nonadherence and they seem to be different among different populations. Determining these possible reasons, could lead to finding suitable strategies to overcome or reduce them.

KEYWORDS

Ulcerative colitis, Crohn's disease, Nonadherence, Medication, Treatment

Please cite this paper as:

Ghadir MR, Bagheri M, Vahedi H, Ebrahimi Daryani N, Malekzadeh R, Hormati A, Kolahdoozan S, Chaharmahali M. Nonadherence to Medication in Inflammatory Bowel Disease: Rate and Reasons. *Middle East J Dig Dis* 2016;8:116-121. DOI :10.15171/mejdd.2016.16

INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic idiopathic inflammatory gastrointestinal disease, including ulcerative colitis (UC), Crohn's disease (CD) and indeterminate. The pathogenesis of IBD is not well understood and there is no certain cure yet.^{1,2}

The overall worldwide incidence rates of IBD vary from 0.5 to 24.5 per 100000 person-years. IBD is becoming a major health problem in Iran. The incidence of IBD is not known in Iran, however, an increasing trend in the incidence rate of IBD has been observed in recent years which are similar to

results from studies in other developing Asian countries such as China and India.³⁻⁵

Patients with IBD need life-long medical treatments and gastrointestinal specialist's observation. The disease is manifested as intermittent remissions and unpredictable relapse. Patients may experience many symptoms during relapses including diarrhea, constipation, bleeding, abdominal cramps, abdominal pain, vomiting, etc. They may be either asymptomatic or demonstrate less severe symptoms in their relapses. The treatment strategy is based on either controlling the symptoms in relapses or maintenance treatment in remissions.^{6,7}

Adherence to medication in IBD is correlated with better outcomes.⁸ Adherence is the cooperation of the patients in taking prescribed drugs, which includes timing, dosage and frequency.^{3,9} Nonadherence to medication can be defined as failure by patients to follow any of their medication recommendations.⁷ It is classified into two groups: unintentional and intentional. Multiple factors have been suggested to contribute to nonadherence in IBD including age, single status or not being in a relationship, full time employment, male sex, new patient status, duration of disease, multiple medications, 3 times or more daily dosing, and depression.^{3,10-14}

In addition to long-term medical treatment, patients with IBD have to use several types of drugs in alternative dosages. This kind of medical regimen influences the patients normal life and significantly affects their life quality.^{6,13} It could also negatively influence the patients adherence as a result of which morbidity is increased due to more systemic relapses and risk of colorectal cancer (CRC). The risk of CRC in patients with IBD is significantly increased by nonadherence.⁶

Medical treatments decrease the relapses but patients nonadherence has a negative influence in this regard. Medication nonadherence in the field of IBD is highly prevalent and affects 40-60% of the patients.^{6,11}

IBD is more common in young-age groups who are the economically productive group of the society. As the treatment period is long and needs a lot of time and costs a lot of money which in turn negatively affects the economy of the society, it seems that one of the effective strategies is to recognize the probable reasons of non-adherence in patients with IBD in order to implement appropriate interventions to decrease their rate of non-

adherence.^{6,12} We aimed to investigate the nonadherence to treatment in patients with IBD and identify the most common related factors.

MATERIALS AND METHODS

The study was conducted during October 2010 to July 2011 in the Digestive Disease Research Center (DDRC) affiliated to Tehran University of Medical Sciences. Five hundred patients (150 with CD, 341 with UC, and 9 indeterminate) were recruited from four major gastrointestinal clinics consecutively.

Patient with disease duration less than 4 months, incompatible patients and those who were unable to fill the questionnaire even with the help of interviewers were excluded from the study.

We explained the aim of the study to the participants and insured them that their responses will have no influence on their treatment process. The interviews were performed by trained staff.

Demographic data, clinical information including: type of disease, duration of disease, duration of treatment, current activity (Modified Truelove and Witt's criteria in ulcerative colitis, Crohn's disease activity index), drugs, dosage and the schedules of current treatment were collected from both the patients and their medical records.^{15,16} Patients were interviewed after their visit according to the questionnaire.

Nonadherence was defined in two ways: if the patients stopped or used their drugs less for any reason without their physician's advice or not using drugs according to their physicians direction properly.

A written informed consent was obtained. The study was approved by the Ethics committee of Shariati Hospital, Tehran, Iran. The results were analyzed using SPSS software, version 19. $P < 0.05$ was considered statistically significant. Confidence intervals were set at 95%.

RESULTS

Five hundred patients were included in the study. Demographic and clinical characteristics of the study population are shown in tables 1 and 2, respectively.

The overall rate of nonadherence was 33.3%, 27.6% of which was intentional nonadherence. The most frequent reason for intentional nonadherence was the pa-

Table 1: Demographic characteristics of the patients in study (N=500)

Gender	N (%)
Male	225(45%)
Female	275(55%)
Age mean(range)	36.2(18-78)
Marital status	
Single	136(27.2%)
Married	349(69.8%)
Divorced	6(1.2)
Widow/widower	9(1.8%)
Education	
Illiterate	16(3.2)
<12 years	69(13.8%)
>12 years	198(39.6%)
License	181(36.2%)
Upper	52(10.4%)
Occupation	
Employed, student, collegian	307(61.4%)
Unemployed	193(38.6%)
Smoking	
Smoker	62(12.4%)
Non-smoker	407(81.4%)
Quitted	31(6.2%)

tients' decision to stop taking their drugs when they recovered from symptoms (42.7%). The most frequent reasons are presented in table 3.

The unintentional nonadherence rate was reported to be 5.7%, for which the most frequent reason was forgetfulness (5.4%). From all patients who discontinued their treatment intentionally or unintentionally, 33.6% had an experience of relapse after discontinuing treatment.

We asked patients to evaluate the efficacy of their medical treatment. 54.3% of the patients believed that the medical treatment was absolutely effective. Also, 35.5% of them stated that it had medium efficacy, 7.4% said the efficacy of treatment was low and 2.8% declared the treatment was totally ineffective.

16.1% of the patients stated that they had complete and comprehensive information about their disease and medical therapy, 46.8% said they had adequate information with basic details, 31.4% said they had a little information and 5.7% said they had no information.

Moreover, 30.6% of the patients stated that they were more comfortable if they took their medicines once daily,

Table 2: Clinical characteristics of the patients in the study (N=500)

Type of disease	N (%)
Crohn's disease	150(30.0%)
Ulcerative colitis	341(68.2%)
Indeterminate	9(1.8%)
Duration of disease(mean)	7.67 years
Min	6 months
Max	40 years
Duration of treatment(mean)	6.65years
Min	7 months
Max	38 years
Ulcerative colitis	
Activity	
Mild	131(38.5%)
Moderate	176(51.6%)
Sever	34(10.0%)
Extention	
Proctitis	38(11.1%)
Left side	182(53.4%)
Extensive	69(20.2%)
Pancolitis	52(15.3%)
Crohn's disease	
Activity	
Remission	67(44.6%)
Chronically active	58(38.6%)
Flare-up	24(16.8%)

24% said they were comfortable with taking drugs twice daily, 42.8% said they preferred to use their medicines three times daily, and 2.4% of said it did not differ for them.

With respect to re-visiting the clinics on time, we found that 19.6% of the patients did not do it and they preferred to refill their pervious prescribed drugs from drugstore. The most frequent reason of not visiting was the clinics' distance for them. The other reasons are displayed in table 4.

The patients were asked if the drug schedule was important for them. 87.2% of the patients stated they follow the drug schedule as per the physician's order, while 12.8% stated that the schedule was not important for them.

We compared demographic and clinical variables with nonadherence, but no significant relationship was found.

Table 3: Reasons of Nonadherence to the treatment (N=138)*

I stopped my treatment when my symptoms were collapsed	59**	42.7%
I am tired of eating too many drugs	51	36.9%
I feel that the treatments have no effect on my recovery	27	19.5%
I can't tolerate the side effects of drugs	18	13.0%
I can't tolerate the rectal drugs	7	5%
I can't tolerate the rectal drugs	11	8%
The cost of treatment is a lot, I can not afford it	17	12.3%
There is not a near drugstore to where I live	8	5.7%
Other reasons	6	4.3%

* Patients who reported nonadherence in treatment.

** Some patients have more than one reason for Nonadherence

Table 4: Reasons of not resourcing to clinic on time (N=98)*

Accessing a clinic is not easy for me	54**	10.8%
I am tired of remissions and relapses of my disease.	28	5.6%
Visiting doctor costs me a lot	23	4.6%
I feel visiting my doctor is not effective for my recovery.	16	3.2%
Other reasons	8	1.6%

* Patients who didn't revisit clinics on time.

** Some patients have more than one reason for Nonadherence

DISCUSSION

Although there are many studies about nonadherence in developed and developing countries, to the best of our knowledge there is still no data from Iran. This study is the first study to evaluate the rate and the reasons of nonadherence in a group of Iranians.

There is a considerable risk of nonadherence to treatment in chronic disorders including IBD.^{9,19-21} We should be more concerned not only about the accurate diagnosis but also about the patients adherence to medication because adherence is as important as correct diagnosis and appropriate therapy. We should be careful about how the treatment process proceeds because it influences the patients' normal life. In addition, drug side effects can complicate the course of treatment.⁹

The studies which have been done on medication nonadherence in patients with IBD have increased in recent years. These studies suggested that several factors could be associated with nonadherence.^{11,22}

The rate of nonadherence varies and it could be one of the most important reasons of treatment ineffectiveness. As the nonadherence is divided into intentional and unintentional, we aimed to study both.

The nonadherence rate in this study is in the same range as reported by other community-based studies. For example in a study in Europe the overall nonadherence rate was 29%. However, our rate varies considerably between countries such as France (13%), UK (33%), Germany (46%), and Italy (26%). In this study intentional nonadherence was more frequent than unintentional as in other studies.^{11,23}

The most important reasons of intentional and unintentional nonadherence in our study were forgetfulness and discontinuing treatment after recovery, respectively; which is similar to the results of some other studies.^{7,10}

Patients' beliefs about the effectiveness of treatment could highly affect adherence to treatment. Patients who emphasis on the effectiveness of treatment are less at risk of nonadherence.¹⁰

One of the reasons of nonadherence reported by some studies was patients' lack of useful and sufficient information about the nature of their disease and types of treatments. In an open questionnaire study, nonadherence was higher in patients who had not been informed adequately about prescribed drugs. It is shown that better information about treatment leads to better adherence.^{6,10}

Since one of the reasons that patients deprived themselves from appropriate and timely treatment is not visiting their physicians on time, some studies have tried to find the reasons.²⁴⁻²⁶ We found that the most frequent reason of delayed visit was the inaccessibility of advanced medical clinics, especially in rural areas and small towns in Iran.

Variables including sex, marital status, education, smoking, full time employment, being a new patient, prolonged and chronic disease and low disease activity are suggested as the predictors of nonadherence in some studies.¹² But we did not find any relationship between mentioned variables and nonadherence.

The large sample size of our study is one its main strengths. Since Iran is geographically a wide country with different types of cultures; therefore our sample size could be a small representative of the Iranian society because it is collected from clinics which accept patients from all parts of the capital as well as other cities.

Informing the patients appropriately about medications, having better connection with them, avoiding prescriptions that need to be followed several times daily, considering and explaining complications of drugs to patients are among the factors that could reduce the rate of nonadherence.^{7,9}

Other factors including unavailability of drugstores and advanced clinics in small cities and villages are not related to the patients and physicians. Therefore, there is a need for more investments in infrastructures and policies. It is clear that implementing a strategy to improve medication adherence in patients with IBD will have a greater effect on both the individual's health and the health economy of the society than the improvements in medical therapies per se.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

REFERENCES

1. Lu Y, Markowitz J. Inflammatory bowel disease in adolescents: what problems does it pose? *World J Gastroenterol* 2011;**17**:2691-5.
2. Jackson CA, Clatworthy J, Robinson A, et al. Factors associated with non-adherence to oral medication for inflammatory bowel disease: a systematic review. *Am J Gastroenterol* 2010; **105**:525-39. doi:10.1038/ajg.2009.685
3. Lakatos PL. Prevalence, predictors, and clinical consequences of medical adherence in IBD: how to improve it? *World J Gastroenterol* 2009;**15**:4234-9. doi: 10.3748/wjg.15.4234
4. Leong RW, Kamm MA, Hu PJ, Sung JJ; Asia Pacific Inflammatory Bowel Disease Working Party. Inflammatory bowel disease in Asia. *J Gastroenterol Hepatol* 2010;**25**:436-8. doi: 10.1111/j.1440-1746.2010.06256.x.
5. Vahedi H, Merat S, Momtahan S, Olfati G, Kazzazi AS, Tabrizian T, et al. Epidemiologic characteristics of 500 patients with inflammatory bowel disease in Iran studied from 2004 through 2007. *Arch Iran Med* 2009;**12**:454-60.
6. Kane SV. Systematic review: adherence issues in the treatment of ulcerative colitis. *Aliment Pharmacol Ther* 2006; **23**:577-85. doi: 10.1111/j.1365-2036.2006.02809.x
7. Robinson A. Review article: improving adherence to medication in patients with inflammatory bowel disease. *Aliment Pharmacol Ther* 2008;**27** Suppl 1:9-14. doi:10.1111/j.1365-2036.2008.03604.x
8. Trindade AJ, Morisky DE, Ehrlich AC, Tinsley A, Ullman TA. Current practice and perception of screening for medication adherence in inflammatory bowel disease. *J Clin Gastroenterol* 2011;**45**:878-82. doi:10.1097/MCG.0b013e3182192207.
9. López San Román A, Bermejo F, Carrera E, Pérez-Abad M, Boixeda D. Adherence to treatment in inflammatory bowel disease. *Rev Esp Enferm Dig* 2005;**97**:249-57.
10. Horne R, Parham R, Driscoll R, Robinson A. Patients' attitudes to medicines and adherence to maintenance treatment in inflammatory bowel disease. *Inflamm Bowel Dis* 2009;**15**:837-44. doi: 10.1002/ibd.20846.
11. Červený P, Bortlík M, Kuběna A, Vlček J, Lakatos PL, Lukáš M. Nonadherence in inflammatory bowel disease: results of factor analysis. *Inflamm Bowel Dis* 2007;**13**:1244-9. doi: 10.1002/ibd.20189
12. Hawthorne AB, Rubin G, Ghosh S. Review article: medication non-adherence in ulcerative colitis--strategies to improve adherence with mesalazine and other maintenance therapies. *Aliment Pharmacol Ther* 2008;**27**:1157-66. doi: 10.1111/j.1365-2036.2008.03698.x.
13. Kane S, Shaya F. Medication non-adherence is associated with increased medical health care costs. *Dig Dis Sci* 2008;**53**:1020-4.
14. Greenley RN, Stephens M, Doughty A, Raboin T, Kugathasan S. Barriers to adherence among adolescents with inflammatory bowel disease. *Inflamm Bowel Dis* 2010; **16**:36-41. doi: 10.1002/ibd.20988.
15. Truelove SC, Witts LJ. Cortisone in ulcerative colitis: final report on a therapeutic trial. *Br Med J* 1955;**2**:1041-8. doi: 10.1136/bmj.2.4947.1041
16. Walters TD, Steinhart AH, Bernstein CN, Tremaine W, McKenzie M, Wolff BG, et al. Validating Crohn's disease activity indices for use in assessing postoperative recurrence. *Inflamm Bowel Dis* 2011;**17**:1547-56. doi: 10.1002/ibd.21524.

17. Kane S, Shaya F. Medication non-adherence is associated with increased medical health care costs. *Dig Dis Sci* 2008;**53**:1020-4.
18. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care* 2004;**42**:200-9.
19. Naidoo P, Dick J, Cooper D. Exploring tuberculosis patients' adherence to treatment regimens and prevention programs at a public health site. *Qual Health Res* 2009;**19**:55-70. doi: 10.1177/1049732308327893
20. Billimek J, Sorkin DH. Self-reported Neighborhood Safety and Nonadherence to Treatment Regimens Among Patients with Type 2 Diabetes. *J Gen Intern Med* 2012;**27**:292-6. doi: 10.1007/s11606-011-1882-7.
21. Ediger JP, Walker JR, Graff L, Lix L, Clara I, Rawsthorne P, et al. Predictors of medication adherence in inflammatory bowel disease. *Am J Gastroenterol* 2007;**102**:1417-26. doi:10.1111/j.1572-0241.2007.01212.x
22. Kane S, Huo D, Aikens J, Hanauer S. Medication nonadherence and the outcomes of patients with quiescent ulcerative colitis. *Am J Med* 2003;**114**:39-43. doi: 10.1016/S0002-9343(02)01383-9
23. Rabinson A. Patients-reported compliance with 5-ASA drugs in inflammatory bowel disease:a multi-national study. *Gastroenterology* 2002;**122**:A-499.
24. Westwood N, Travis SP. Review article: what do patients with inflammatory bowel disease want for their clinical management? *Aliment Pharmacol Ther* 2008;**27** Suppl 1:1-8. doi: 10.1111/j.1365-2036.2008.03605.x.
25. Bosworth HB, Granger BB, Mendys P, Brindis R, Burkholder R, Czajkowski SM, et al. Medication adherence: a call for action. *Am Heart J* 2011;**162**:412-24. doi: 10.1016/j.ahj.2011.06.007
26. Russell CL, Ruppar TM, Matteson M. Improving medication adherence: moving from intention and motivation to a personal systems approach. *Nurs Clin North Am* 2011;**46**:271-81, v. doi: 10.1016/j.cnur.2011.05.004