IBD REVIEWS REVIEW ARTICLE

Adherence to Treatment in Inflammatory Bowel Disease

Guillermo Veitia* and Beatriz Pernalete

Gastroenterology Unit, Hospital Militar de Caracas, Caracas, Venezuela

Abstract

Today one of the most important aspects of the management of patients with inflammatory bowel disease (IBD) is strict compliance with the advice they are given in order to improve disease activity, which in turn will lead to better quality of life.

Nonadherence to medication is associated with higher levels of disease activity, greater use of health services, and reduced quality of life[1].

Treatment goals in ulcerative colitis (UC) and Crohn's disease (CD) have changed in recent years due to increases in knowledge about these complex and heterogeneous diseases, which has led to concepts such as inverted pyramid, early accelerated and/or combination therapy, mucosal healing, and deep remission.

Although many patients may be satisfied with the healthcare services because of the impact on their quality of life, including personal and professional relationships, it is necessary to improve the speed of diagnosis and communication between patients and healthcare providers[2].

A new goal-oriented treatment approach is needed, with increased monitoring and stricter control of symptoms and inflammation. To reach these goals it is extremely important for every doctor's office, hospital, and multidisciplinary team working in IBD to understand and stress to the patients and their families the importance of adhering to treatment so that they are fully aware of the direct relationship between treatment and the improvement that it seeks to achieve. Adherence to treatment is important for it to succeed. (IBD Rev. 2016;2:22-9)

Corresponding author: *Guillermo Veitia, gveitia@gmail.com*

Key words: *Adherence. Ulcerative colitis. Crohn's disease. Inflammatory bowel disease.*

What is adherence to treatment?

This term may be defined as the active and informed participation of patients in decisions about treatment, which in turn has the immediate effect of ensuring that compliance with the prescribed treatment regimen will be optimal[3,4]. We use this definition to refer to the patient's degree of compliance with the medication regimen that has been prescribed by the specialist.

Good adherence to treatment requires the commitment of the patient and entails the patient receiving all of the medications at the proper doses and at the right time, which means

Corresponding author:
*Guillermo Veitia
E-mail: gveitia@gmail.com

Received for publication: 11-04-2016
Accepted for publication: 10-04-2016

that all of the instructions for their administration should be very clear.

Adherence also means strict compliance with any advice or recommendations given by the physician or health providers with regard to diet, personal care, and giving up of certain habits (smoking, drinking alcohol, etc.) in order to improve the health of the patient.

The concept of adherence involves both the patient and the physician, who must work together to achieve a common goal. It is also important to understand that the term "adherence" does not refer exclusively to the patient and the attending physician, but also includes in its definition all of the persons involved in the care of the patient, such as the nursing staff who are now more and more involved in the management of patients with IBD.

What factors have an influence on adherence?

Nonadherence is multidimensional and is influenced by several factors that are important to understand. It has been shown that there is a direct relationship between compliance with treatment, its efficacy, and the course of the disease. It is therefore necessary for patients to be made aware of the relevance of their treatment, for them to know the medications that have been prescribed, and to commit to taking them.

In some cases poor adherence is involuntary because of forgetting to take a dose or because they have misunderstood the instructions they have been given. In other cases it is voluntary when it is related to the absence of confidence in the effectiveness of the drug or a fear of the side effects that it may cause. It is therefore necessary to remind the patients that they should tell their doctor about any decision regarding the treatment, as communication and expressing doubts and fears are essential for making the best decisions.

In chronic diseases, adherence to treatment and medical advice is low. Different studies have concluded that between 50 and 70% of patients do not follow their physician's treatment plan as prescribed. In a Spanish study of a sample of 107 patients with IBD, 63% of whom had CD, it was reported that 66% (2 of 3) said they forgot to take a dose involuntarily, and as many as 27% acknowledged being somewhat careless at times about taking their medication. Voluntary nonadherence was only acknowledged by 16% of those surveyed[5].

Adherence to long-term treatment for chronic illnesses in developed countries averages 50% and is even lower in developing countries[6].

Another factor that has a significant effect on adherence is the support of family, friends, or caregivers. To be surrounded by people who are reliable ensures that someone will remind the patient when to take the medication.

Likewise, leading a life with irregular meal and sleep schedules may have a negative impact on adherence: adopting a routine will help to avoid the forgetfulness that affects compliance[7].

Noncompliance can be related to loss of treatment efficacy or early relapse, so it is necessary to understand the subjective factors that will affect the patient's adherence to the medication.

A case-control study of triggers of factors that trigger IBD flares evaluated the use of nonsteroidal anti-inflammatory drugs (NSAID), antibiotics, stressful events, smoking, medication adherence, infections and travel in the preceding three months and concluded that only nonadherence to medication was significantly associated with disease flares[8].

It is known that noncompliance with treatment is related to a decrease in the efficacy of the medication, poor control of the disease, greater susceptibility to complications, and higher economic costs. It is therefore obvious that optimizing compliance with treatment will lead to patients having fewer symptoms, feeling better, presenting with fewer complications, and not requiring either more medications or surgery because of inadequate control of the disease.

The physician and the patient must share the decision on the treatment plan, which means

that a patient's beliefs about the treatment of chronic diseases play a decisive role when it comes to compliance with the therapeutic regimen that is established, and therefore that they will have an influence on its effectiveness, outcome, and the costs associated with the disease.

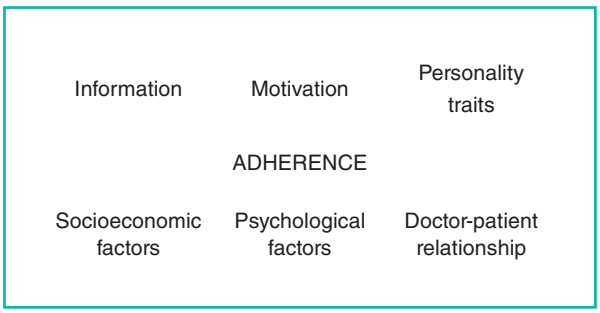

Figure 1. Importance of information to achieve a greater adherence.

Informed patients, greater adherence to treatment

Patients should be provided with the best advice and information available about their disease and everything related to it because at times they may have false beliefs and fears (psychological aspects) that can be solved by consulting the specialist, which is why the doctor-patient relationship is so important (Fig. 1).

When patients do not have the necessary information about their disease and treatments, their mechanisms of action, side effects, and the consequences of not complying properly with treatment, adherence decreases.

It is important to have proper knowledge, in line with medical recommendations that are based on clinical evidence, to provide patients with the best care[9].

Better compliance has been reported when patients are convinced of the need to take their medication and have fewer concerns about it. In addition, belonging to an IBD patient association is associated with greater adherence[10].

A recently published study reports that limited knowledge of the prescribed medication, being under 30 years of age, and monitoring visits at intervals of more than three months were associated with lower adherence to medication and a higher rate of relapse[11].

Good communication between doctor and patient is the cornerstone of effective management of the disease. After a diagnosis of IBD, people are likely to feel great uncertainty about their future. They may be worried about the effects the disease and its treatment will have on their day-to-day lives, their ability to work, their ability to have children, and the eventual need for hospitalization and surgery. By proactively discussing these issues with patients who have been newly diagnosed, doctors can begin to build a relationship of trust that will be open and long lasting[12].

Clear communication with regard to the risk/benefit relationship of other treatment strategies and alternative therapeutic options is essential to every doctor/patient relationship. That said, the physician must keep in mind the treatment goals that are important for the patient and, therefore, understand that the perspective from which the patient assesses the risk/benefit trade-offs may differ from his own (Table 1).

To help the integration of these two perspectives, the physician must clearly communicate the rationale for a long-term treatment plan. The consequences of progression of the disease is an important element in the discussion about risks and may be discussed along with other subjects such as steroid dependence, frequent or unusual adverse events associated with specific treatments and the complications of surgery. The potential risks of "undertreatment" (development of complications, need for surgery and nutritional problems) must be balanced carefully with those of "overtreatment" (potential impact on quality of life of toxicities associated with anti-TNF drugs)[13,14].

Proper information that is open about potential medication-induced toxicity is crucial to building a relationship of trust, so as to prevent patients from using the Internet or anecdotal evidence from other patients as the only source of reference. This may form part of a broader

Table 1. Management of Crohn's Disease: Priorities of physicians and patients

Physicians (longer-term perspectives)
Avoid surgery (use only as last resort)
Induce rapid remission with acceptable side effects
Modify the natural history of the disease (avoid complications)
Avoid steroid toxicity
Patients (short-term perspectives)
Minimize symptoms as much as possible
Minimize side effects of medication as much as possible
Have the opportunity to discuss anxieties with physician
Have the opportunity to address related issues (fatigue, sexuality, esthetic changes, fertility, uncertainty)

Source: What do changes in inflammatory bowel disease management mean for our patients? J Crohn's Colitis 2012;6:S243-9.

conversation that includes health education on important aspects of the treatments (Table 2)[15,16].

One of the main concerns is the risk of infection, which can be reduced to the minimum by having detailed discussions with the patients to determine whether they have any history of infection, risk of latent or active tuberculosis, their vaccination status against hepatitis B, travel history and future travel plans, and appropriate vaccination. It is also important to talk with the patients about the need to consult with their doctor and postpone anti-TNF medication if they have any fever or symptoms and signs of infection develop.

There are other aspects of IBD and its treatment that should also be discussed. Fatigue, esthetic concerns, sexual problems, and complications, such as metabolic bone disease, are frequent in patients, but are often not spoken about[17,18].

Improving communication to motivate patients

Motivational communication is a technique to improve dialogue and cooperation between healthcare providers and patients. It uses a patient-centered approach to identify the thoughts and behaviors that may interfere with optimal management of the disease (Table 2)[19]. The ultimate goal is to involve and motivate the patients so they become partners in their own healthcare in order to achieve better adherence to treatment and an optimal response[20].

Table 2. Main differences between conventional and motivational communication

Conventional	Motivational
Argues that the patient has a problem and needs to change	Seeks to understand the patient's frame of reference, particularly through reflective listening
Offers direct advice or prescribes solutions to the problem without the patient's permission or without actively encouraging the patient to make his/her own choices	Expresses acceptance and affirmation
Uses an authoritative/expert stance, leaving the patient in a passive role	Elicits and selectively reinforces the patient's own self-motivational statements, expressions of problem recognition, concerns, desire and intention to change, and ability to change
Does most of the talking, or functions as a unidirectional information-delivery system	Monitors the patient's degree of readiness to change, and ensures that resistance is not generated by jumping ahead of the patient
Imposes a diagnostic label	Affirms the patient's freedom of choice and self-direction

Adapted with permission from Ghosh, et al.[11].

In the conversation about the risk/benefit relationship, this approach may be useful in addressing the concerns and expectations of the patients with regard to a given treatment or proposed management strategy, allowing appropriate decisions to be made. Some patients with IBD show resistance to taking an intensive approach to management of the disease and the establishment of treatment with biological agents (anti-TNF drugs) despite having severe symptoms and/or a high risk of disease progression. The trans-theoretical model of behavior change has been well validated and has been used in a number of diseases[21,22] to promote behavior change as a progressive process, undertaken in a series of voluntary steps. It examines how patients make decisions over time and provides a useful framework for helping patients identify and approach their ambivalence about change in their maladaptive way of thinking or behaving (Fig. 2). The gastroenterologist can help patients in the "pre-contemplation stage" (when they are not yet ready to change), by building trust and encouraging an open dialogue about any doubts they may have. In the contemplation stage (preparing for change), the patients experience mixed feelings associated with a growing understanding of the risks and complications associated with the disease, and this is where the doctor can be useful in helping to "tip the balance in the decision-making process", by encouraging a discussion on the pros and cons of specific treatments or management strategies, while emphasizing the patients' responsibility and choice.

The patients' resistance to change can take the form of arguing, interrupting, denying, or ignoring communications with the medical team[23]. Doctors who practice motivational communication avoid answering back, but instead respond without resistance, repeating the patient's statement in a neutral form. In this way they acknowledge what the patient has said and a different response may be elicited. It is also important to instill a sense of self-efficacy in patients after having made them feel

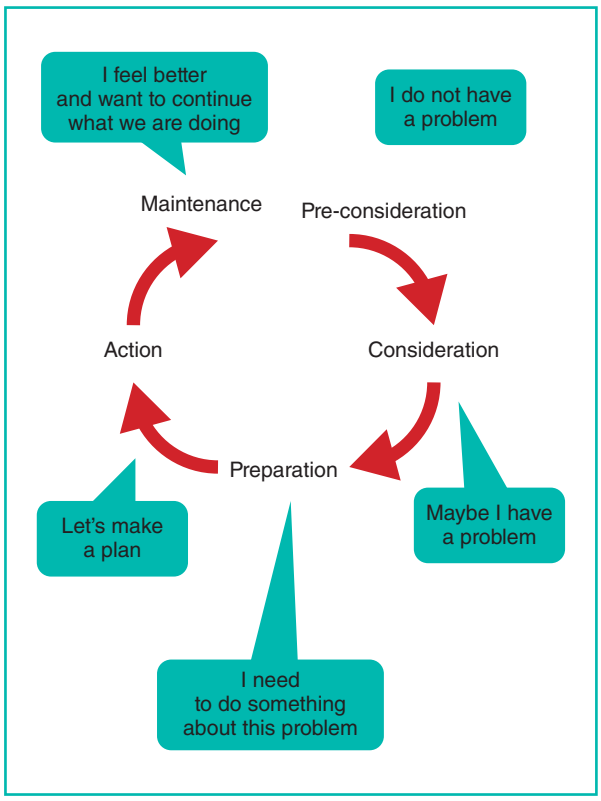

Figure 2. Stages of change in health behavior *(adapted with permission from Ghosh, et al.[11])*.

"empowered" to take charge of their health, as it is known that belief in the possibility of change is an important motivator. For example, to create a positive expectancy in a patient with CD who wishes to quit smoking, the doctor can point out that if they have already succeeded in cutting down, they have already shown they have the ability to advance towards the goal of complete abstinence. This type of positive reinforcement may be useful for triggering other desirable health behaviors. Motivational communication is intended to help patients describe the discrepancies between their life with active disease and their life with the disease in remission (Fig. 2).

Role of the multidisciplinary team in inflammatory bowel disease

Management of patients with IBD is a team effort: gastroenterologists, psychologists, surgeons,

dermatologists, rheumatologists, radiologists, pathologists, nutritionists, and nurses, who all play an important role in building the trust relationship. The IBD treatment centers can do a lot to facilitate effective communication between the patients and the multidisciplinary team.

People who have UC and CD need quick, flexible, and comprehensive care that will consider their physical, emotional, social, and professional needs. For this reason, many hospitals have set up IBD Comprehensive Care Units.

The role played by specialized nursing services varies considerably and the functions carried out by their staffs are very different, depending on each hospital. Keeping this in mind and with the aim of integrating all of these functions, standardize criteria, and define the role of nursing, the Grupo Enfermero de Trabajo en Enfermedad Inflamatoria Intestinal (GETEII - IBD Nurse Working Group) was set up in Spain, which is something we should emulate all over Latin America.

Providing a telephone or Internet hotline, educational leaflets and materials, sources of further information in addition to patient support groups, are just some of the ways in which accessibility and information exchange can be improved.

Specialists from the Gastroenterology Unit of the University Hospital Complex of El Ferrol (Spain) have launched www.educainflamatoria.com, a website for IBD patients that allows a multidisciplinary approach to the disease. One of the main innovations of this website is that through use of telemedicine, patients can improve their adherence to treatment.

Feedback has been very positive. The most noteworthy benefit for the patients who use educainflamatoria.com is the interactive tool that allows them to communicate with their doctor about their illness and its treatment. This has had a great impact on patients by increasing their knowledge of the disease, improving their levels of adherence to treatment and their quality of life.

Advice to improve compliance with treatment: Strategies to boost adherence

Here are some of the recommendations that can be found on the website[7]:

- Make sure the information regarding the treatment plan is very clear, including where the medications are listed, the time of day they have to be taken, the dosages, and how to take them.
- Simplify the process of taking your medications whenever possible. Generally speaking, it is preferable to take your medication in a single dose. This will not reduce the efficacy of the medication and increases adherence.
- Try to link the schedule for taking your medications to daily activities. Having a regular routine will help you remember when to take your medication.
- Using a daily or weekly pillbox to organize your medication will make planning easier and allow you to keep track of whether or not you have taken your medication.
- Set an alarm on your cell phone as a reminder to take your medication. A great variety of mobile apps that can facilitate adherence to treatment are now available for free, specifically tailored to patients and caregivers.

Patients are involved in the day-to-day management of their disease, actively participating by sharing their experiences or questions anytime they need to through email and social networks. Questions are answered individually by each specialist through the website forums, and if required can remain anonymous.

Using a combination of different measures to boost adherence is often the best strategy for achieving it.

If side effects occur, it is important to let your doctor know as he/she may prescribe medications to relieve them or advise you on how to handle them.

Patients should not feel bad or guilty about forgetting to take their medication. It is recommended to simply follow the advice above

and let your doctor know about it at your next visit.

How is adherence measured? The Morisky-Green questionnaire

There are at present several methods of measuring patients' adherence to treatment for their disease, which can be divided into direct and indirect methods. Direct methods are based on the measurement of levels of the drug in blood, urine, or other body fluids, although their use in clinical practice is limited because they are costly and time-consuming.

Indirect methods that are based on patient questionnaires are easy to use and affordable, allowing them to be used in routine practice.

The Morisky-Green treatment adherence questionnaire is one of the most widely used because of its simplicity. Patients need only respond "yes" or "no" to four questions about their medication taking[3,24].

This method, which has been validated for various chronic diseases, was originally developed by Morisky, Green, and Levine to assess compliance of medication taking in patients with hypertension. From the time the test was first created, it has been used to assess treatment compliance in different diseases[25,26]. It consists of four questions that allow dichotomous yes/no answers regarding the patients' behavior with respect to compliance. Patients are considered to be compliant if they respond correctly to all four questions, i.e. No/Yes/No/No; self-administered questions with true/false answers intended to evaluate adherence to treatment (Table 3).

It is important to be aware that the questionnaire should be answered in accordance with each person's behavior and should never be answered on the basis of what one thinks is the most adequate or suitable behavior. The results of the questionnaire can help assess the level of adherence a patient may have to a given treatment and, on that basis, allow for recommendations that will help improve or increase adherence to the treatment to be made, thereby improving its effectiveness or causing it to be changed.

Table 3. Morisky-Green questionnaire

1	Have you ever forgotten to take your medicine?	True	False
2	Do you take your medicine at the right times?	True	False
3	When you feel better, do you sometimes stop taking your medicine?	True	False
4	If you feel worse when you take your medicine, do you stop taking it?	True	False

Adapted with permission from López San Román, et al.[24].

In a study conducted by the Spanish National Health System[23], a urine sample was collected from patients who were taking mesalazine or one of its derivatives and analyzed for salicylates by fluorescence polarization immunoassay (FPIA). This technique has proved to be adequate for the assessment of levels of 5-aminosalicylic acid and its metabolites in urine[28].

In order to obtain information with regard to compliance by patients of the Inflammatory Bowel Disease Center of the Division of Gastroenterology of the Hospital Vargas in Caracas, a survey was conducted during February and March 2015 that used the Morisky-Green questionnaire with a few additional questions to broaden the scope of the research: a study of a total of 42 IBD patients, of whom 27 had UC and 15 had CD that was presented at the 1st Congress of the Pan American Crohn's and Colitis Organization, which took place in Guadalajara, Mexico in June 2015. According to the results of our investigation, 42.85% of patients adhered to treatment, a figure that is somewhat higher than that reported in the majority of the studies that have investigated this issue.

We must note that the results obtained give the IBD team cause for satisfaction as we see that the work performed for the last six years is bearing fruit. Since we are aware that education is fundamental to achieving

strict compliance by our patients, we have been holding meetings of the Club for IBD Patients every three months, where information about the disease and its complications is provided, in which psychologists and nutritionists also participate, and where we conduct activities such as laugh therapy, yoga, dance therapy, etc. However, we need to improve the rate of adherence considerably so, among other things, we need to step up the program for IBD patients by holding meetings on a monthly basis, maintaining permanent information available through the www.grupovenezolanoeii.org website, which is under construction and is now nearly finished, so we can respond quickly to whatever questions the patients ask without their needing to visit the doctor, as in this way we will bring the assistance and support they require closer to them.

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