Review article: improving adherence to medication in patients with inflammatory bowel disease

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SUMMARY

Background
Adherence to medications in inflammatory bowel disease is associated with a reduced risk of both relapse and colorectal cancer development in the long term. However, many patients are non-adherent to their prescribed treatment regimen.

Aim
To review and discuss the extent of medication non-adherence in inflammatory bowel disease patients, the predictors of non-adherence, and strategies for optimizing patient adherence.

Results
More than 40% of inflammatory bowel disease patients do not adhere to their medication and thus a significant number of patients are not receiving the full benefits from their treatment – that is, remission and disease maintenance. The causes of medication non-adherence are multi-factorial. Improving medication adherence in patients is an important challenge for physicians; understanding the different patient types, the reasons given by patients for non-adherence and the predictors of non-adherence will help devise suitable plans to optimize patient adherence. Approaches such as improving the physician–patient relationship, individualized therapy, providing patient information and support, self-management programmes and practical aide memoires can be beneficial.

Conclusions
Implementation of strategies to improve medication adherence in inflammatory bowel disease patients increases the likelihood of patients achieving disease remission and maintaining remission in the long term, thereby improving symptom control and quality of life.

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INTRODUCTION

In inflammatory bowel disease (IBD), which encompasses ulcerative colitis (UC) and Crohn’s disease (CD), medication adherence is associated with a reduced risk of disease relapse and colorectal cancer (CRC) development in the long term. In clinical practice, however, a large number of patients are non-adherent to their prescribed medication, and the resultant increases in hospital admissions as a result of disease ‘flare-ups’ impact negatively on the healthcare service utilization, with an overall rise in healthcare costs.

The terms ‘compliance’, ‘adherence’ and ‘concordance’ are often used synonymously, but for the purpose of this meeting-proceedings article, which was to identify strategies for improving patient adherence to medication, the terms ‘adherence’ and ‘non-adherence’ are used throughout.

Non-adherence can be applied to a number of situations, such as failure of patients to adopt preventative health behaviours, or failure to attend follow-up appointments. Non-adherence to medication can be defined as, ‘a failure by patients to undertake activities or follow treatment recommendations made by health service providers’.

PREVALENCE OF MEDICATION NON-ADHERENCE IN IBD

Clinical trials reporting efficacy and safety of treatment therapies available in the management of IBD have reported patient adherence rates of between 70% and 95%. This high rate of medication adherence is not, however, mimicked outside the clinical trial setting, as patients do not receive the same level of medical supervision. In some areas of medicine, such as hypertension and pain, rates of medication non-adherence have been reported to be approximately 50% and as high as 90%, respectively. In the field of IBD, rates of non-adherence to medication range from 41% to 60%. Furthermore, cultural differences in self-reported medication non-adherence rates in IBD have been found in a European population survey (Figure 1). Nonetheless, an overall non-adherence rate of 29% was reported in this study, where non-adherence was defined as taking <80% of prescribed medication.

Therefore, a high percentage of IBD patients are not receiving the full benefits of their medication, not achieving disease remission and not maintaining their disease. Thus, improving medication adherence in patients is a major challenge for physicians in the treatment of IBD as well as other therapeutic areas. Understanding the different types of patients in terms of their medication-taking behaviour could be the first step towards overcoming this challenge.

PATIENT TYPES

Patients can be sub-categorized into four main types according to their adherence behaviour towards prescribed medication: gamblers, teacher’s pets, rebels and distractibles. Gamblers are aware of the potential benefits of medication but often take a chance that they will come to no harm if medication is missed, akin to smokers who take a chance that they will avoid cancer. An example that clearly illustrates this is in the case of statin therapy. Despite good evidence showing that continued statin therapy over 5 years can save approximately one life in 20 patients who previously suffered a myocardial infarction, more than half of the patients stop taking their medications after about 2 years. Those patients who fall within the category of ‘teacher’s pets’ are likely to do what their physician asks them to do, whereas ‘rebels’ will do the exact opposite of what is requested. The fourth category of patients are classed as ‘distractibles’, primarily because they are often pre-occupied and forget to do the things they have been asked.

Adherence rates may be improved if we gain a greater understanding of individual patient characteristics and an insight into the drivers for non-adherence. Gamblers may be more likely to adhere to medication if their medication beliefs are strengthened in favour of efficacy and fears of side-effects are diminished. ‘Teacher’s pets’ are usually good adherers to medication, although this is the group of patients who may be more likely to report good adherence even if it is untrue, so as to avoid ‘upsetting’ the doctor.

Figure 1. Cultural differences in self-reported medication non-adherence rates.
Patterns of medication non-adherence include failing to redeem prescriptions, altering the dosing regimen and in rare circumstances, incorrect administration. Kane et al.’s study (2003) of quiescent UC patients showed that at 12 months, 19 out of 86 patients had recurrent disease, 13 (68%) of whom were non-adherent to their 5-aminosalicylic acid (5-ASA) medication. The most commonly cited reasons were self-confessed ‘forgetfulness’ by the patients (50%), ‘too many pills’ (30%), and ‘no need for so much medicine’ (20%). A multitude of other factors have been associated with medication non-adherence, including the approach/attitude of the healthcare professional, the perceptions/beliefs of patients, illness-related factors (i.e. the reduction/absence of symptoms) and the dosing regimen.3, 9, 14–16

Dosing regimens
The effect of different dosing regimens on medication adherence rates has been a contentious topic of debate in IBD. An early literature review has shown significantly better medication adherence rates with once daily and twice daily dosing (i.e. 73% and 70%, respectively) compared with three times (52%) and four times daily dosing (42%) regimens.17 However, a small, pilot, feasibility study showed no significant difference in adherence rates at 6 months between once daily and conventional twice daily and three times dosing regimens (i.e. 75% and 70%, respectively; P = 0.8) in quiescent UC patients on mesalazines.18 Medication non-adherence is multi-factorial and is, therefore, not simply a case of dosing regimens/frequencies.

Number of doctor visits
An important contributing factor to medication non-adherence is poor communication between the physician and the patient, i.e. the lack of rapport and poor quality of relationship.16 Therefore, another possible reason for non-adherence may be that patients do not see their physicians often enough to be reminded about taking their medication, especially when the patient is seemingly well during the quiescent stages of their disease.16 However, a European cohort showed no correlation between the number of times the IBD patient had seen the physician and self-reported medication adherence rates.11

Physicians make direct enquiries with their patients about their medication consumption,9 but detecting medication non-adherence can be difficult as patients are not always honest with their physicians. For example, urine analysis showed disparities between self-reported medication rates and that as detected by urine analysis of 5-ASA and N-acetyl-5-ASA.9 Self-reporting of medication non-adherence only identified 66% of patients who were indeed non-adherent according to their urinary drug measurements.9 Thus, it is conceivable that for a number of reasons, such as fear of upsetting the physician, patients would lie about the actual amount of medications they had taken. The fact that patients may be inclined to over-estimate their adherence rates during a clinical study, which they know they are being monitored for medication adherence, may mean that other methods of detecting non-adherence are needed, especially outside a clinical trial setting.

Because of the time-constraints that gastroenterologists face and the fact that patients may feel more comfortable talking to another member of the multidisciplinary team, other methods can be deployed. These methods include the involvement of an IBD nurse specialist or the physician’s assistant who can also ask the patients directly, or via questionnaires. In some cases, especially with medications that are associated with severe side effects, an indication as to whether or not a patient has been adherent can be obtained by probing them about any side effects experienced. However, as 5-ASAs are not associated with significant side effects,19 this may not be applicable to IBD patients.

An indirect route to the patients could be via their spouse, who may know more about their medication-taking behaviour and are more prepared to report the truth. The patient’s pharmacy could also give an indication as they will have a record of when each repeat prescription was dispensed. Patients often have a relationship with their pharmacist and are likely to keep using the same pharmacy. For these reasons, some clinical trials on medication adherence have relied on pharmacies to provide repeat prescription data. Patients can be requested to bring their medication with them when they are attending their prescheduled visits, and if the date of dispensation is on the medication, the number of tablets remaining can be counted, which may give an indication of their adherence. In addition, there are various clinical trial methods that
can be adopted including bottles that record every time the lid is removed. One weakness of this approach is, however, that the lid can be removed and replaced without the medications actually being taken. Therefore, there is no one way of determining a true reflection of the degree of medication adherence.

**PREDICTORS OF NON-ADHERENCE**

Some patients are at a greater risk of non-adherence than others and several studies have identified predictors of non-adherence. Evidence suggests that being male (especially young males) and taking multiple medications increase the risk of becoming non-adherent by approximately twofold and 2.5-fold, respectively – see Table 1. Thus, these factors are strong predictors of medication non-adherence, whereas being married, having greater disease extent and undergoing a recent procedure are not.

In another study, a clear relationship was shown between partial non-adherence and full time employment, and total non-adherence and depression. Therefore, it may be possible to identify those patients who fall into the various predictive categories, and as they are considered to be at ‘high-risk’ of non-adherence, physicians may target these patients with treatment strategies to improve medication adherence rates.

**THE IMPACT OF NON-ADHERENCE ON CLINICAL RECURRENCE**

Evidence shows that patient non-adherence to medication impacts adversely on disease symptoms. For example, Kane et al.’s study (2003) showed that of those quiescent UC patients who experienced clinical recurrence of disease symptoms by 12 months, 68% of these patients were non-adherent to their medication. Furthermore, the authors also reported a greater than fivefold increased risk of recurrence in patients who were non-adherent to their 5-ASA therapy compared with those who were adherent ($P < 0.001$). Therefore, the more adherent the patients are to their medication, the less likely they are to experience clinical relapses.

Multivariate analyses revealed other risk factors for disease relapse including significantly shorter length of remission (hazard ratio 2.7 [95% CI: 1.2–5.8]; $P = 0.01$), and significantly shorter duration of disease (hazard ratio 2.4 [95% CI: 1.1–5.1]; $P = 0.02$). However, it appears that medication non-adherence is the single most important predictive factor for disease relapse [hazard ratio 5.5 (95% CI: 2.3–13); $P < 0.001$]. A Kaplan-Meier curve constructed to compare outcomes stratified by adherence status for 24 months also showed that UC patients adherent to their 5-ASA therapy had a significantly greater chance of remaining in remission than those who were non-adherent (i.e. 89% vs. 39%, respectively; $P = 0.001$).

**STRATEGIES FOR OPTIMIZING PATIENT ADHERENCE**

Improving patient adherence to medication in IBD may improve clinical outcomes and reduce the risk of developing CRC in the long term. Communication is a key component in improving patient adherence and a good physician–patient relationship has been shown to be associated with higher medication-adherence rates.

**Physician–patient relationship**

Psychology literature points out using COPE principles (see below) as a way for physicians to improve their relationship with patients and optimize patient adherence to their medication. COPE principles encompasses the following: communicate with patients; obtain patient’s commitment to therapeutic objectives; promote emotional/psychological/physical support as necessary; educate the patient and their family.

The physician–patient relationship is complex as it involves two individuals who have been brought together by illness, and each individual may hold different health beliefs. A prospective study involving IBD patients has shown that patient–physician discordance correlated with patient non-adherence. The findings of this study support the fact that poor communication, as reflected by higher discordance, increased the risk of intentional non-adherence in all patients, and raised the risk of overall and unintentional non-adherence in psychologically non-distressed patients.

<table>
<thead>
<tr>
<th>Table 1. Odds ratios for medication non-adherence factors</th>
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<td><strong>Factors</strong></td>
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<td>&gt;4 medicines</td>
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<tr>
<td>Male gender</td>
</tr>
<tr>
<td>Recent procedure</td>
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<tr>
<td>Greater extent of disease</td>
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<td>Married</td>
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Studies have also shown that the interaction between the patient and the physician has a huge impact on health outcomes. For example, resolution of symptoms including abdominal, back, neck or chest pains, fatigue and rectal bleeding, have been shown to be improved when physicians and patients collaborated in partnership to reach agreement on the nature of the medical problem.  

Therefore, a good physician–patient relationship requires close mutual co-operation towards shared goals, and an agreed commitment to therapeutic objectives, i.e. adherence to medication. Moreover, the physician’s willingness to allow a patient to become involved in their illness may facilitate treatment decisions that are meaningful to both parties. In addition, for the co-operative approach to be successful, physicians must ascertain a patient’s ability to make decisions, empathize with their needs and concerns, and ensure that patients feel as involved in the treatment decision-making process as they are comfortable.

Individualized therapy

Another approach that could be taken to optimize patient adherence include individualized therapy where physicians review the patient’s disease and therapeutic history, i.e. identify which treatment(s) were effective/ineffective in the past, to avoid prescribing them the same medication that was unsuccessful. Through this approach, the physician could also keep track of a patient’s level of adherence by requesting them to keep a log of each time their medication was taken and suggest other means of improving adherence when necessary. Furthermore, this patient review process could also provide predictive information on medication non-adherence behaviour, and thus help identify those patients at high risk who may require longer consultation slots than those who are at low risk.

Patient information and support

In addition to the information and support provided by the IBD nurse specialists, other sources of information/support are available from patient advocacy groups, such as the National Association for Crohn’s and Colitis Disease and the CORE Charity. Patients and their families, who play an important supportive role, can log on to their websites to learn more about the disease and disease-related issues (via http://www.nacc.org.uk and http://www.corecharity.org.uk).

Physicians could also recommend their UC patients to enrol in patient support programmes such as PGtP’s Everyday-Living Support Programme (http://www.everyday-living.co.uk), which may help patients to understand better their condition and the importance of taking their medication as prescribed. Physicians can recommend this programme to their recently diagnosed UC patients who have been prescribed mesalazines and provide them with a starter pack, which contains details for registration.

Self-management training programmes

Patients who take responsibility for their own health and self-manage their disease could improve medication adherence rates, as they would have a vested interest in maintaining their symptoms and quality of life. Over the past few years, the UK Department of Health have launched their Expert Patients Programme (EPP) as a Community Interest Company (EPP CIC), enabling Primary Care Trusts to commission self-management courses for people with long-term conditions.

Practical aide memoires

Patients could also be prompted to take their medications via simple pill-taking cues, such as placing pills close to something they use daily, e.g. the toothpaste, breakfast table, glasses/contact lenses case, night-time beverage, etc. In addition, telephone support, postal reminders, setting alarms on watches/mobile phones, vibrating key fobs and even a robotic pet that taps the patient’s leg at set times have been suggested. However, intervention studies are needed to evaluate the beneficial effects of each of these cues on disease outcomes.

CONCLUSIONS

Medication non-adherence in IBD patients is an important factor in predicting disease relapse and is associated with an increased risk of developing CRC in the long term. It also impacts significantly on the healthcare system because of increased hospital visits and resultant economic burden. The causes of medication non-adherence are multi-factorial and factors other than dosing frequency may play an important role. Medication non-adherence rates in IBD range
from between 41% and 60% and clinical relapses are inversely proportional to adherence rates. Strategies for optimizing patient adherence include improving physician–patient relationships, individualized therapy, self-management programmes and interventions such as aide memoires. Through the implementation of these strategies, patient adherence to medication could be significantly improved, increasing the likelihood of the patient achieving disease remission and sustaining remission for longer, which could in turn have a positive impact on their symptomatic control and quality of life.

REFERENCES


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