Adherence Issues in the Patient with Inflammatory Bowel Disease

While literature on other chronic diseases such as coronary artery disease, congestive heart failure, and diabetes has tried to address the issue of medication non-adherence and its effect on disease outcomes, the impact of medication adherence on specific inflammatory bowel disease (IBD) outcomes has not been fully explored. The published literature of the efficacy of IBD maintenance medications underestimates the extent of the problem, as patients often conceal their failure to take medications as directed once outside of controlled clinical trial environments. The remainder of this article will discuss the state of knowledge regarding the issues surrounding non-adherence in the management of IBD, presented in a case presentation format with each highlighting a commonly encountered adherence related problem.

Who is more likely to be non-adherent? A study by Kane, et al demonstrated in their population that noncompliant patients were more likely to be male (67% vs. 52%, p < 0.05), single (68% vs. 53%, p = 0.04) and to have disease limited to the left side of the colon vs. pancolitis (83% vs. 51%, p < 0.01) (1). Sixty-eight percent of patients who took >4 prescription medications were found to be noncompliant versus only 40% of those patients taking fewer medications (p = 0.05). Age, occupation, a family history of inflammatory bowel disease, length of remission or quality-of-life score was not associated with non-adherence. The median amount of medication dispensed per patient was 71% (range 8%–130%) of the prescribed regimen over a six-month period.

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THE PATIENT WHO DOES NOT WANT TO TAKE PILLS WHEN WELL

What are the consequences of a patient who does not continue to take his medication for maintenance of remission? A follow up study on the above mentioned cohort revealed that after 12 months of observation, 19 of 86 patients originally in remission had recurrent disease, 13 (68%) of whom were noncompliant (2). A Multiple Cox proportional hazards model revealed that patients not compliant with medication had more than 5-fold greater risk of recurrence than the compliant patients (hazard ratio 5.47, 95% confidence interval 2.26–13.22, p < 0.001) (Figure 1).

One method that has proven to increase short-term adherence is direct physician contact with the patient (3). Patients respond to additional attention, and this can be by any one of several health care providers.

Maybe even more important are the cumulating data regarding continued medication consumption and protection from colon cancer, which is an important concern for the long-term natural history of UC. Eaden and colleagues found in a case-control study that mesalazine at a dose of 1.2 g/day or greater reduced colorectal cancer risk by 91% in patients with UC compared to no treatment (4). There are now five additional studies and a recent meta-analysis that show that continued consumption of roughly 2.0 g of 5-ASA per day decreases the risk of the development of colorectal cancer by at least 30%. This finding is independent of folic acid use, disease duration and extent.

THE PATIENT WHO DOES NOT QUIT SMOKING

The detrimental effects of tobacco smoking on Crohn’s disease are well known. However, it is difficult to encourage patients to remain non-smokers long term and the recidivism rate is high. Cosnes, et al has followed prospectively 59 patients who quit smoking and were able to remain adherent to the smoking cessation program (5). During a median follow up of 29 months, the risk for need for steroids or immunosuppressive medications was similar to that in non-smokers, and lower than in current smokers. Emphasizing the long-term benefits in terms of medication use can be one way to encourage non-smoking behavior.

THE PATIENT WHO FORGETS TO TAKE HIS MEDICINE

As part of the previously described study, non-adherent patients were asked why they were not taking their medications (1). The majority stated that they simply forgot one of their doses. Fewer than 10% of patients complained of side effects and cost (Figure 2). If this is true, then helping patients simplify their regimens will help increase overall medication consumption.

Farup, et al in their trial of mesalazine versus hydrocortisone foam enemas, incorporated the issue of tolerability, ease and adherence into the data collection (6). In this 4-week trial, patients were asked to mark on a 100 mm visual analog scale an assessment of their medication regimen with regard to ease of administration and practicality. Adherence, as measured by the return of unused bottles, was >80% at 2 weeks in both groups, then dropped to 73% for the foam patients but remained >90% for the mesalazine group. The authors suggested that the better outcome in the mesalazine group was in part due to convenience and simplicity and thus better adherence to that treatment regimen.

In a study by Robinson, et al self-reporting of medication consumption revealed non-adherence

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Adherence Issues in the Patient with IBD

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![Bar chart of non-adherence in quiescent UC](chart.png)


**Figure 2.**

(taking less than 80% of the prescribed dose) in 42 patients (43%) (7). Logistic regression revealed three times daily dosing [OR 3.1 (95% CI 1.8–8.4)] was one of the only independent predictors of non-adherence. Urinary drug measurements revealed 12 patients with no detectable 5-ASA or N-acetyl 5-ASA. Of interest, self-reporting correctly identified 66% of patients judged to be non-adherent on the basis of urinary drug measurements but only two of the 12 patients with undetectable drug levels admitted to complete non-adherence.

Simplifying patient regimens is an effective way to increase adherence. A recent pilot feasibility trial assessed short-term outcomes in patients on once daily mesalamine compared to a conventional (twice or three times daily) regimen for maintenance of ulcerative colitis (8). Secondary aims included overall medication consumption rates and patient satisfaction. Twenty-two patients were randomized, and followed for six months. The number of clinical relapses after six months was similar in the once daily and conventional dosing groups. While there was no statistically significant difference in six-month adherence rates between the two groups, there was a numerical advantage for overall consumption with a once daily regimen and patients in the once daily group were on the whole more satisfied with their regimen as compared to the conventional dosing patients.

It has been suggested that physicians may overestimate patient comprehension in regard to instructions and education. Martin and colleagues showed that of IBD patients polled, 62% of ulcerative colitis patients felt ill informed about their disease (9). While eighty-six percent of patients responding knew of the increased risk of cancer, only 44% knew that it was possible to screen for dysplasia and possible prevention of invasive cancer.

Other literature also suggests that non-adherence is linked to patient non-comprehension (10). A recent study yet to be published in full form reported that in a GI outpatient clinic 15% of patients did not know how their medication worked, 22% felt dissatisfied with their medications, primarily from unexpected side effects, and 12% admitted they do not tell their physician all the medications that they take (11).

Patient autonomy is also a means to enhance adherence with medications. Realizing the potential difficulties for long term adherence with sulfasalazine, Dickinson et al studied continuous versus “on demand” sulfasalazine in 28 patients with quiescent ulcerative colitis (12). Of the 18 patients in the “on demand” group, directed to take 3 grams of sulfasalazine per day starting within 24 hours of symptom

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<th>Adherence Issue</th>
<th>Possible Interventions</th>
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<tr>
<td>1. Patient does not take his medication</td>
<td>Emphasize long term outcome, and Role of possible chemoprophylaxis Educate patient regarding role of medicines</td>
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<tr>
<td>2. Patient does not quit smoking</td>
<td>Emphasize long term benefits on disease</td>
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<td>3. Patient forgets to take medication</td>
<td>Simplify regimen Work with patient regarding medication-taking behaviors</td>
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<td>4. Patient does not come for colonoscopy</td>
<td>Emphasize improved outcomes with regular surveillance</td>
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recurrence, seven relapsed within the study period, four within the first two months of the trial. Three of the ten patients randomized to the continuous group relapsed. Adherence was measured by serum sulfapyridine levels every four months for one year or until relapse, and was reported as adequate for patients in either group. The authors concluded that because there was no difference in relapse rates between the two groups, and that by serologic testing sulfapyridine levels were therapeutic, that an “on demand” regimen may be as efficacious as continuous therapy. These results were published as preliminary, and unfortunately no larger studies have been published to date that corroborate these results.

This patient-centered, self-management approach offers the opportunity to improve outcomes through patient education and empowerment. In a British study, 203 patients with UC were randomized to either routine treatment by a specialist or patient-centered self-management in the primary care setting (13). Patient training included a written algorithm for treatment and a 15–30 minute training session. In the self-management group, relapses were treated significantly more rapidly than in the conventional group (14.8 vs. 49.6 hours, p < 0.01), had fewer office visits (0.9 vs. 2.9/year, p < 0.01), and the length of the flares that did occur was shorter (Figure 3).

**THE PATIENT WHO DOES NOT COME FOR COLONOSCOPY**

Patient adherence rates with surveillance colonoscopy are not well documented. In the only study that directly addressed this issue, Woolrich, et al reported on seven patients of their cohort of 121 that were found to have cancer (14). In two of these patients, previous colonoscopy had found dysplasia in the setting of quiescent disease, and neither of these patients were adherent with recommendations for close follow up colonoscopy or colectomy. It was the conclusion of the authors that quiescent disease was a risk factor for non-adherence with physician recommendations.

**References**