Improving Adherence to Mesalamine Therapy Among Patients With Ulcerative Colitis

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Introduction
Ulcerative colitis (UC) is a chronic inflammatory bowel disease of the colon characterized by exacerbation and remission of core symptoms, including bloody diarrhea, abdominal pain, urgency, and tenesmus.1 Pharmacologic treatment is necessary to induce remission, and protracted therapy often is required to maintain remission. First-line therapeutic options for induction of remission in patients with mild to moderate UC include 5-aminosalicylic acid (5-ASA) and steroids, whereas various oral and topical formulations of 5-ASA (ie, pH-dependent mesalamine, balsalazide, sulfasalazine, and olsalazine) generally are prescribed for maintenance of remission.2,3 Differences among these formulations revolve around the mechanisms that prevent absorption of 5-ASA within the small intestine.2 These include attachment of the parent 5-ASA molecule to protective moieties (eg, sulfapyridine or benzoic acid derivatives) or encapsulation of mesalamine within protective, pH-dependent coatings.2 Because each dosing formulation has specific medication-release properties, multiple-daily administration may be required to maintain therapeutic concentrations of mesalamine within the colon.2 However, multiple-daily dosing may affect adherence to prescribed pharmacologic regimens. This article briefly reviews the impact of nonadherence to mesalamine therapies for UC and provides practical advice for improving therapeutic compliance.

Importance of Adherence
A significant percentage of patients with UC (ie, ≥40%) are nonadherent to their prescribed maintenance therapy despite evidence that nonadherence may significantly influence the clinical course of their disease. For example, after 2 years, 89% of adherent patients maintained UC remission compared with only 39% of those who were nonadherent (Figure).4 An increased occurrence of flares in nonadherent patients can translate into an increased need for hospitalization and medications such as prednisone, thereby resulting in higher medical costs.5 Additionally, patients with UC may have a greater risk for developing colorectal cancer (CRC) because of the increased inflammation associated with UC. Mesalamine is thought to be chemoprotective through reduction of colon inflammation; therefore, nonadherence to mesalamine therapy may result in an increased risk for CRC. In support of this hypothesis, a meta-analysis of 9 studies demonstrated a protective association between the use of mesalamine and CRC in patients with UC.6 Concomitant with a reduction in flares, adherent patients have higher health-related quality of life,7 and may be more likely than nonadherent patients to avoid the stress and worry associated with flares that may occur immediately before the weekend (so-called Friday flares). Given these observations, increasing adherence to medication regimens is paramount in terms of clinical, economic, and psychological well-being.

Science of Adherence
Multiple factors contribute to how well patients adhere to their medication regimen (Table).3,10-14 Insight into these factors (eg, patient perception, treatment formulations, and demographic and disease characteristics) can guide health care professionals in their discussions and educational efforts with patients, with the ultimate goal of increasing clinical remission and patient well-being.

Table. Factors Contributing To Nonadherence With Mesalamine Treatments

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<th>Demographic</th>
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<tr>
<td>Male sex</td>
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<td>Unmarried status</td>
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<td>Full-time employment</td>
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<td>Large number of concomitant medications</td>
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<table>
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<tr>
<th>Treatment-specific</th>
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<tr>
<td>Rectal therapy</td>
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<td>Multiple-daily dosing</td>
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<td>Prescription drug costs</td>
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<tr>
<th>Disease status</th>
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<tr>
<td>Quiescent of symptoms</td>
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<td>Longer duration of disease</td>
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<td>Less-extensive disease (eg, proctitis, proctosigmoiditis)</td>
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Figure. Maintenance of clinical remission after 2 years in adherent and nonadherent patients with ulcerative colitis.

A greater percentage of patients who were adherent to their maintenance treatment regimen (89%) remained in clinical remission than nonadherent patients (39%). Figure adapted from Kane S, Huo D, Aikens J, Hanauer S. Medication nonadherence and the outcomes of patients with quiescent ulcerative colitis. Am J Med. 2003;114(1):39-43. With permission from Elsevier.
Medication Formulation and Dosing

Compliance typically is greater with oral than with topical mesalamine formulations, and negatively correlates with treatment duration (ie, compliance with treatment regimens for the induction of remission [short-treatment duration] is greater than that for maintenance therapy [long-term duration]). Dosing frequency also significantly affects compliance. More frequent dosing (eg, 3 times daily) may be considered more disruptive because patients are required to take medication in the middle of the day when they are at work or school. They may feel embarrassed about taking medication outside of their home or they may forget entirely. Thus, it is not surprising that patient compliance was less with 3-times-daily treatment regimens than with once- or twice-daily regimens. However, patient preference and cost also should be taken into account. Some studies have reported no significant difference in adherence between different dosing regimens, and patients may prefer increased dosing frequency if it is concomitant with lower pill burden at each administration.

Demographic and Disease Characteristics

On the basis of data from questionnaires addressing medication-taking behavior, specific patient populations or characteristics may be associated with a greater risk for noncompliance (Table). Young age, male sex, unmarried status, full-time employment, disagreeable temperament, multiple concomitant medications, and advanced education were associated with noncompliance. Additionally, nonadherence was greater in patients with inactive disease, those without a history of complex disease (ie, steroid dependency, steroid refractoriness, intestinal resection, infliximab requirement, or UC-related hospitalization), and patients with left-sided UC. These demographic and clinical characteristics may aid in the identification of patients who are at increased risk for nonadherence and thus help focus interventional and educational efforts accordingly.

Identification of Patients at Risk for Poor Adherence

Practical Tips for Assessment

Assessing medication compliance in clinical practice can be difficult, and no gold standard for doing so exists. Patients who experience frequent flares despite medication may be suspected of nonadherence, but, given the relapsing and remitting nature of UC and the observation that patients who receive no treatment may not experience a flare for years, flares may be a poor indicator of compliance. Frank questioning of patients verbally or through the use of questionnaires may provide some insight into patient adherence and may act as a catalyst for discussions about compliance. Although patients may inflate their adherence rate and self-reporting techniques are limited by patients’ recollections, subjective assessment of patients’ responses and body language during questioning may be informative. Prescription refill rates may provide a more definitive perspective on patient adherence, but they do not accurately reflect actual medication consumption. However, failure to refill prescriptions for long periods of time likely indicates noncompliance. Pill counting and comparison with patients’ prescribed dose also is hindered by the lack of definitive information, but asking patients to bring in their medication and inspecting the remaining doses may be beneficial in initiating a dialogue about adherence and may be seen by the patient as a gesture of the physician’s interest and compassion. More objective measurements of patient compliance include biologic assays that measure blood or urine concentrations of the medications or their metabolites. Although effective, these tests provide time-limited adherence information (eg, adherence only within the previous 24 hours), and their cost-effectiveness has not been ascertained. Thus, identification of patients who are nonadherent remains challenging, and the principal strategy to overcome this problem may be the use of practical measures to augment adherence in all patients with UC.

Practical Tips for Increasing Adherence

A strong physician–patient relationship is paramount for ensuring proper disease management and medication adherence. Discord with the physician or feeling uneducated about the disease correlated with nonadherence. Patients often feel that the disease disrupts their daily life, although their physicians may not agree. They also may feel that their physicians do not fully appreciate their situation. To overcome these perceptions, physicians should actively listen to patients talk about their disease and ask questions accordingly. This not only may make patients feel that their situation is understood but also may provide physicians with valuable insight regarding the patients’ disease course, adherence, and barriers to adherence. Patients’ attitude toward medications, their belief and support systems, and knowledge of their disease should be explored. Physicians also should review the patient’s disease and therapeutic history and examine the efficacy and disruption associated with previous treatments (eg, switching from a multiple-daily to a once-daily medication). These types of discussions can lead to dialogue concerning treatment alternatives and distribution of educational materials that are pertinent to the patient and, therefore, are more likely to be remembered and followed.

Conclusion

Patient adherence to mesalamine treatment directly affects the clinical outcome of UC, the overall health care cost associated with the disease, and the development of long-term complications. Understanding the factors that contribute to treatment nonadherence may help identify at-risk patients and allow the development of appropriate strategies to target less-adherent patient populations. The physician–patient relationship is essential to this process, and open discussions about the patient’s disease may provide insight into adherence barriers, a forum for disease education, and evaluation of treatment options that may increase patient compliance. (eg, once-daily vs multiple-daily medications).

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References