Towards Better Patient Compliance in IBD: Report of an International Compliance Consensus Meeting

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Introduction

Poor compliance with medical therapy is a common problem; approximately half of all medicines prescribed for patients with chronic conditions are not taken as prescribed.\(^1\) Similar rates of noncompliance have been reported amongst patients with inflammatory bowel disease (IBD),\(^2,3\) and there is a clear association between rates of relapse and compliance with 5-aminosalicylic acid (5-ASA) therapy.\(^4\) Modeling studies suggest that health beliefs, quality of life, and the physician-patient relationship play an important role in compliance,\(^5\) and another study found that being male, single, or having distal colitis were associated with greater noncompliance.\(^4\)

Treatment with 5-ASA significantly reduces the rate of relapse in patients with IBD,\(^6,7\) and there is mounting circumstantial evidence that 5-ASA may be protective against colorectal cancer.\(^8,9\) In most clinical trials, the reported rates of compliance are in excess of 95%, but there is a predictable reduction in efficacy with real-life compliance, with rates of 60% or less.

Pharmaceutical companies also have a vested interest in increasing patient compliance—not just to increase sales of their drug, but to improve the effectiveness of their product, and hence the satisfaction of prescribers and patients. It is interesting to note that if current rates of compliance with prescribed 5-ASA therapy were increased by 25%, the outcome would be similar to that of treatment with a new 5-ASA preparation that was 25% more effective than current preparations.

The issue of noncompliance in IBD was the subject of a 1-day roundtable consensus meeting (Marlow-on-Thames, UK, March 2004, supported by an unrestricted educational grant from Ferring Pharmaceuticals), at which data on 5-ASA treatment and compliance were reviewed and discussed in detail. The objectives were to identify the causes and consequences of noncompliance and to develop practical solutions to take into clinical practice. The multidisciplinary team of panelists had clinical and/or research interests in compliance and included 6 physicians, a pharmacist, a behavioral psychologist, a patient’s, and a patients’ advocate representing the European Federation of Crohn’s and Ulcerative Colitis Associations.

The following is a summary of the presentations and recommendations of the panelists for improving patient compliance in IBD.

Presentations

Background and Natural History of IBD

Ebbe Langholz (Denmark) reported up-to-date statistics on the epidemiology of IBD based on the Copenhagen population-based cohort. The incidence of ulcerative colitis (UC) is fairly stable, at around 10 per 100,000 population, whereas the incidence of Crohn’s disease (CD) is rising (currently 6–7 per 100,000 population). The overall prevalence of IBD in Denmark is approximately 0.5%. In 90% of patients, the disease runs a relapsing-remitting course with less than 5% of patients experiencing continuous disease.

Simon Travis (UK) reviewed the development of pharmacologic therapy and the natural history of IBD, recalling mortality rates in severe colitis of up to 70% prior to drug therapy. He emphasized the importance of establishing the correct diagnosis to engender patient confidence and tailor treatment to the distribution of disease. The diagnosis may change from CD to UC (or vice versa) in up to 5% of cases\(^10\) but disease extent is more variable. In 467 patients with distal colitis, disease progressed in 53% over 25 years,\(^11\) while in another 399 patients with UC, disease extent regressed in 22%.\(^12\) The most recent data from the UK General Practice Research Database indicate
that the overall mortality in IBD is modestly increased (by 44% for UC, and 73% for CD) compared with standard mortality data, which is similar to the mortality difference between manual and nonmanual workers.13

Giuseppe Frieri (Italy) reviewed safety and efficacy data relating to 5-ASA. Several trials show that 5-ASA is up to twice as effective as placebo for inducing and maintaining remission in UC and may reduce the risk of colorectal cancer in this group of patients. In large population studies involving over 3,000 patients taking up to 7 g of 5-ASA daily for up to 5 years, remarkably, only 1.5% of patients withdrew from treatment. As the active agent of all 5-ASA preparations is the same, the most important factor for efficacy is the ability of the delivery system to target inflamed tissue.

**Essence of the Compliance Problem**

Amy Trachter (behavioral psychologist, USA) reported that noncompliance rates in acute illness range from 70–95%, falling to less than 50% for chronic illness. The priorities for any intervention are to change patient behavior so that patients feel an increased sense of control of their illness, and hence accept more responsibility for their own treatment. Improved communication between doctor and patient is needed to: 1) increase understanding of drugs and their effects (and unwanted effects); 2) understand the consequences of noncompliance; and 3) identify barriers to nonadherent behavior (for example, previous experiences with other medicines). Many patients are unintentionally noncompliant and behavioral interventions can be used to address forgetfulness and other inadvertent behavior leading to nonadherence. The panel agreed that time and understanding are critical factors for improving both compliance and the doctor–patient relationship, and that consultations should be of sufficient length to ensure appropriate communication. It was recommended that patients be accompanied by a friend or family member, when possible, to reinforce the importance of treatment. Micke Lindholm (Finland) provided a personal insight into compliance, having lived with CD for 30 years and also having a son with IBD. He reported that he had been noncompliant with treatment shortly after diagnosis, and stressed the importance of the doctor–patient relationship, having been treated by a series of different doctors during the early years. Patients and doctors should share responsibility for treatment, and good communication is paramount. Lindholm’s own noncompliance was partly due to a poor understanding of the relapsing/remitting pattern of disease. He listed a number of reasons why patients are noncompliant:

- Lack of resources, related to the cost of medicines
- Fear pertaining to side effects, safety, and efficacy
- General anxiety of long-term illness
- Previous experiences and failure to recognize patterns of illness
- Forgetting to take their medicines
- Lack of understanding of their disease or medication
- Differing educational and social levels; lack of family support
- Lack of continuity of care and/or patients missing appointments
- Use of alternative remedies
- Size and/or number of pills per day, difficulty in swallowing pills, and dosing regimen
- Poor communication/inadequate supervision
- Religion, culture, and customs.

Sarah Cripps (Pharmacist, UK) presented the results of a patient survey conducted by the pharmacy department of the John Radcliffe Hospital, Oxford, identifying IBD patients’ beliefs about their illness and medication as well as the implications of these beliefs for treatment adherence and patient education. An association was demonstrated between patients with strong beliefs about the necessity of medication (oral or rectal) and self-reported adherence. Certain groups of patients expressed greater concerns, particularly females, younger patients, and those newly diagnosed with IBD. Long-term side effects were the most common concern for patients receiving oral therapy, whereas embarrassment and lifestyle disruption were cited for rectal therapy. In addition, 41% patients had not been shown how to use rectal preparations. Patients identified the important role of the pharmacist in IBD management and joint working between pharmacists and doctors resulted in improved medication information pamphlets. Andrew Robinson (UK) presented Dr. Sunanda Kane’s data1 showing that noncompliance correlated strongly with clinical recurrence of IBD (87% of noncompliant patients relapsed vs 26% of compliant patients) and compliance with 5-ASA therapy reduced the risk of relapse by 50%. Noncompliance was the most important predictor of relapse (hazard ratio [HR] 5.47), followed by length of remission (HR 2.65), positive family history (HR 2.42), and disease duration (HR 2.41). The main reasons for noncompliance reported by patients were forgetfulness and perceived lack of benefit; fear of side effects and cost were minor issues. The main risk factors for noncompliance were male gender and multiple medications; of note, married patients were more likely than unmarried patients to comply with treatment.

Drug therapy is only 1 part of a patient’s healthcare requirement. Appropriate, timely information, participation in decision-making, convenient access to specialist information, and opportunity for self-care should be part of the IBD management service. It was noted that increased frequency of clinician visits does not correspond with improved compliance; the quality of the patient–physi-
Table 1.  Reasons for Treatment Noncompliance: Poor Physician–Patient Communication (Time, Quality, Rapport)

<table>
<thead>
<tr>
<th>Why Does This Occur?</th>
<th>How Can This Be Improved?</th>
<th>Clinical Practice and Resource Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Poor postgraduate education of physicians, especially communication skills</td>
<td>• Establishment of multidisciplinary teams incorporating high-quality patient information and care plans</td>
<td>• Physician communication—warmth, empathy, unconditional regard, trust</td>
</tr>
<tr>
<td>• Lack of integrated multidisciplinary teams, resulting in lack of continuity and poor information</td>
<td>• Incorporating interpersonal skills into postgraduate education</td>
<td>• Easily accessible, tailored patient information</td>
</tr>
<tr>
<td>• Use of medical jargon by health professionals</td>
<td>• Investment of increased multidisciplinary time with newly diagnosed patients</td>
<td>• Manage clinic templates to allow longer consultations with patients who need more time</td>
</tr>
<tr>
<td>• Lack of time for clinicians to explain all the relevant information to patients</td>
<td>• Continuity of healthcare provider—building on previous consultations</td>
<td>• Separate clinics for newly diagnosed, relapsing, and routine follow-up patients</td>
</tr>
<tr>
<td></td>
<td>• See same clinician if possible</td>
<td>• IBD school</td>
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IBD = inflammatory bowel disease.

Table 2.  Reasons for Treatment Noncompliance: Fear—Side Effects, Safety, and Efficacy

<table>
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<tbody>
<tr>
<td>• Patient misconceptions, eg, equating increased frequency/dosing to higher frequency of side effects</td>
<td>• Use of clear, balanced information about drugs, indications, effects and side effects</td>
<td>• Clear information leaflets</td>
</tr>
<tr>
<td>• Fear of adding to pre-existing symptoms with drug side effects</td>
<td>• Simplify wording on the package insert</td>
<td>• Simplified package insert</td>
</tr>
<tr>
<td>• Unclear communication about medicine—nature of prophylaxis</td>
<td>• Anticipate patient fears, eg, pregnancy, rectal preparations</td>
<td>• Well-reasoned discussions relating to benefit-versus-safety concerns</td>
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<tr>
<td>• Previous reactions to medication deterring patients from all forms of medication</td>
<td>• Better use of pharmacists</td>
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Table 3.  Reasons for Treatment Noncompliance: Size and Number of Tablets, Dosing Frequency

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</thead>
<tbody>
<tr>
<td>• Large numbers of tablets</td>
<td>• Minimum number of tablets/day</td>
<td>• Patient participation in choice of preparation and administration</td>
</tr>
<tr>
<td>• Too frequent administration</td>
<td>• Reduced dosing frequency</td>
<td>• More patient-friendly formulations</td>
</tr>
<tr>
<td>• Large tablets</td>
<td>• Smaller tablets</td>
<td></td>
</tr>
<tr>
<td>• Inconvenient, impractical administration, eg, enemas</td>
<td>• Alternative preparations</td>
<td>• Training to administer topical therapy</td>
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</tbody>
</table>

Physician interaction is much more important than frequency. Guided self-management provides patients with the skills to participate actively in their own disease management, reduces delays between symptoms and treatment, and reduces the number of consultations.14

Ad van Bodegraven (Holland) discussed strategies to identify and target noncompliant patients using the Dutch Patient Empowerment Programme as an example. Strategies include sharing responsibility for management between patients and physicians; increased education of patients and physicians about IBD, its treatment, side effects of therapy, and the rationale for compliance; simplification of drug regimes; ensuring easy access to healthcare professionals for help and advice; and better use of physician time by increasing the input of IBD specialist nurses.
How Can This Be Improved?

Drug metabolites to inform compliance discussion, may

Expert patient training, and measurement of urinary

Extended consultations for newly diagnosed patients,

Patient questionnaires to evaluate risk of noncompliance,

Coordination of services, including multidisciplinary service and active patient participation, by providing appropriate, tailored information about the disease and treatment. Also as easy access to specialist advice and services, and by facilitating active patient participation in decision-making and disease management. Additional services, including multidisciplinary team management, questionnaires to evaluate risk of noncompliance, extended consultations for newly diagnosed patients, expert patient training, and measurement of urinary drug metabolites to inform compliance discussion, may increase compliance still further. Compliance is likely to improve with the development of simplified, once-daily dosing regimens, and the supportive/educational role of patient support organizations could complement existing programs by training “expert” patients.

There is clearly no simple solution to noncompliance in IBD—it is over 20 years since van Hees reported noncompliance rates of 40%.—but our understanding of the reasons and consequences of noncompliance is greater and presents opportunities to evaluate the effectiveness of remedial interventions.

Declaration of Competing Interests

Andrew Robinson has attended and presented at several IBD conferences organized by Ferring Pharmaceuticals and has received payment for participation in advisory board meetings. Bernd Bokemeyer has been reimbursed by Ferring Pharmaceuticals (manufacturers of PENTA) for attending several conferences and has also received fees from them for speaking and consulting. Sarah Cripps has no competing interests to declare. Giuseppe Frieri was reimbursed by Ferring Pharmaceuticals for attending the Consensus meeting and received a fee for speaking. Ebbe Langholz has no competing interests to declare. Micke Lindholm was reimbursed by Ferring Pharmaceuticals for attending the Consensus meeting and received a fee for speaking. Amy Trachter has no competing interests to declare. Simon Travis has been reimbursed by Ferring Pharmaceuticals for speaking at several conferences or acting as an advisor. He has received an unrestricted educational grant in support of a research meeting. Ad van Bodegraven has received partial reimbursements (according to Dutch Law) from Ferring Pharmaceuticals for attending symposia and reimbursements/fees from them for lectures concerning treatment.

Table 4. Reasons for Treatment Noncompliance: Patient in Remission, Feeling Well

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<tbody>
<tr>
<td>• Poor education about relapsing/remitting nature of disease and value of prophylaxis</td>
<td>• Better patient education; reduced relapse rates, possible reduction in colorectal cancer rates</td>
<td>Motivation and reinforcement during clinical interactions</td>
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<tr>
<td>• Patients unaware of long-term therapy</td>
<td>• Positive reinforcement of link between remission and treatment</td>
<td>Development and implementation of compliance risk questionnaires</td>
</tr>
<tr>
<td>• Medication costs; patients stop treatment to save money, especially when drug costs are high</td>
<td>• Use of risk questionnaires to identify patients at high risk of noncompliance and to target interventions</td>
<td>Exploration of patient expectations and role of clinician during remission</td>
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Panel Discussion

Following the presentations, panel members discussed the data at length in an attempt to classify the major components of poor patient compliance and identify workable interventions to address these issues. Using the list of reasons for noncompliance presented by Micke Lindholm (above), the panelists were asked to rate each factor in order of importance. There was a clear multinational consensus between clinicians and nonclinicians that poor doctor–patient communication (time, quality, and rapport) was the single most important factor contributing to noncompliance (Table 1). Other key reasons were patient fear (safety, side effects, and efficacy of treatment) (Table 2); dosing frequency and size and number of pills (Table 3); and patients stopping treatment when they were well (Table 4). Each of these factors was explored in depth to provide a deeper insight into the perceived problems and a list of suggested solutions was presented.

Conclusion

Poor compliance with long-term medication is widespread and presents a significant challenge to clinicians managing patients with IBD, particularly as patients are frequently in remission. Following a comprehensive review of the literature, the panel agreed unanimously that improved communication is the key to maximizing compliance. Communication can be improved at many levels, including during the physician–patient consultation, by providing appropriate, tailored information about the disease and its treatment as well as easy access to specialist advice and services, and by facilitating active patient participation in decision-making and disease management. Additional services, including multidisciplinary team management, questionnaires to evaluate risk of noncompliance, extended consultations for newly diagnosed patients, expert patient training, and measurement of urinary drug metabolites to inform compliance discussion, may increase compliance still further. Compliance is likely to improve with the development of simplified, once-daily dosing regimens, and the supportive/educational role of patient support organizations could complement existing programs by training “expert” patients.

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(Continued on page 215)
Conclusions

Well-conducted systematic reviews and meta-analyses of relevant trials provide the strongest inference for clinical decision making. Systematic reviews can identify and appraise the quality of the most relevant articles for busy clinicians. Meta-analyses can provide clinicians with the best estimates of treatment effects. This article has provided an introduction to clinicians wishing to understand and apply the results of meta-analyses, particularly with regard to the between-study differences in magnitude of effect that are, to some degree, always present.

References


(Continued from page 209)
of IBD. Sunanda Kane has received reimbursement for organizing an academic roundtable discussion regarding adherence issues in IBD from Ferrin Pharmaceuticals.

References

16. van Hees PA, van Tongeren JH. Compliance to therapy in patients on a main-