An Analysis of Factors That Influence Selection of the Induction Dose of Delayed Release Oral Mesalamine (Asacol) in Ulcerative Colitis in the Community Setting

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INTRODUCTION

In the United States, the dose of Asacol® (mesalamine) Delayed Release Tablets (Procter & Gamble, Cincinnati, OH) approved for treatment of flares of ulcerative colitis (UC) is 2.4 g/day. Previous clinical trials reported greater response with 4.8 g/day[1,2], and some physicians employ higher doses in clinical practice in some patients. The ACG's UC Practice Guidelines[3] state, "From a practical standpoint, the anatomic extent and clinical severity of an acute attack determine the approach to therapy." Thus we hypothesized extent and severity would be the primary determinants of induction dosing for an acute UC flare.

The aims of this study are to:

- Determine the range and frequency of Asacol doses currently used in clinical practice
- Identify factors that influence selection of the induction dose

MATERIALS and METHODS

Study Design. A retrospective survey of community-based gastroentrological practices. Thirty-nine geographically dispersed practices provided data.

Patient Selection. A total of 411 patients met the following inclusion criteria:

- UC flare between 1999-2003
- at least 18 years old
- successfully induced with Asacol
- not in a controlled clinical trial for UC
- no prior or current history of Crohn's disease, infectious colitis, colon cancer, colectomy or ileostomy

Variables. Data elements used for these analyses were: patient's age; gender; ethnicity; smoking history; prior disease and treatment history; physician's global assessment of symptom severity (PGA); stools per day; percentage of stools with blood; initial dose of Asacol for induction (g/day). Also collected were anatomic extent and severity of disease from most recent endoscopy.

Statistical Analysis. The joint impact of the potential predictors on starting induction dose was assessed using stepwise logistic regression. All significance levels were $p < 0.05$, two-tailed.

RESULTS

Figure 1.
Distribution of Starting Induction Dose of Asacol

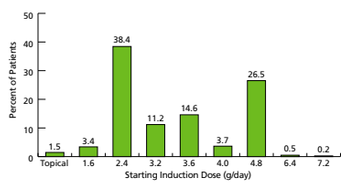
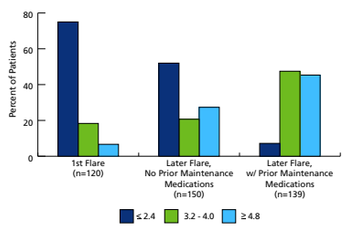


Table 1 displays the results of the regression analysis performed after dosages were grouped into low dose (n=178, 43.3%), intermediate dose (n=121, 29.4%), high dose (n=112, 27.3%).

Figure 2.
Prior Treatment History Was Found to Be the Most Significant Predictor of Dosing Behavior



An unambiguous inverse relationship exists between prior history and dose, with 1st flare patients overwhelmingly receiving 2.4 g/day (75%).

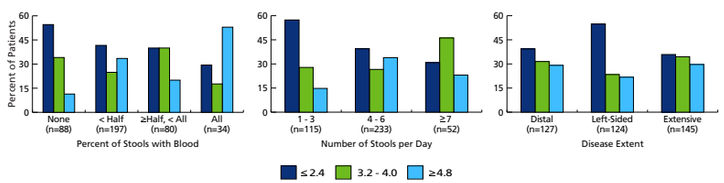
Table 1.
Results of Stepwise Logistic Regression Analysis: Characteristics significantly predictive of dose (in order of entry into the model), p-values, area under the curve (AUC), odds ratios (OR) and 95% confidence limits (CI)

Characteristic	p-value	AUC	Contrast†	OR	95% CI
Prior Treatment History	< .0001	0.744	1st Flare	27.5	14.0 - 54.1
			Later Flare, No Prior Meds	5.7	3.4 - 9.6
% Stools with Blood	< .0001	0.786	None	9.5	3.7 - 24.4
			< Half	7.4	3.0 - 17.8
			≥ Half, < All	6.8	2.7 - 16.8
# Stools/Day	< .001	0.804	1-3	3.1	1.3 - 7.1
			4-6	1.0	0.5 - 2.2
Endoscopic Extent	< .05	0.813	Proctitis/ Proctosigmoiditis	1.1	0.6 - 1.9
			Left-Sided	1.9	1.1 - 3.3

†Contrasts are the level shown vs. the omitted level

RESULTS (cont'd.)

Figure 3.
Relationship Between Induction Dose and the Remaining Significant Predictors of Dose in Order of Model Entry



The percentage of patients initially treated with the low dose declines as the percent of stools with blood and the number of stools per day increases. However, 68.1% of patients with more than 3 stools per day (the ACG Guidelines' definition of a "moderate" patient) received a dose of less than 4.8g/day.

CONCLUSIONS

- Clinicians use a wide range of initial doses of Asacol for induction
- Prior disease and treatment history, symptom severity and disease extent are major determinants of dose selection
- Patients experiencing their first flare are less likely to receive a dose greater than 2.4 g/day, regardless of symptom severity or extent of disease
- As recommended by the ACG Guidelines, physicians may want to consider weighting symptom severity more heavily in their treatment decisions to assure that the moderate patient is appropriately dosed

References:

1. Sandborn WJ, Hanauer SB, Katz S, et al. Efficacy and safety of Asacol 4.8 g/day (800 mg tablet) compared to 2.4 g/day (400 mg tablet) in treating moderately active ulcerative colitis. Paper presented at 69th Annual Scientific Meeting of the American College of Gastroenterology, 2004, Orlando, FL
2. Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. N Engl J Med 1987;317:1625-1629
3. Kornbluth A, Sachar DB. Ulcerative colitis practice guidelines in adults (update). Am J Gastroenterol 2004;99:1371-1385

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