

Diarrhea-Predominant Irritable Bowel Syndrome: Health Outcomes Associated with Loperamide or Bismuth Subsalicylate Therapy

George J. Wan, PhD, MPH¹; Charles Laudadio, MD, MBA¹; Susan C. Bolge, MA²

¹McNeil Consumer & Specialty Pharmaceuticals, Fort Washington, PA; ²Consumer Health Sciences, Princeton, NJ.

ABSTRACT

Objective: To describe health outcomes, including quality of life and satisfaction with medication, in patients with diarrhea-predominant irritable bowel syndrome (DP-IBS) treated with loperamide or bismuth subsalicylate. **Methods:** Cross-sectional data from Consumer Health Sciences June 2003 National Health and Wellness Survey, a nationally representative sample of a noninstitutionalized, U.S. civilian population. Patients were currently taking either loperamide (n=176) or bismuth subsalicylate (n=192) to treat DP-IBS. Quality of life in the past month was assessed using the Medical Outcomes Study (MOS) 8-item Short-Form Health Survey (SF-8). Patient satisfaction with the studied medication (PSM) was measured using a 5-point scale from 1 to 5, with 1=not at all satisfied and 5=extremely satisfied. Satisfaction rates were computed as the percentage of patients reporting a 4 or 5 on the PSM. **Results:** Mean age of patients was 51 years and 77% were female. Quality of life reports were comparable between treatment groups for both the mental and physical component summary scores of the SF-8. Significantly more patients reported that they were satisfied with loperamide (82%; 144/176) versus bismuth subsalicylate (50%; 96/192; $p<0.001$), with an odds ratio of 4.50 (95% CI: 2.80, 7.24). **Conclusions:** Patients taking loperamide or bismuth subsalicylate for DP-IBS reported similar quality of life. However, patients treated with loperamide were 4.5 times more likely to be satisfied with their medication than patients treated with bismuth subsalicylate. These factors may prove important for physicians when considering DP-IBS therapy.

INTRODUCTION

- Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder, marked by:
 - ≥ 12 weeks of abdominal discomfort or pain during the preceding 12 months
 - 2 of the following 3 characteristics: relieved with defecation; onset associated with change in frequency of stool; and/or onset associated with a change in form (appearance) of stool.^{1,2}
- Treatment is based on predominant symptom presentation: constipation-predominant, diarrhea-predominant (DP-IBS), or pain-predominant. Antidiarrheal agents are the recommended course of treatment for DP-IBS.²⁻⁷
- Though not approved for the treatment of DP-IBS, loperamide is an effective treatment for urgency and loose stools that are symptomatic of DP-IBS. Loperamide alone is less effective for pain and bloating.^{2,6} However, loperamide in combination with simethicone effectively reduces gas-related abdominal discomfort.⁸
- Loperamide has become a common treatment for DP-IBS and may be appropriate for long-term use. Loperamide is available as an over-the-counter product, has no anticholinergic component, and does not induce euphoria.³
- Numerous studies have been conducted on the comparable efficacy of loperamide versus bismuth subsalicylate in the treatment of acute diarrhea.⁹⁻¹¹ However, to date, there has been insufficient evidence in the literature to determine relative efficacy in the treatment of DP-IBS.
 - In double-blind studies, loperamide has shown significantly greater efficacy, defined as fewer unformed stools, than bismuth subsalicylate in the treatment of acute diarrhea.⁹⁻¹⁰
 - In an open-label, parallel comparison, loperamide reduced the average number of unformed stools, prevented recurrence of diarrhea for a longer period of time, showed a quicker onset of action, and was rated better in providing overall relief by subjects than bismuth subsalicylate.¹¹
- Treatment satisfaction has recently become an accepted patient-reported outcome in clinical investigations. There are several domains of satisfaction including: symptom relief/efficacy, side-effects, ease and convenience, and impact on quality of life.¹²

OBJECTIVE

- To describe health outcomes, including quality of life and satisfaction with medication, in patients with DP-IBS treated with loperamide or bismuth subsalicylate.

METHODS

Study Sampling Design and Data Collection

- Data were obtained from the Consumer Health Sciences 2003 National Health and Wellness Survey (NHWS), an annual cross-sectional study of attitudes, behaviors, and treatment choices related to healthcare.
- Data were collected through self-administered Internet-based questionnaires in June 2003 from a U.S. nationally representative sample of community-based adults at least eighteen years of age.

Inclusion Criteria for Analysis

- Men and women at least 18 years old.
- Experience DP-IBS (self-reported).
- Report currently taking either loperamide (Imodium[®]) or bismuth subsalicylate (PeptoBismol[®]), but no other prescription or over-the-counter treatment for IBS.

Outcomes Measures

Health-Related Quality of Life (HRQoL)

- HRQoL during the month preceding the questionnaire was assessed using the Medical Outcomes Study (MOS) 8-item Short-Form Health Survey (SF-8).¹³
- The SF-8 is a generic HRQoL measure designed to assess physical functioning, role limitations due to physical health problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health.¹³
- Standardized physical and mental component summary scores are calculated based on the responses.¹³

Treatment Satisfaction

- Patient satisfaction with the studied medication (PSM) was measured using a 5-point scale from 1 to 5, with 1=not at all satisfied and 5=extremely satisfied.
- Satisfaction rates were computed as the percentage of patients reporting a 4 or 5 on the PSM scale.

Statistical Analyses

- Bivariate descriptive analyses were performed to compare loperamide users and bismuth subsalicylate users.
- Significance testing of HRQoL differences was performed using 2-tailed t-tests assuming equal variances.
- Significance testing of treatment satisfaction was performed using Fisher's exact test.

RESULTS

Patient Characteristics (Table 1)

- 368 patients met the inclusion criteria.
 - 176 were taking loperamide (92% reported using Imodium[®])
 - 192 were taking bismuth subsalicylate (100% reported using PeptoBismol[®])
- 77% were female, 85% were Caucasian, and average age was 51 years.
- 64% were diagnosed with IBS, 64% experienced moderate to severe symptoms, and 56% experienced symptoms at least once per week.
- Loperamide and bismuth subsalicylate users did not significantly differ with respect to baseline demographics or disease characteristics.

RESULTS, cont.

Table 1 – Patient Characteristics

	Patient Number (% or SD) (n=368)
Mean Age (SD)	50.8 (15.3)
Females	284 (77%)
Race or Ethnicity	
Caucasian	313 (85%)
African-American	16 (4%)
Other/Decline to Answer	39 (11%)
Diagnosed with IBS	235 (64%)
Severity of IBS Symptoms	
Very mild	39 (10%)
Mild	95 (26%)
Moderate	168 (46%)
Severe	66 (18%)
Frequency of IBS Symptoms	
Daily	24 (7%)
4-6 times per week	44 (12%)
2-3 times per week	93 (25%)
Once per week	46 (12%)
2-3 times per month	91 (25%)
Once per month or less often	70 (19%)

Duration of Treatment (Table 2)

- Though bismuth subsalicylate users have a longer duration of use than loperamide users, more than half of both treatment groups have been treated with their current product for more than five years.

Table 2: Treatment Duration*

	Total (n=368)	Loperamide (n=176)	Bismuth Subsalicylate (n=192)	P Value
Years of Tx				<0.001
< 1	41 (11%)	17 (10%)	24 (12%)	
1 to 4.9	104 (28%)	63 (36%)	41 (21%)	
5 to 9.9	74 (20%)	46 (26%)	28 (15%)	
≥ 10	149 (40%)	50 (28%)	99 (52%)	

*Values may sum to 99% or 101% due to rounding.

Health-Related Quality of Life (Table 3)

- HRQoL reports were comparable between treatment groups both for the mental and physical component summary scores of the SF-8.

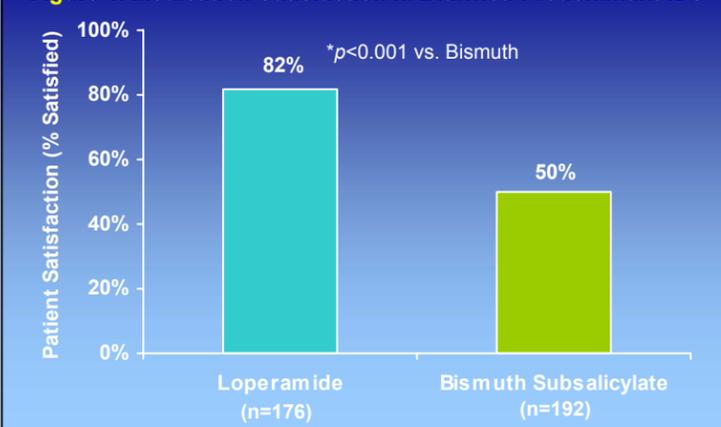
Table 3: Health-Related Quality of Life

Scale score	Statistic	Total	Loperamide	Bismuth Subsalicylate
SF-8 Physical Component Summary Score	Mean	368	176	192
	SD	41.8	41.6	42.0
	Range	11.8	11.8	11.8
		13.2-65.3	15.0-63.1	13.2-65.3
		P = 0.747		
SF-8 Mental Component Summary Score	Mean	368	176	192
	SD	44.5	45.1	43.8
	Range	10.5	10.6	10.5
		16.2-62.6	16.2-62.6	16.4-62.5
		P = 0.235		

Medication Satisfaction (Figure 1)

- Significantly more patients reported that they were satisfied with loperamide versus bismuth subsalicylate treatment (82% versus 50%; $P<0.001$).
- Loperamide users were 4.50 times as satisfied as bismuth subsalicylate users (95% CI: 2.80, 7.24).

Figure 1: Medication Satisfaction in Diarrhea-Predominant IBS



DISCUSSION AND CONCLUSIONS

- Loperamide patients were 4.50 times more likely to be satisfied with their medication than bismuth subsalicylate patients.
- However, while impact on quality of life is a domain of satisfaction, patients taking loperamide or bismuth subsalicylate reported similar HRQoL at a single point in time as measured by the SF-8.
- Differences in satisfaction ratings may be attributed to the domain of symptom relief/effectiveness. Studies comparing efficacy of loperamide versus bismuth subsalicylate in the treatment of acute diarrhea have consistently concluded that loperamide is more effective in reducing frequency of unformed stools, preventing recurrence of diarrhea for a longer period of time, showing a quicker onset of action, and providing overall relief.⁹⁻¹¹
- Other domains of satisfaction, such as side-effects and ease/convenience may contribute to the differences in general satisfaction of loperamide patients versus bismuth subsalicylate patients, and should be investigated in future research.
- Because of the positive correlation of treatment satisfaction and adherence to treatment regimen found in other studies, physicians should consider patient satisfaction in their decision to recommend antidiarrheal agents.¹²

REFERENCES

- Drossman DA, Corazzari E, Talley NJ, Thompson WG, Whitehead WE. Rome II: the functional gastrointestinal disorders: diagnosis, pathophysiology, and treatment: a multinational consensus. *Gut* 1999; 45(suppl 2):1-81.
- Viera AJ, Hoag S, Shaughnessy J. Management of irritable bowel syndrome. *Am Fam Physician* 2002; 66(10):1867-74.
- Mertz HR. Irritable Bowel Syndrome. *N Engl J Med* 2003; 349(22):2136-46.
- Camilleri M. Management of irritable bowel syndrome. *Gastroenterology* 2001; 120(3):652-68.
- Spiller RC. Treatment of irritable bowel syndrome. *Curr Treat Options Gastroenterol* 2003; 6(4):329-37.
- Talley NJ. Pharmacologic therapy for irritable bowel syndrome. *Am J Gastroenterol* 2003; 98(4):750-8.
- Horowitz BJ, Fisher RS. The irritable bowel syndrome. *N Engl J Med* 2001; 344(24):1846-50.
- Kaplan MA, Prior MJ, Ash RR, McKonley KI, Helsner EC, Nelson EB. Loperamide-simethicone vs loperamide alone, simethicone alone, and placebo in the treatment of acute diarrhea with gas-related abdominal discomfort: a randomized controlled trial. *Arch Fam Med* 1999; 8(3):243-8.
- Johnson PC, Ericsson CD, DuPont HL, Morgan DR, Bitsura JA, Wood LV. Comparison of loperamide with bismuth subsalicylate for the treatment of acute travelers' diarrhea. *JAMA* 1986; 255(6):757-60.
- Steffen R. Worldwide efficacy of bismuth subsalicylate in the treatment of travelers' diarrhea. *Rev Infect Dis* 1990; 12(Suppl 1):S80-6.
- DuPont HL, Flores Sanchez J, Ericsson CD, Mendiola Gomez J, DuPont MW, Cruz Luna A, Mathewson JJ. Comparative efficacy of loperamide hydrochloride and bismuth subsalicylate in the management of acute diarrhea. *Am J Med* 1990; 88(6A):15S-9S.
- Shikar R, Rentz AM. Satisfaction with medication: an overview of conceptual, methodological, and regulatory issues. *Value in Health* 2004; 7(2):204-15.
- Ware, JE, Kosinski M, Dewey JE, Gandek B. A Manual for Users of the SF-8 Health Survey. Lincoln, Rhode Island: QualityMetric Incorporated; 2001.

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Disclaimer: Loperamide and bismuth subsalicylate are indicated for the treatment of acute diarrhea and have not been approved for the treatment of DP-IBS.