Factors Leading Patients to Discontinue Multiple Sclerosis Therapies

Kimberly K. Daugherty, J.S. Butler, Michelle Mattingly, and Melody Ryan

ABSTRACT

Objectives: To determine the percentages of patients who discontinued treatment with the multiple sclerosis medications intramuscular interferon beta-1a (IFN-beta-1a; Avonex—Biogen), interferon beta-1b (IFN-beta-1b; Betaseron—Berlex), and glatiramer acetate (Copaxone—Teva) and to determine the factors that led to discontinuation of the medications.

Design: Cross-sectional study.

Setting: University-based neurology clinic.

Patients: 108 patients with multiple sclerosis who were prescribed intramuscular interferon beta-1a, subcutaneous interferon beta-1b, or subcutaneous glatiramer acetate.

Intervention: Telephone survey.

Main Outcome Measures: Discontinuation percentages and the factors that contributed to discontinuation.

Results: There was no significant difference between the percentages of patients who discontinued and did not restart treatment with the products (interferon beta-1b, 41%; intramuscular interferon beta-1a, 34%; and glatiramer acetate, 28%). Four main reasons for medication discontinuation emerged: adverse effects (52%), physician-documented disease progression (40%), patient perception of drug ineffectiveness (20%), and cost (4%). No statistical differences were identified among the three agents for any of the reasons for discontinuation.

Conclusion: Patient education on adverse effects and realistic patient expectations may be potential areas of study to improve discontinuation percentages with these agents.

Keywords: Multiple sclerosis, adherence, persistence, drug-related problems, interferon beta, glatiramer acetate.

J Am Pharm Assoc. 2005;45:371–375.

Received November 20, 2003, and in revised form June 15, 2004. Accepted for publication July 8, 2004.

Kimberly K. Daugherty, PharmD, is Assistant Professor, Department of Pharmacy Practice, Ferris State University, Grand Rapids, Mich.; at the time of this research, she was Primary Care Pharmacy Resident, University of Kentucky, Lexington. J.S. Butler, PhD, is Professor, Division of Pharmacy Practice and Science, University of Kentucky, Lexington. Michelle Mattingly, PhD, is Assistant Professor, Department of Neurology, College of Medicine, University of Kentucky, Lexington. Melody Ryan, PharmD, is Assistant Professor, Department of Pharmacy Practice and Science and Department of Neurology, University of Kentucky, Lexington.

Correspondence: Melody Ryan, PharmD, University of Kentucky Medical Center, 800 Rose Street, C117, Lexington, KY 40536-0293. Fax: 859-323-0069. E-mail: maryan1@email.uky.edu

Disclosure: Teva Pharmaceuticals funded Dr. Daugherty's attendance for poster presentation at the American College of Clinical Pharmacy meeting listed below. Dr. Ryan has received honoraria from Biogen Idec, Berlex Inc., and Teva Pharmaceuticals. Drs. Butler and Mattingly declare no conflict of interest or financial interests in any product or service mentioned in this article, including grants, employment, gifts, stock holdings, or honoraria.

Acknowledgments: To Jingyu Luan for assistance in statistical analysis and Frederick A. Schmitt, Ph.D. and Chantel Dearth, MA, for assistance with scoring and interpretation of the Profiles of Mood States.

Previously presented at the American College of Clinical Pharmacy Spring Practice and Research Forum, Savannah, Ga., April 7–10, 2002.

Multiple sclerosis (MS) is a chronic recurrent inflammatory disorder of the white matter of the central nervous system characterized by injury to the myelin sheaths, the oligodendrocytes, the axons, and the nerve cells.[1] The location of demyelination determines symptom presentation. Common symptoms include visual changes, paresthesias, gait problems, pain, weakness, and tremors.[2] The Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the Multiple Sclerosis Council for Clinical Practice Guidelines recommend that all patients with MS be treated with medications that slow disease progression and prevent relapses.[1]

Intramuscular interferon beta-1a (IFN-beta-1a; Avonex—Biogen), interferon beta-1b (IFN-beta-1b; Betaseron—Berlex), glatiramer acetate (Copaxone—Teva), and subcutaneous interferon beta-1a (Rebif—Serono) are approved for treatment of the relapsing forms of multiple sclerosis (Table 1). All of these agents have demonstrated efficacy over placebo.[3–7] Two trials have prospectively compared these agents in a blinded manner.[8,9]

Discontinuation rates as high as 42% for IFN-beta-1b have been reported during the first 3 months of therapy.[10] Another study with intramuscular IFN-beta-1a showed a 4-month discontinuation rate of 11%.[11] Little work has been performed on discontinuation rates in clinical use with the other treatments. Theories to explain high discontinuation rates include: adverse effects, inadequate medication knowledge, unrealistic patient expectations, and depression.[10–13] However, the degree to which each factor contributes to the overall discontinuation rate is unknown. We undertook a study to define the degree to which these factors contribute to overall lack of persistence with therapy.

AT A GLANCE

Synopsis: Among 108 patients with multiple sclerosis (MS), treatment-discontinuation percentages were statistically similar for three agents approved for treating relapsing forms of the disease, ranging from 28% to 41%. The most frequent determinants of discontinuation included incidence of adverse effects, reported by more than 50% of the patients surveyed, and physician-documented disease progression, reported by 40% of patients.

Analysis: *Treatment with disease-modifying agents is recommended to slow MS progression and reduce relapses for patients with the condition. Previous studies have reported higher percentages of discontinuation for interferon beta-1b (Betaseron—Berlex) than for interferon beta-1a administered intramuscularly (Avonex—Biogen). Discontinuation percentages for glatiramer acetate (Copaxone—Avonex) have not been reported previously. The discontinuation percentages observed in this study were comparable with those of previous reports but did not differ significantly by agent. Patient-reported reasons for discontinuation of treatment also were similar for the three medications.*

Objectives

The objectives of this study were twofold: to determine the proportion of patients who had discontinued IFN-beta-1a, IFN-beta-1b, and glatiramer acetate therapy after prescribing in a university neurology clinic and to determine the factors leading to discontinuation.

Methods

This telephone survey was performed in a university-based neurology clinic. With approval of the institutional review board of the University of Kentucky, the informed consent requirement was waived. Investigators identified subjects through a billing database (*International Classification of Diseases, Ninth Revision,* code 340) and subsequent chart review. Inclusion criteria were: diagnosis of MS; age 18 years or older; and current or any past use of intramuscular IFN-beta-1a, IFN-beta-1b, or glatiramer acetate. Subcutaneous IFN-beta-1a was not available at the time this study was undertaken. Patients were excluded if they had no telephone or access to a telephone, did not speak or understand English, or were unwilling to be interviewed.

Once identified, patients were telephoned and administered a survey designed by the investigators. Patients were removed from the study pool if they could not be reached by telephone in three attempts.

Patients who were no longer using the prescribed study drug were allowed to freely describe the reason or reasons for drug discontinuation, and the investigator categorized the response. The response categories were predetermined based on the investigators' clinical experiences discussing discontinuation with patients and theories advanced to explain medication discontinuation.[10–13] Categories of response included: physician-documented disease progression, patient felt drug was not working, fear of injection, adverse effects, cost, and other. If adverse effects contributed to the discontinuation, the patient was queried regarding the nature of those effects. The same investigator conducted all interviews and categorized all responses to ensure consistency.

Statistical Analysis

The primary endpoints were discontinuation rates for the individual agents and the factors that contributed to discontinuation. For age, length of diagnosis, and mean months of use variables, analysis of variance was used to compare medication groups. Other demographic variables and reasons for medication discontinuation