Changes in Resource Use and Outcomes for Patients With Migraine Treated With Sumatriptan

A Managed Care Perspective

Jennifer H. Lofland, PharmD; Nelda E. Johnson, PharmD; Alice S. Batenhorst, PharmD; David B. Nash, MD, MBA

Background: Migraine headaches result in significant patient suffering and high costs to managed care organizations and employers. Studies that evaluate patient outcomes and the financial consequences of migraine treatment are important from a clinical and an economic perspective.

Methods: This prospective, observational study assessed the outcomes of migraineurs in a mixed model staff/independent practice association managed care organization for patients previously diagnosed as having migraine who received their first prescription for sumatriptan. Data collected included medical as well as pharmacy claims and patient surveys to measure changes in satisfaction, health-related quality of life, workplace productivity, and nonworkplace activity after sumatriptan therapy was initiated.

Results: A total of 178 patients completed the study. Results showed significant decreases in the mean number of migraine-related physician office visits, emergency department visits, and medical procedures in the 6 months after sumatriptan therapy compared with the 6 months before sumatriptan was used (P<.05). Four of the health-related quality-of-life dimensions and the physical component summary score measured by the SF-36 (which is a valid, reliable general health status instrument) showed significant improvements at 6 months compared with patients’ scores before use of sumatriptan (P<.05). Health-related quality of life measured by the disease-specific instrument MSQ (Migraine-Specific Quality of Life Questionnaire-Version 1.0, 1992 Glaxo Wellcome Inc, Research Triangle Park, NC) showed significant improvement at 3 and at 6 months compared with baseline scores (P<.05). There were also improvements in patient satisfaction and significant reductions in time lost from workplace productivity and nonworkplace activity.

Conclusion: In the 6 months after sumatriptan therapy was initiated, health care resource use and time lost from workplace productivity and nonworkplace activity were reduced, while health-related quality of life and patient satisfaction scores improved for the managed care migraineurs enrolled in this study.

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MIGRAINE HEADACHE has been associated with significant medical costs to the health care system, as well as pain and suffering by patients, and the loss in productivity for employers.1-3 For the patient, migraine headaches result in debilitation during a migraine attack as well as impairment in physical, social, and mental health between attacks.3-5 In the United States alone, there are more than 9 million patient visits a year to internal medicine and family practice physicians for the treatment of migraine.6 As a result, the economic burden of migraine is significant, both in terms of the direct costs for medical care as well as the indirect costs associated with patients’ lost productivity at work.4,5,7 In 1992, researchers estimated that US employers may lose up to $17 billion a year because of decreased productivity attributable to migraine6 and that patients spent 3 million days a month bedridden during migraine attacks.8 In addition, studies have shown that patients who have migraine headaches have lower quality of life than do patients who have diabetes, hypertension, or depression.2 The effective treatment of migraine headaches has the potential to benefit not only patients but the health system as well. The serotonin (5HT1) receptor agonist sumatriptan (Imitrex, Glaxo Wellcome Inc, Research Triangle Park, NC) has been shown to be a safe and effective treatment for acute migraine headache and its associated symptoms.9,10 Sumatriptan was first introduced as a subcutaneous injection in 1993, followed by an oral formulation in 1995. In addition to providing relief during an acute migraine attack,
PATIENTS AND METHODS

STUDY SITE AND DESIGN

This was a prospective, observational study conducted at an MCO in Pittsburgh, Pa. This 210,000-member mixed-model MCO had patients in both a staff and an independent practice association. The study protocol was approved by the institutional review board and research committee of the MCO and was designed through the collaborative efforts of the MCO’s medical director and quality manager, outcomes researchers at Thomas Jefferson University, Philadelphia, Pa, and Glaxo Wellcome Inc, Research Triangle Park, NC. A prospective, observational, pretest-posttest study design was used to describe what happened to patients over time after the introduction of the independent variable, sumatriptan. This study design would characterize how patients used and responded to the therapy while under their provider’s care. It was also selected because it would result in the least amount of interference with routine patient care.

PATIENTS

Patients who received new prescriptions for sumatriptan were identified through the MCO's pharmacy prescription authorization system, screened for eligibility criteria by a study coordinator at the MCO, and then invited by telephone to participate in the study. As part of the MCO’s prescription authorization system, patients received a test dose of sumatriptan in the physician’s office before receiving a sumatriptan prescription. This allowed the physician to evaluate patients for response to therapy and potential adverse events.

The injection has also been shown to improve health-related quality of life (HRQoL), decrease health care costs, and decrease workplace productivity lost for patients who have migraine.

Several studies have been conducted to evaluate the impact of sumatriptan on economic, clinical, or social outcomes; however, these studies had several limitations. They were retrospective analyses, were conducted within a clinical trial, and may have not been representative of outcomes from a managed care perspective. In addition, these studies were conducted in a staff-model managed care setting and it is possible that different results may be found in a different managed care model. To address these issues, we conducted a prospective study to measure the economic, patient-centered, and productivity outcomes of using sumatriptan for patients with migraine in a mixed-model managed care organization (MCO).

The primary study objectives were to measure changes in (1) health care resource use; (2) HRQoL; (3) migraine-related workplace productivity; (4) nonworkplace activity; and (5) patient satisfaction with the migraine medications after initiation of sumatriptan therapy.

Eligible patients were those with a physician diagnosis of migraine, who received a new prescription for sumatriptan during the study period (October 1994-August 1996), who had not previously taken any formulation of sumatriptan, who had been continuously enrolled in the MCO for at least 6 months before their first sumatriptan prescription, and who would be continuously enrolled in the MCO for 6 months after study enrollment. Patients who met the inclusion criteria as well as completed a written informed consent form and returned the baseline survey were enrolled in the study.

HEALTH CARE RESOURCE ANALYSIS

Medical and pharmacy claims data were obtained from the MCO for each study patient’s health care encounters for the 6 months prior to study enrollment (before sumatriptan) and the 6 months after the first prescription for sumatriptan (after sumatriptan). Medical claims were classified as either related to migraine or not related to migraine based on the International Classification of Diseases, Ninth Revision, Clinical Modification codes present. Medical claims were then grouped into 1 of 4 categories according to the type of medical service provided: primary care physician office visit, physician specialist office visit, emergency department visits, or hospital admissions. Pharmacy claims were classified as being definitively related to migraine if the medications would only be used for treating migraine headaches (such as dihydroergotamine). If the medication could have been used for multiple indications including migraine (such as narcotic pain medications), the claim was classified as being possibly related to migraine. All other prescription claims were classified as being not related to migraine treatment. These categories were developed from the current literature, information provided by pharmaceutical manufacturers, and clinical pharmacy expertise. All data

RESULTS

PATIENTS

There were a total of 220 managed care patients who were eligible for enrollment during the study period and 206 who completed informed consent. Of these, 178 patients (86%) successfully completed the entire study protocol. Reasons for study dropout included failure to return all surveys (n = 19); no longer a member of the MCO (n = 5); physician changed the patient’s medication (n = 2); pregnancy (n = 1); and lost to follow-up (n = 1). The most common reason patients gave for not returning surveys was lack of time to participate in the study. No patients dropped out due to an adverse effect with the use of sumatriptan.

Of the 178 patients who completed the study, 90% were women (161 women, 17 men), 96% of them were white, and the average age was 39 years (age range, 17-63 years). Most patients had completed high school, were married, and reported the following symptoms associated with their migraine attacks: nausea, phonophobia, photophobia, aura, unilateral migraine, vomiting, and throbbing/pulsating migraine. Approximately 26% of the patients reported having migraine attacks once a month, and 69%
were analyzed using SAS statistical software (version 6.11), with α set at 0.05. Descriptive statistics were used to summarize patient characteristics and Wilcoxon signed rank test was performed to detect significant differences in the number of medical and pharmacy claims in the 6 months before and after sumatriptan therapy.

PATIENT QUESTIONNAIRES

Questionnaires were mailed to patients at their homes for self-completion 3 times during the study. The first questionnaire was completed at baseline after receipt of the first prescription for sumatriptan. Follow-up questionnaires were completed at 3 and at 6 months after enrollment in the study. Each questionnaire consisted of a battery of instruments, including a general HRQoL instrument, a migraine-specific HRQoL instrument, time lost from workplace productivity and nonworkplace activity, and patient satisfaction questions.

HRQoL ANALYSIS

Health-related quality of life was measured using a valid, reliable general health status instrument, the Short Form 36 (SF-36), which has previously been used in patients with migraine.5,11,13,17 The SF-36 was scored according to guidelines published by the Medical Outcomes Trust (Boston, Mass).21 A disease-specific instrument, the MSQ (Migraine-Specific Quality of Life Questionnaire-Version 1.0, Glaxo Wellcome Inc), was used to detect changes in HRQoL as related to migraine following treatment with sumatriptan. The MSQ has been shown to be a reliable and valid instrument for measuring HRQoL in patients with migraine.21,22 Health-related quality-of-life data were analyzed using repeated-measures analyses of variance for all eligible patients (intent to treat) and for those who completed all questionnaires per protocol.

HEALTH CARE RESOURCE USE

Medical Claims

In the 6 months before sumatriptan, the 178 patients had a total of 260 medical claims that were related to migraine. This decreased to a total of 172 migraine-related claims in the 6 months after sumatriptan (34% decrease). There were statistically significant decreases in the number of migraine-related visits to primary care providers and to the emergency department for treatment of migraine in the 6 months before sumatriptan (P<.05) (Table 1). There were no migraine-related hospital claims. When the claims data were analyzed by the number of medical procedures (such as computed tomography or magnetic resonance imaging) performed, there were 138 fewer migraine-related medical procedures in the 6 months before sumatriptan compared with the 6 months after sumatriptan (P<.05). There were no significant changes in nonmigraine-related medical claims.

In a subgroup analysis by dosage form of sumatriptan (oral or injection), the results were similar for all types of medical claims except for emergency department visits. Patients who used injection had a larger, significant decrease of 93% in emergency department visits (P<.05). Those patients using sumatriptan orally had a 70% decrease in emergency department visits.

Pharmacy Claims

The pharmacy claims were further categorized into medication classifications. The categories with the most number of pharmacy claims were antidepressants, nonsteroidal anti-inflammatory agents, β-blockers, narcotics, and barbiturates (Table 2). There appeared to be no significant change in the number of possibly migraine-related pharmacy claims between the before and after period within medication categories. There appeared to be no significant difference in the percentage of all possibly migraine-related prescription claims for each medication category from the periods before and after sumatriptan.

We wanted to determine if the use of sumatriptan decreased the use of other definitely migraine-related medications in the 6 months after sumatriptan. There was
a statistically significant decrease in the mean number of definitely migraine-related pharmacy claims in the 6 months after sumatriptan (P<.05) and a corresponding increase in the use of sumatriptan. The mean number of definitely migraine-related pharmacy claims decreased from 0.24 per patient in the before period to 0.08 claims in the after period. There were 42 pharmacy claims for medications that were definitely related to migraine in the before period compared with 14 in the after period and an increase from 0 to 686 for sumatriptan claims. It should be noted that all pharmacy claims, other than sumatriptan, represent a 1-month supply of medication. Therefore, the number of sumatriptan claims is not directly comparable with the number of pharmacy claims. There were no significant changes in the mean number of claims for medications that were possibly or not related to migraine treatment.

Health-Related Quality of Life

At baseline, the study population had average baseline HRQoL scores that were lower than the general US population normative scores20 in 7 of the 8 dimensions measured by the SF-36. At baseline, only the physical functioning scores were similar to the population norm (Figure 1). Within 3 months, 5 of the SF-36 dimension scores had shown improvement, and at 6 months there were statistically significant improvements in 4 of the HRQoL dimensions (Figure 2). There were clinically significant improvements in 3 dimensions: role-physical, bodily pain, and social functioning (Figure 2). The greatest improvement was seen in role-physical scores, which, on average, improved 25% over baseline. Compared with baseline, bodily pain scores improved by 15%, social functioning scores improved by 10%, and vitality scores improved by 9%. Scores of the remaining dimensions improved to within at least 5.8 points of population norms. In addition to improvements in individual dimension scores, one of the summary scores, the physical component score, showed both a clinical and statistically significant improvement from baseline to 6 months after sumatriptan (P<.05).

In a subgroup analysis by dosage form of sumatriptan (oral or injection), the results showed variability across the different SF-36 dimensions. Patients who used injection had significant improvements in role-physical scores (P<.05). Those patients using sumatriptan orally had significant improvements in vitality and social functioning scores (P<.05).

Health-related quality-of-life scores measured by the disease-specific questionnaire, the MSQ, showed statistically significant improvements in all the measured dimensions within 3 months of starting sumatriptan therapy (Figure 3). Patients showed additional improvement...
improvements in these HRQoL scores 6 months after sumatriptan. Average scores for the role restrictive and emotional dimensions improved by 22% and the role-preventive dimension improved 14% compared with baseline in the 6 months after starting sumatriptan ($P<.05$).

In a subgroup analysis by dosage form of sumatriptan (oral or injection), the results showed statistically significant improvements in all the measured dimensions within 3 months of starting sumatriptan therapy ($P<.05$), for both the oral and injection forms. Patients who used injection showed additional significant improvements in the role restrictive and emotional dimensions at 6 months after sumatriptan ($P<.05$). Those patients using sumatriptan orally showed additional significant improvements in all the measured dimensions at 6 months after sumatriptan ($P<.05$).

**WORKPLACE PRODUCTIVITY AND NONWORKPLACE ACTIVITY**

**Total Disability Time**

Total disability time (workplace productivity time and nonworkplace activity time) improved significantly within 3 months of starting sumatriptan and continued to show an improvement 6 months after treatment started. At baseline, patients reported missing an average of 16 days from workplace and nonworkplace activities due to migraine in the 3 months before using sumatriptan. In the 3 months after starting sumatriptan, patients reported missing on average 11 days of workplace and nonworkplace activities due to migraine, and, at 6 months, patients reported missing on average 8 days of workplace and nonworkplace activities in the preceding 3 months (Figure 4). This change was statistically significant at 3 months and at 6 months ($P<.05$). Overall, patients gained an average of 8 additional days of combined workplace productivity time and nonworkplace activity time 6 months after starting sumatriptan. This combined gain was a result of several factors including (1) missing fewer days of work due to migraine, (2) reductions in time loss while working during a migraine attack, (3) missing fewer days of nonworkplace activities, and (4) reductions in time loss from nonworkplace activities during a migraine attack.

**Workplace Productivity**

On average, the number of workdays reported missed due to migraine decreased by 0.5 days in the 3 months after starting sumatriptan and continued to decrease 6 months after starting sumatriptan. At 6 months, the number of workdays reported missed had decreased by an additional 0.7 days in the preceding 3 months ($P<.05$) (Table 3). Patients also reported a significant decrease in the amount of time that they worked while migraine symptoms were present. At baseline, patients reported working on average 4 days with migraine symptoms in the 3 months preceding sumatriptan therapy. At 6 months,
this decreased to 2 days worked with migraine symptoms in the preceding 3 months ($P<.05$).

### Nonworkplace Activity

On average, the number of days reported missing from nonworkplace activities due to migraine decreased by 2 days in the 3 months after starting sumatriptan and continued to decrease 6 months after starting sumatriptan. At 6 months, the number of days reported missing from nonworkplace activities had decreased by a total of 3 days in the preceding 3 months ($P<.05$) (Table 3). In addition, the number of days in which nonworkplace activities were performed while migraine symptoms were present decreased by an average of 2 days from baseline to 6 months ($P<.05$).

### Patient Satisfaction

At baseline, more than half the patients reported that they were either dissatisfied with how well their migraine medication worked, how well their migraine medication worked for other migraine symptoms, or how easy the medication was to use. After starting sumatriptan therapy, patient satisfaction scores improved dramatically. Within 3 months, more than 64% of the patients reported that they were very satisfied with how well their medication worked (Figure 5), 50% were very satisfied with how fast the medication worked, and more than 80% were very satisfied with how easy sumatriptan was to use. Patients who used the oral form of sumatriptan were more likely to be very satisfied with the ease of use (90% very satisfied) than those who used the injection (70% very satisfied) at 6 months. Patients who used the injection form of sumatriptan were more likely to be very satisfied with how fast sumatriptan worked (67% very satisfied) than those who used sumatriptan orally (36% very satisfied) at 6 months.

Our study reports the data we analyzed from patients who completed the entire study. However, we also analyzed data for all patients who completed at least 1 follow-up questionnaire (intent to treat) and found no significant differences in the study results. In addition, since only 2 patients (1.1%) were withdrawn from the study because their physician discontinued the use of sumatriptan, it is unlikely that data from these individuals would have changed the overall findings of the study.

This study examined the changes in outcomes for managed care patients who began using sumatriptan for the treatment of acute migraine headaches. The results of our study showed that in the 6 months after using sumatriptan, patients made fewer visits to their primary care providers and had fewer visits to the emergency department for treatment of migraine. This study also showed that patients experienced improvements in HRQoL and reductions in time lost from workplace productivity and nonworkplace activity after starting sumatriptan therapy. These results can help health care providers and formulary decision makers better quantify the potential benefits of using the 5HT$_1$ serotonin receptor agonist, sumatriptan, within the context of a mixed model MCO.

Our findings are consistent with the results of other studies within different MCO models, including a prospective study previously completed in a large staff-model MCO. Results were similar to previous investigations even though our study was (1) conducted in a mixed-model MCO, (2) did not use specific migraine diagnostic criteria for study entry, and (3) did not provide patients unlimited access to sumatriptan doses as did other studies. Since our protocol did not exclude patients with mild migraine headaches, our results may be more applicable to the general population of managed care patients with migraine who receive sumatriptan prescriptions.

There are several findings in our study that are particularly interesting. We found that the disease-specific HRQoL questionnaire, the MSQ, was able to detect small but significant improvements in HRQoL within 3 months of starting sumatriptan. Even though general health status instruments are considered less sensitive than disease-specific instruments in measuring the effects of therapeutic treatments on HRQoL, the changes in HRQoL were detected with the SF-36 within 6 months of therapy. However, MCOs that wish to measure outcomes for patients with migraine to support the National Council for Quality Assurance (NCQA) accreditation may want to use a disease-specific questionnaire such as the MSQ to save time.

Patients missed more days of nonworkplace activities than days missed from work. It is likely that patients are re-
luctant to miss work but continue to suffer the effects of migraine while at home. For the age group included in our study, a reduction in the number of days lost from nonworkplace activities has the potential to provide a significant benefit to migraine sufferers, their families, and society.

Throughout the study, the productivity and HRQoL measures continued to improve from baseline to 6 months. Since this investigation had a limited timeline of 6 months, we were not able to determine if this trend would have continued. However, in an open-label, 42-month, clinical trial, patients had significant improvements in HRQoL with long-term use of sumatriptan therapy for migraine.28 The most notable improvements occurred during the first 6 to 12 months, and were sustained over the 42-month study period. It is possible that similar results may have been demonstrated in our patient population had the study continued longer than 6 months.

As with many other outcomes studies, our study has some limitations that include not being a randomized study or including an external control group. However, since patients served as their own controls and repeated measures were conducted over time, we believe that the changes in health care resources were most likely due to the initiation of sumatriptan. We found that only the migraine-related health care visits decreased and that there were no changes in medical claims for nonmigraine-related visits, showing that there was a general trend toward decrease resource use. There were no concurrent migraine initiative programs implemented by the MCO during the time of this study.

Because our study did not include a control group, the effects of sumatriptan on HRQoL, time lost from workplace productivity, time lost from nonworkplace activity, and patient satisfaction may be difficult to distinguish from the effects of participating in an observational research study. Even though contact with the patients was limited to intermittent telephone follow-up, it is possible that the effects of participating in a study could have influenced the patients’ self-reports. Patients may have thought there was an improvement in these subjective measures simply because they knew they were participating in a study.

Another limitation of this investigation is that it does not report cost data. Such cost information would be of great interest. We are currently analyzing the cost data associated with the health care resource use, lost workplace productivity, and nonworkplace productivity data. This information will be published at a later date.

The findings of this study offer evidence that sumatriptan counters the detrimental effects of migraine headaches to patients. The improvements in health care resource use, HRQoL, and reductions in time lost from workplace productivity and nonworkplace activity suggest that the clinical benefits of sumatriptan may also translate into reduced migraine-related costs for the patient, the MCO, and employers.

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Reprints: Jennifer H. Lofland, PharmD, Office of Health Policy and Clinical Outcomes, Thomas Jefferson University, 1015 Walnut St, Suite 621, Philadelphia, PA 19107.

REFERENCES


described in our patients. There was no sex predominance, the median time from initiation of ticlopidine therapy to the onset of symptoms was 3 weeks (range, 1-16 weeks), and there was a 50% (11/22) mortality rate in patients who did not receive plasma exchange therapy compared with 24% (9/38) in those who received plasma exchange therapy.

The incidence of ticlopidine-associated TTP is unknown and cannot be determined from case series. Steinhubl et al identified 9 cases of TTP out of 43,322 patients treated with ticlopidine following coronary stenting in 1996 and 1997 in 63 centers throughout the United States and Canada. This suggests that the incidence of ticlopidine-associated TTP is 0.02%. Bennett et al identified 5 cases of TTP out of 7842 patients who received coronary stents followed by ticlopidine therapy between July 1996 and December 1997 in a single metropolitan area in the United States. Their estimated frequency of ticlopidine-associated TTP was 0.06%. These results contrast with an estimated population incidence of TTP of 0.0004%. However, based on a review of the diagnostic codes of patients readmitted following coronary stent placement performed in California, Brown found that TTP was rare. No cases of TTP were identified in 16,819 patients who had coronary stents placed in 1996, although the rate of ticlopidine therapy for this indication in 1996 was not specified.

Clopidogrel is an antiplatelet agent that selectively inhibits the adenosine diphosphate receptor. Since its release in 1998 in the United States for prevention of stroke, there have been trials involving more than 19,000 patients, and no association with TTP has been reported. Given its antiplatelet effects and the absence to date of complicating blood dyscrasias, clopidogrel therapy may provide a safer alternative to ticlopidine therapy. This remains to be confirmed by randomized prospective clinical trials.

Although based on case reports, the accumulation of cases of ticlopidine-associated TTP makes a progressively stronger argument for causation. This is further supported by the large multicenter retrospective trial that found an increased incidence of TTP in patients receiving ticlopidine therapy following coronary stent placement compared with the estimated incidence of TTP in the general population. Because of the serious and potentially fatal outcomes resulting from TTP, physicians and patients should be made aware of this complication of ticlopidine therapy. The development of safer alternative agents should also be pursued.

Danny K. Chen, MD
David M. C. Sutton, MD
Toronto, Ontario


In the Original Investigation titled “Changes in Resource Use and Outcomes for Patients With Migraine Treated With Sumatriptan,” published in the April 26 issue of the ARCHIVES (1999;159:857-863), several errors were inadvertently printed. The corrections appear below, with corrected terms in italic typeface.

**Errors in Chronology.** On page 859, the third sentence in the first paragraph of the “Medical Claims” subsection of “Health Care Resource Use” should have read as follows:

There were statistically significant decreases in the number of migraine-related visits to primary care providers and to the emergency department for treatment of migraine in the 6 months after sumatriptan (P<.05) (Table 1).

The fifth sentence in that same paragraph should have read as follows:

When the claims data were analyzed by the number of medical procedures (such as computed tomography or magnetic resonance imaging) performed, there were 138 fewer migraine-related medical procedures in the 6 months after sumatriptan compared with the 6 months before sumatriptan (P<.05).

**Errors in Expansion of Abbreviations.** On page 860, the legends to Figure 1 and Figure 2 incorrectly state that the abbreviation RP indicates role-playing. The correct expansion of RP in both figures is role-physical.

**Errors in P Values.** On page 861, the legend of Figure 4 incorrectly reports 2 P values as being less than .049. They are actually less than .05 (P<.05).