Patient Preferences for Migraine Therapy: Subcutaneous Sumatriptan Compared with Other Medications

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Background. This study was conducted to identify, from the patient's perspective, the important attributes of a migraine therapy and to assess the performance of subcutaneous sumatriptan, aspirin, acetaminophen, and patients' usual therapies with respect to these attributes.

Methods. Six hundred forty-eight patients who had received subcutaneous sumatriptan (one or two doses, 6 mg per dose, for a single migraine episode) or placebo in a clinical trial completed questionnaires.

Results. According to patients, the four most important attributes of a migraine therapy are "how well it works," "how safe it is," "how fast it works," and "side effects." The least important attribute is "cost of drug." Subcutaneous sumatriptan received significantly more favorable scores than did aspirin, acetaminophen, or patients' usual therapies with respect to the attributes of how well it works, how fast it works, and number of doses needed to relieve pain. Subcutaneous sumatriptan was also rated more favorably than either aspirin or patients' usual therapies with respect to side effects. Acetaminophen and aspirin were rated significantly more favorably than subcutaneous sumatriptan on the attributes "easy to take" and "easy to buy." Asked which drug they would use again for migraine, more patients selected subcutaneous sumatriptan than any other single medication. More patients also ranked subcutaneous sumatriptan as the best overall performer compared with other migraine medications taken in the last 12 months.

Conclusions. These data indicate that according to patients' preferences, subcutaneous sumatriptan possesses many of the attributes of an ideal migraine therapy.

Key words. Sumatriptan; migraine; headache; consumer satisfaction; patient satisfaction; injections, subcutaneous. (*J Fam Pract 1995; 41:147-152*)

It has been reported that at least four of 100 Americans suffer from migraine,[1] a condition characterized by episodes of moderate to severe headache that may be accompanied by photophobia, phonophobia, nausea, and vomiting. In a United States survey involving 600 migraineurs, most patients reported experiencing two to three migraine episodes per month, and more than one half of the patients indicated that migraine caused them to miss at least one day per month of work.[2] Patients' responses indicated that they were far less effective (mean=58%) when they work during a migraine episode. Consistent with these data reflecting the debilitating aspect of migraine, measurements of health-related quality of life reveal that the impact of migraine on mental health, pain, and physical functioning is at least as great as the impact of chronic conditions such as arthritis, diabetes, and gastrointestinal disease.[3]

The serotonin ($5HT_1$) receptor agonist sumatriptan was introduced in 1993 in the United States for the treatment of acute migraine with or without aura.[4] In two double-blind, parallel-group clinical studies conducted in the United States[5] and one conducted internationally,[6] subcutaneous sumatriptan (6 mg) reduced moderate or severe headache to mild or no headache by 1 hour after administration in 70% to 72% of patients, compared with 22% to 25% of placebo-treated patients ($P<.001$). Relief generally began within 10 minutes of dosing and peaked 90 minutes to 120 minutes thereafter. Subcutaneous sumatriptan was effective regardless of whether it was used to treat migraine with aura or migraine without aura, and whether the headache was treated sooner or later than 4

Submitted, revised, March 20, 1995.

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ISSN 0094-3509

hours after onset.[6] The most common adverse event after subcutaneous administration of sumatriptan was burning, redness, or stinging at the injection site, which occurred in about 60% of patients in these studies.

Patients' perceptions regarding subcutaneous sumatriptan and other migraine medications were assessed in the two United States studies. Patients completed a questionnaire in which they were asked to identify important attributes of a migraine medication and to rate the performance of subcutaneous sumatriptan and other migraine medications, particularly aspirin and acetaminophen, with respect to these attributes. The results of this survey are described in this report.

Methods

Patients

Eligible patients were adults who had a ≥1-year history of migraine, diagnosed according to International Headache Society criteria,[7] and had participated in one of two clinical trials[5] in which they had received either sumatriptan, 6 mg subcutaneously, or placebo for a migraine episode during one clinic visit. Some sumatriptan-treated patients whose headache was not alleviated 1 hour after this treatment received a second administration of 6 mg of sumatriptan subcutaneously.

Procedure

A questionnaire was mailed to 940 of 1104 patients who had received either subcutaneous sumatriptan (6 mg; one or two doses) or placebo in one of two clinical trials. In the questionnaire, patients were asked to use a 5-point Likert-type scale (ranging from 1=important to 5=unimportant) to rank the importance of 10 medication attributes that influence their choice of treatment: (1) how well it works, (2) how safe it is, (3) how fast it works, (4) side effects, (5) physician recommendation, (6) number of doses needed to relieve pain, (7) total treatment cost, (8) how easy it is to buy, (9) how easy it is to take, and (10) cost of the drug.

In the second section of the questionnaire, patients were asked to list the medications they normally take for migraine and to rate these medications and subcutaneous sumatriptan, identified only as "the experimental drug they received in a recent study," with respect to the 10 medication attributes. Because sumatriptan-treated patients had been exposed to subcutaneous sumatriptan only during a clinical trial, they could not accurately evaluate it on the attributes of cost of the drug or total treatment cost. Therefore, these two attributes were not included in the performance ratings for subcutaneous sumatriptan. Patients were also asked to rate aspirin and acetaminophen if they had ever used these medications for a migraine. For all attributes except side effects, total treatment cost, and cost of drug, medications were rated on a 6-point scale, ranging from 1=very good to 5=very poor, and 6=no opinion. Side effects were rated on a separate 6-point scale, from 1=none to 5=severe, and 6=no opinion. Total treatment cost and cost of drug were each rated on another 6-point scale, from 1=very inexpensive to 5=very expensive, and 6=no opinion.

Patients' weightings of the importance of the various attributes of a medication were made independently of the medication. The properties of a particular medication (eg, sumatriptan) were thus independent of the importance of the attributes to the patients.

In the last section of the questionnaire, patients were asked to list the medications they would use again to treat a migraine and to rank migraine medications taken during the past 12 months according to overall performance (1=best performer, 2=second-best performer, etc).

Statistical Analysis

Statistical significance was set at $P<.05$. Differences in the importance rankings of the 10 medication attributes were established using 95% confidence intervals (CI) around the means.

Performance ratings for the four medication groups (subcutaneous sumatriptan, acetaminophen, aspirin, or usual therapy) with respect to the medication attributes were compared between sumatriptan- and placebo-treated patients using analysis of variance (ANOVA). This comparison was made to determine whether, as expected, patients who received placebo rated attributes of the experimental drug differently from those patients who received sumatriptan. It was also important to determine whether the placebo group rated acetaminophen, aspirin, or usual therapy differently from the sumatriptan group. Differences in performance ratings on the medication attributes were also compared between medication groups (subcutaneous sumatriptan, acetaminophen, aspirin, or usual therapy) using ANOVAs.

For each medication that patients indicated they would use again to treat a migraine episode, the number and percentage of patients who indicated that they would use the medication again were tabulated. For each medication patients had taken during the last 12 months, the number and percentage of patients ranking that medication first, second, or third best overall performer were tabulated.

Results

Respondent Characteristics

Eleven of the 940 questionnaires were undeliverable by the post office. Six hundred forty-eight of the remaining 929 questionnaires were completed and returned. Analyzable responses were obtained from 70% (648/929) of sampled patients. Of the 648 respondents, 418 (65%) received either one (n=205) or two (n=213) administrations of subcutaneous sumatriptan during a clinical trial; 189 (29%) respondents received placebo only. The treatment that 41 (6.3%) respondents received during the clinical trial could not be determined. Respondents represented approximately 59% of the 1104 participants in the two United States clinical trials, and respondents' distribution across treatment groups (one dose sumatriptan vs two doses sumatriptan vs placebo) was similar to that of the 1104 clinical trial participants. Because preliminary analyses revealed that the questionnaire responses of patients receiving one dose vs two doses of sumatriptan did not systematically differ, the data from these two groups were combined for analysis of the patient preference results.

Demographic characteristics of respondents are depicted in Table 1. Most respondents indicated that they had two or three migraine episodes per month, and over 90% of respondents rated their migraine episodes as being either severe or very severe (Table 1). Medications that patients normally took for a migraine episode included Tylenol (acetaminophen, 29.2% of patients), Demerol (meperidine, 24.7% of patients), Fiorinal (butalbital, aspirin, caffeine; 23.6% of patients), Midrin (isomethептene, dichloralphenazone, acetaminophen; 23.5% of patients), Tylenol with codeine (22.8% of patients), and aspirin (22.1% of patients).

Table 1. Characteristics of Respondents (N=648)

Characteristic	Percentage
Sex	
Men	10.2
Women	88.4
Not reported	1.4
Age, y	
19–24	2.9
25–34	21.1
35–44	39.5
45–54	23.9
55–64	10.2
65–77	0.9
Not reported	1.4
Education	
≤Grade school*	0.2
Some high school	2.6
High school diploma	19.1
Technical school	6.6
Some college	31.9
College degree	19.0
Some graduate school	8.2
Graduate degree	10.8
Other	1.5
Migraine attack frequency	
<1 per month	4.6
1 per month	14.0
2 per month	23.8
3 per month	23.8
1 per week	12.2
2 to 3 per week	15.6
4 to 6 per week	4.0
Daily	1.4
Not reported	0.6
Migraine severity	
Very severe	49.1
Severe	43.2
Moderate	7.1
Mild	0.2
Very mild	0.0
Not reported	0.5

**Grade school includes grades 1 through 8.*

Questionnaire Data

Important Attributes of Migraine Therapy

According to patients, the most important of the 10 attributes of a migraine therapy is how well it works (Table 2). Over 99% of respondents rated this attribute as being important (mean score=1). How safe it is and how fast it works, which had the same mean importance ratings, were the second most important attributes (Table 2). Side effects was rated as an important attribute by 65% of patients and was the next most important attribute. The least important attributes were easy to take and cost of drug.

Migraine Medications' Performance Ratings on Important Attributes

Performance ratings for subcutaneous sumatriptan were significantly different ($P<.05$) between patients who had received subcutaneous sumatriptan in the clinical trial (n=418) and patients who had received placebo (n=189). In contrast, performance ratings for aspirin, acetaminophen, and patients' usual therapy did not differ significantly between patients who had received subcutaneous sumatriptan and patients who had received placebo. Therefore, in statistical comparisons of performance ratings among the four medication groups (subcutaneous sumatriptan, aspirin, acetaminophen, usual therapy), performance ratings for subcutaneous sumatriptan were based on data from patients who had received subcutaneous sumatriptan in a clinical trial, while

Table 2. Patient-Rated Importance of the Attributes of a Migraine Medication

Migraine Medication Attribute	Mean	95% CI	% of Respondents Rating Attribute Important	Relative Importance of Attribute to Patients*
How well it works	1.00	0.99–1.02	99.8	A
How safe it is	1.18	1.14–1.22	86.5	B
How fast it works	1.18	1.15–1.22	84.6	B
Side effects	1.45	1.41–1.49	64.5	C
Physician recommended	1.61	1.54–1.68	61.1	D
No. of doses to relieve pain	1.63	1.56–1.70	57.3	D
Total treatment cost	1.81	1.72–1.90	53.7	E
How easy to buy	2.01	1.92–2.09	42.1	F
How easy to take	2.22	2.13–2.31	32.8	G
Cost of drug	2.32	2.22–2.43	32.6	G

**Attributes are listed in descending order of importance from A to G. Attributes assigned the same letter were rated equivalently. CI denotes confidence interval.*

performance ratings for acetaminophen, aspirin, and patients' usual therapy were based on data from patients who had received either subcutaneous sumatriptan or placebo.

Subcutaneous sumatriptan received more favorable scores than aspirin, acetaminophen, or patients' usual therapy on the attributes of how well it works, how fast it works, and the number of doses needed to relieve pain (Figure 1). Subcutaneous sumatriptan was also rated significantly more favorably than either aspirin or patients' usual therapy with respect to side effects (Figure 1). Acetaminophen and aspirin were rated significantly more favorably than subcutaneous sumatriptan on the attributes of easy to take and easy to buy. For the attribute easy to take, mean scores were 2.72 for subcutaneous sumatriptan, 1.70 for usual therapy, 1.64 for aspirin, and 1.57 for acetaminophen. For the easy-to-buy attribute, mean scores were 4.21 for subcutaneous sumatriptan, 2.23 for usual therapy, 1.19 for aspirin, and 1.21 for acetaminophen.

Asked which medication they would use again for migraine, more patients selected subcutaneous sumatriptan than any other single medication (Figure 2; data from sumatriptan- and placebo-treated patients pooled). Seventy-two percent of patients treated with subcutaneous sumatriptan in a clinical trial indicated that they would use it again. Also, more patients ranked subcutaneous sumatriptan as the best overall performer compared with other migraine medications that they had taken in the last 12 months. Two hundred sixty-eight patients (41.4%) ranked subcutaneous sumatriptan as the best overall performer. Demerol (meperidine) and Midrin

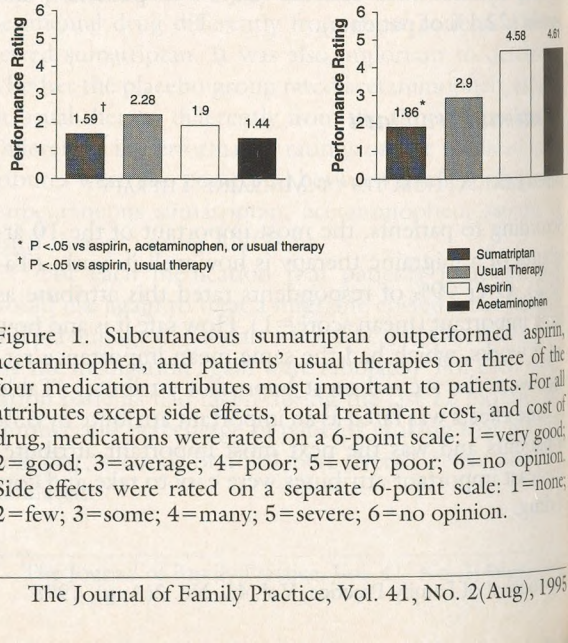

Figure 1. Subcutaneous sumatriptan outperformed aspirin, acetaminophen, and patients' usual therapies on three of the four medication attributes most important to patients. For all attributes except side effects, total treatment cost, and cost of drug, medications were rated on a 6-point scale: 1=very good; 2=good; 3=average; 4=poor; 5=very poor; 6=no opinion. Side effects were rated on a separate 6-point scale: 1=none; 2=few; 3=some; 4=many; 5=severe; 6=no opinion.

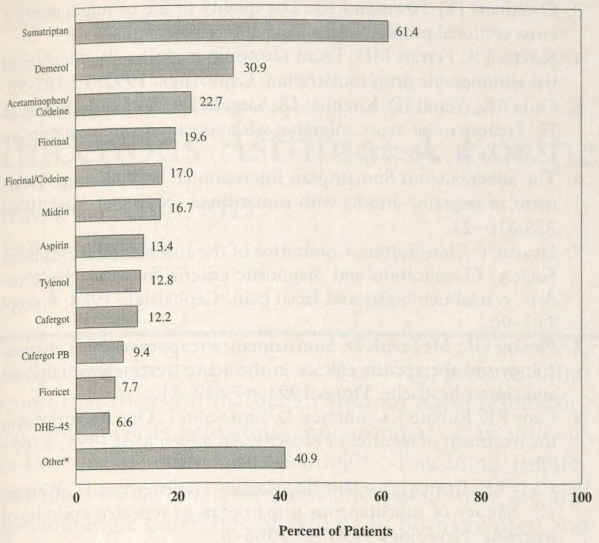

Figure 2. More patients indicated that they would take subcutaneous sumatriptan compared with any other single migraine medication again for migraine. Note: Percentages sum to greater than 100% because some patients listed more than one medication. Each percentage represents the fraction of the 648 patients surveyed.

(isometheptene, dichloralphenazone, acetaminophen), the medications that received the next most favorable ratings for overall performance, were ranked as best by 85 patients (13.1%) and 31 patients (2.8%), respectively.

Discussion

The results of this study indicate that migraineurs view subcutaneous sumatriptan more favorably than aspirin, acetaminophen, or their usual therapy with respect to medication attributes they consider important. Subcutaneous sumatriptan was rated significantly more favorably than patients' usual therapy on three of the four attributes patients consider most important: how well it works, how safe it is, how fast it works, and side effects. Patients overwhelmingly preferred sumatriptan to their usual therapies, aspirin, or acetaminophen, perhaps because subcutaneous sumatriptan ranked highest on attributes they considered most important. Seventy-two percent of patients who had received subcutaneous sumatriptan in a clinical trial indicated that they would use it again. Furthermore, when compared with other medications taken during the last 12 months, subcutaneous sumatriptan was ranked as best overall performer by the greatest number of patients.

With respect to the attributes of easy to take and easy to buy, patients rated subcutaneous sumatriptan less favorably than their usual therapy, aspirin, or acetaminophen. Since patients had received sumatriptan in a clinical trial, they had no previous experience in buying the drug. Thus, ratings for sumatriptan on the attribute of easy to buy were made on the basis of conjecture, rather than personal experience. Unlike sumatriptan, which is currently available only in an injectable formulation, aspirin, acetaminophen, and some other migraine medications are available in tablet form and are nonprescription drugs. The relative ease associated with obtaining and administering these over-the-counter tablet preparations may have contributed to patients' perceptions that they are easier to buy and take than subcutaneous sumatriptan. Apparently, easy to take and easy to buy, which, along with cost of drug, were ranked as important by the fewest patients, are not as influential as other attributes in determining patients' satisfaction with a medication and their willingness to use it. Indeed, more patients selected subcutaneous sumatriptan than any other single medication as the drug they would use again to treat a migraine episode.

Subcutaneous sumatriptan was rated more favorably than other medications for migraine by patients who had received either one or two doses for a single migraine episode. In contrast, aspirin, acetaminophen, and patients' usual therapy had probably been used repeatedly over the long term to treat separate migraine episodes. Whether patients' ratings of subcutaneous sumatriptan used over the long term are as favorable as ratings after treatment of a single migraine episode is a subject of ongoing study. It would be particularly interesting to examine patient preferences for sumatriptan since concerns about its safety in patients with cardiovascular disease have arisen[8] and the phenomenon of headache recurrence after sumatriptan has been shown to occur in some patients.[9] The clinical efficacy and tolerability of subcutaneous sumatriptan is consistently maintained with repeated administration for separate migraine episodes.[10] If patients' perceptions correspond with clinical data, the favorable patient ratings should also be consistent with repeated administration.

The patients surveyed in this study had participated in a sumatriptan clinical trial. Most of these patients were long-term migraine sufferers who may have been experienced patients and who may have used a variety of medications during their migraine histories. Although the sample is probably representative of the population of migraineurs that receives treatment, it is not known how representative this sample is of the general migraine population, including those who do not seek treatment.

Incorporating patient ratings such as these into clinical studies is an important step in thoroughly evaluating the therapeutic significance of a drug, as patients' percep-

tions of a medication may affect their willingness to use it as well as to comply with a therapeutic regimen. Subcutaneous sumatriptan has favorable efficacy and safety profiles, and patients in this study rated it more positively than their other migraine medications on attributes they considered most important.

Acknowledgments

This research was sponsored by Glaxo Research Institute, Research Triangle Park, North Carolina.

References

1. Stang PE, Osterhaus JT. Migraine headache in the 1989 National Health Interview Survey: demographics. Headache 1992; 32:258.
2. Osterhaus JT, Gutterman DL, Plachetka JR. Healthcare resource and lost labour costs of migraine headache in the US. Pharmacoeconomics 1992; 2:67–76.
3. Osterhaus JT, Townsend RJ. The quality of life of migraineurs: a cross sectional profile. Cephalalgia 1991; 11(suppl 11):103.
4. Saxena PR, Ferrari MD. From serotonin receptor classification to the antimigraine drug sumatriptan. Cephalalgia 1992; 12:187–96.
5. Cady RK, Wendt JD, Kirchner JR, Sargent JD, Rothrock JF, Skaggs H. Treatment of acute migraine with subcutaneous sumatriptan. JAMA 1991; 266:2831–5.
6. The Subcutaneous Sumatriptan International Study Group. Treatment of migraine attacks with sumatriptan. N Engl J Med 1991; 325:316–21.
7. Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Cephalalgia 1988; 8(suppl 7):1–96.
8. Plosker GL, McTavish D. Sumatriptan: a reappraisal of its pharmacology and therapeutic efficacy in the acute treatment of migraine and cluster headache. Drugs 1994; 47:622–51.
9. Cady RK, Rubino J, Crummett D, Littlejohn T. Oral sumatriptan in the treatment of recurrent headache. Arch Fam Med 1994; 3:766–72.
10. Cady RK, Dexter J, Sargent JD, Markley H, Osterhaus JT, Webster CJ. Efficacy of subcutaneous sumatriptan in repeated episodes of migraine. Neurology 1993; 43:1363–8.