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Research Submission

Patients' Preference for Migraine Preventive Therapy

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Objective.—Preventive treatment is an important part of migraine therapy. When prescribing medication, physicians should understand patients' treatment preferences and select drugs that most closely meet their patients' needs. Understanding the factors that influence patients' preference increases physicians' ability to select appropriate migraine therapy. However, unlike acute migraine treatment, patients' preferences for migraine preventive treatment have never been studied.

Methods.—We enrolled 250 patients who attended the Jefferson Headache Center and Sao Paulo Headache Center and had a primary headache diagnosis. Patients' age, gender, body mass index (BMI), headache diagnosis, headache frequency, duration, and intensity, headache disability (by MIDAS), and current preventive treatments were ascertained. Patients were asked to rate 7 aspects of headache prevention (efficacy, speed of onset, out-of-pocket expenses, adverse events, formulation of therapy, type of treatment, and frequency of dosing) in order of importance (1-7). Each patient also evaluated 12 different clinical scenarios, each one containing a simulation of 2 hypothetical headache preventive treatments, wherein patients could choose Product A, Product B, or neither. Patients were informed of each product's efficacy data (50%, 75%, or 100% headache elimination), adverse event profile (weight gain, concentration difficulty, and/or fatigue), and dosing frequency (once every 3 months, once per day, or twice per day).

Results.—Most patients were Caucasian. Mean BMI was 26.55 $\pm$ 5.34, range (17-45). Mean history of headache was 20.93 years. Fifty patients (40%) had 45 or more headache days in the past 3 months. Mean headache intensity score (0-10 scale) was 5.7 $\pm$ 1.8. Patients were on various preventive treatments, including β-blockers (48 [41%]), calcium-channel blockers (19 [16%]), antidepressants (52 [44%]), antiepileptics (46 [39%]), neurotoxins (16 [14%]), vitamins/herbal therapies (28 [24%]), and nonmedicinal therapy (38 [32%]). Of the 7 aspects of migraine prevention that patients were asked to rate, 72% rated effectiveness the most important aspect. Twelve percent rated speed of onset most important, 6% rated absence of adverse events most important, 3% rated formulation of therapy most important, 3% rated out-of-pocket expenses most important, and 2% rated type of treatment (prescription/vitamin) most important. None rated frequency of dosing as the most important factor. In the area of preventive treatment scenarios, patients were more likely to choose treatments with higher efficacy rates, fewer adverse events and less frequent dosing schedule. Patients indicated that they preferred the treatment options with higher efficacy rates even if side effects were present and a more frequent dosing schedule was necessary.

Conclusion.—Patients' preference regarding migraine prevention is very important in headache management. Patients rated efficacy the most important aspect in preventive therapy and preferred treatment options with higher efficacy rates. Future studies are needed for a better understanding of patients' preference for migraine prevention.

Key words: migraine, preventive treatment, preference

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Preventive treatment is a crucial part of migraine therapy. Indications for migraine prevention include (i) migraine that significantly interferes with the patient's daily routine despite acute treatment; (ii) failure, contraindication to, or troublesome side-effects from acute medications; (iii) overuse of acute medications; (iv) special circumstances, such as hemiplegic migraine; (v) very frequent headaches; or (vi) patient preference.[1]

When prescribing medication for patients with migraine, physicians should respect patients' treatment preferences and select drugs that most closely meet patients' needs.

Understanding which factors influence patients' preference increases physicians' ability to select appropriate migraine therapy; however, patients' preferences regarding migraine preventive treatment have never been studied.

Different approaches have been used to study patient preference for acute migraine therapy. Migraineurs in the general population were surveyed to discover which attributes of acute migraine therapy they considered important.[2] Complete pain relief and no recurrence were rated as important or very important attributes by 87% of patients, followed by rapid onset of pain relief (83%), lack of adverse events (79%), and relief of associated symptoms (76%).[2]

Davies et al[3] studied patient satisfaction with acute migraine treatment and its relationship to clinical trial end points. More than 90% of patients who were pain-free at 2 hours were satisfied with their acute treatment. Sixty to 80% of patients with mild pain were satisfied at 2 hours and 10% of patients with persistent pain were satisfied at 2 hours postdosing.

Hamelsky et al[4] used the willingness-to-pay approach, a more patient-centered strategy for assessing patient preferences for treatment characteristics. Four different domains (speed of relief, consistency of relief, lack of adverse events, and recurrence) were analyzed. The study indicated that a migraine sufferer would be willing to pay $225 per year ($5.6 billion in aggregate) for relief of most severe migraine pain. This is approximately 2.5 times greater than current expenditures in the US on migraine therapy overall.[5]

Patient preference for triptans was also studied. Rizatriptan 10 mg and sumatriptan 50 mg were compared.[6,7] Whether patients preferred rizatriptan or sumatriptan, about 50% identified more rapid pain relief as the most important determinant of preference, followed by only 7% who cited rapid return to normal activity.

One of the major limitations of preventive therapies for migraine prevention is their adverse event profile.[8] Tricyclic antidepressants, neuromodulators, calcium-channel blockers, and β-blockers are the main treatment options. Little is known about how adverse events influence patient preferences. We designed and executed this study to evaluate patients' preference for migraine preventive therapy.

PATIENTS AND METHODS

This was an international clinic-based study. We recruited 250 patients, 125 from the Sao Paulo Headache Center, Brazil and 125 from the Jefferson Headache Center, USA. IRB approval was obtained from both centers, patients gave written informed consent. Age, gender, body mass index (BMI), headache diagnosis, headache frequency, duration, and intensity, headache disability (by MIDAS) and patients' current preventive treatments were ascertained. Race, education, income, and demographic data were similar in both populations, therefore only the cultural aspect was different.

Patients were asked to rate seven aspects of headache prevention (efficacy, speed of onset, out-of-pocket expenses, adverse events, formulation of therapy, type of treatment, and frequency of dosing) in order of importance (1 to 7). Each patient also evaluated 12 different clinical scenarios, each one containing a simulation of 2 hypothetical headache preventive treatments, wherein patients could choose Product A, Product B, or neither. Each product had efficacy data (50, 75, or 100% of headache elimination), adverse event profile (weight gain, concentration difficulty, and/or fatigue), and dosing frequency (once every 3 months, once per day, or twice per day). The questionnaire was interviewer-administered. Interviewers were trained in a like manner to ensure uniform administration of the questionnaire.

Discrete choice modeling, a method that has been widely used in patients preference research,[9-11] was

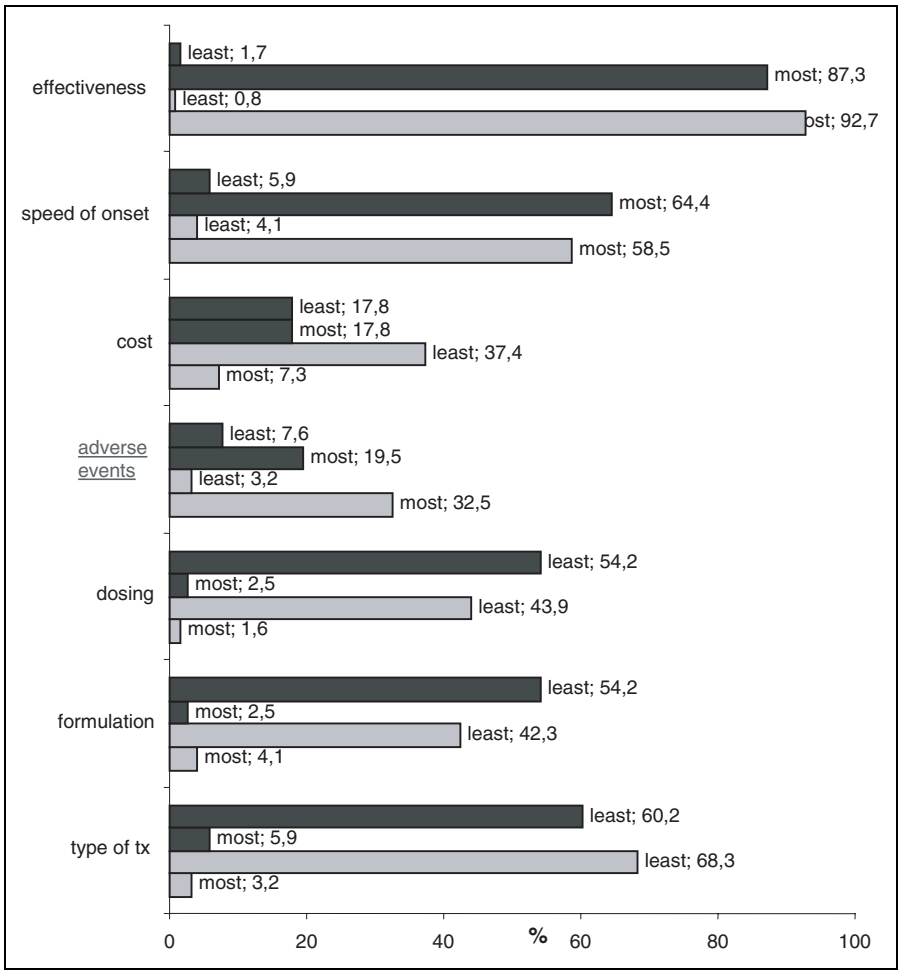

Fig 1.—Distribution of aspects rated by patients, for each country. Most or second most important aspect (most important bar), and least important aspects (least important bar). Numbers are reported in percentages. Black = USA population. Gray = Brazilian population. "Most" represents the most important aspect rated, "Least" represents the least important aspect rated.

used. Discrete choice describes various alternatives (different migraine preventive medications) to respondents in terms of their characteristics ("attributes") and the specific assumptions ("levels") for each of those characteristics. For example, one attribute we studied was efficacy of a migraine treatment, with 3 possible levels: 50% of headaches eliminated, 75% of headaches eliminated, and 100% of headaches eliminated. Other attributes studied included dosage frequency and whether each of 3 potential side effects occurred. By asking respondents which alternatives they most prefer, and observing patterns in the choices made by respondents, one can statistically determine which attributes are most important in driving patient preference, and the extent to which a desirable level on one attribute (eg, lack of a side effect) can or cannot offset an undesirable level on another (eg, lower efficacy, or inconvenient dosing).

We included men or women 18 to 65 years old who had a migraine diagnosis for at least 1 year. We excluded patients with secondary headache disorders. Both episodic and chronic/transformed migraine patients were surveyed.[12,13]

RESULTS

Most patients were Caucasian. In the American population, 114 were Caucasian, 8 African American, 1 Hispanic, and 2 Asian. In the Brazilian population, 97 were Caucasian, 4 African American, 22 Pardo/mixed, and 2 Asian. Mean BMI was 26.55 ± 5.34, range (17-45). Mean history of headache was 20.93 years. Ninety patients (36%) had 45 or more headache days in the

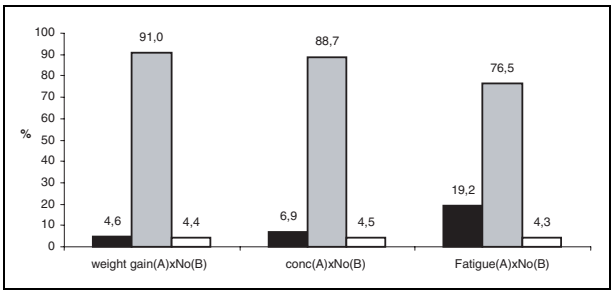

Fig 2.—Patients' preference for migraine preventive therapy according to presence or absence of adverse events. First set of bars comparing Product A causing weight gain versus Product B without weight gain, second set of bars comparing Product A causing concentration difficulties versus product B without it, third set of bars comparing Product A causing fatigue versus Product B without it. Black bar: medication with side effect, gray bar = medication without side effect, white bar = neither.

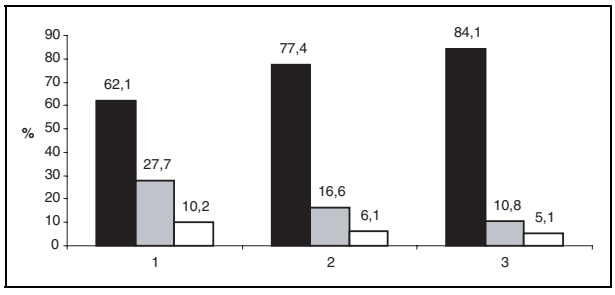

Fig 4—Patients' preference for migraine preventive therapy according to 100% versus 50% efficacy with or without side effects. Black bar = patients' preference for product with 100% efficacy and side effect; gray bar = patients' preference for product with 50% efficacy without side effect; white bar = patients' preference for neither product; 1 = with or without weight gain 2 = with or without concentration problems 3 = with or without fatigue. First set of bars comparing Product A has 100% efficacy causing weight gain versus Product B, which has 50% efficacy without side effects, second set of bars comparing Product A has 100% efficacy causing concentration difficulties versus Product B, which has 50% efficacy without side effects, third set of bars comparing Product A has 100% efficacy causing fatigue versus Product B, which has 50% efficacy without side effects.

past 3 months. Mean headache intensity score (0-10 scale) was 5.7 ± 1.8. Patients were on various preventive treatments, including β-blockers (48 [41%]), calcium-channel blockers (19 [16%]), antidepressants (52 [44%]), antiepileptics (46 [39%]), neurotoxins (16 [14%]), vitamins/herbal therapies (28 [24%]), and nonmedicinal therapy (38 [32%]). These characteristics were similar between the 2 populations.

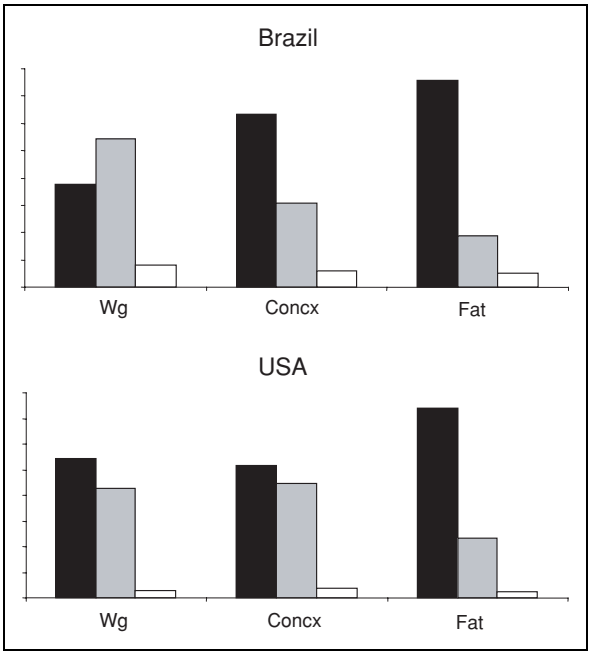

Fig 3.—Patients' preference for migraine preventive therapy according to 100% versus 75% efficacy with or without side effects in the Brazilian population (first bar graph) and USA (second bar graph). Black bar = patients' preference for product with 100% efficacy and adverse event; gray bar = patients' preference for product with 75% efficacy without adverse event; white bar = patients' preference for neither product; Ef = percent headache elimination; Wg = weight gain; Concx = concentration problems >Fat = fatigue.

Of the 7 aspects of migraine prevention that patients were asked to rate, most patients in both populations rated efficacy the most important aspect. Figure 1 shows the distribution of aspects according to what patients rated most or second most important (most important bar), and least important aspects (least important bar). In both the USA and Brazilian populations, efficacy (72%) was followed by speed of onset (12%), absence of side effects (6%), out-of-pocket expenses (3%), formulation of therapy (3%), type of treatment (prescription/vitamin) (2%), and dosing.

In the analysis of preventive treatment scenarios, patients were more likely to choose treatments with higher efficacy rates, fewer adverse events, and a less frequent dosing schedule. When patients separately compared weight gain, concentration problems, and fatigue to a hypothetical medication without those adverse events, the preference was for a medication with fewer adverse events (Fig. 2). Still, as many as 19.2% still prefer a medication despite having fatigue as an adverse event. In the Brazilian population, when 100%

efficacy is combined with weight gain, compared with 75% efficacy without weight gain, patients preferred the second option; however, when concentration or fatigue was taken into account, patients still preferred the more efficacious product. In contrast to the Brazilian population, American patients preferred a 100% efficacy rate even if weight gain occurs (Fig. 3). When a 100% efficacy medication with side effects is compared with a 50% efficacy treatment without side effects, the most effective option was preferred by both populations (Fig. 4).

The results did not change when previous use of preventive therapy, MIDAS results, BMI, and headache frequency were analyzed.

DISCUSSION

Patient preference for acute migraine treatment has been studied, but patient preference for preventive therapy had never been evaluated. This is a unique study, one of the first to evaluate patient preference for migraine preventive treatment. Asking patients about attributes may not be the same as what they experience or decide when taking the drug. We are considering initiation here rather than long term follow up.

Patients preferred treatment options with higher efficacy rates, even if adverse events occurred and a more frequent dosing schedule was needed. The only exception was in the Brazilian population, where a preventive therapy with 75% reduction in frequency without weight gain was preferred over a medication with 100% response rate with weight gain. This may be explained by cultural differences, wherein Brazilians may be more concerned with weight changes than Americans. When 100% rates with weight gain were compared with 50% rates without weight gain, respondents from both countries preferred higher efficacy. The trend of migraine patients to prefer more efficacious therapies should be studied in more detail.

Fatigue and concentration difficulty are common in headache patients pretreatment, and markers for disability in many conditions, patients may think they cannot get more fatigued, modifying their responses.

Clinical endpoints in trials comparing different treatment modalities in migraine prevention should emphasize response rates, higher than 50% in order to bridge the gap between patients' preferences and the treatment options available. Patient preference in migraine prevention is a key aspect in headache management. Future studies are needed for a better understanding of preferences in migraine preventive treatment.

Conflict of Interest: None

REFERENCES

1. Silberstein SD, Goadsby PJ. Migraine: Preventive treatment. *Cephalalgia*. 2002;22:491-512.
2. Lipton RB, Stewart WF. Acute migraine therapy: Do doctors understand what patients with migraine want from therapy? *Headache.* 1999;39(suppl 2):S20-S26.
3. Davies GM, Santanello N, Lipton R. Determinants of patient satisfaction with migraine therapy. *Cephalalgia.* 2000;20:554-60.
4. Hamelsky SW, Lipton RB, Stewart WF, Suh D, Greenberg M, Schneider D. An assessment of the burden of migraine using the willingness to pay model [abstract]. *Cephalalgia.* 2001;21:336.
5. Hu XH, Markson LE, Lipton RB, Stewart WF, Berger ML. Burden of migraine in the United States: Disability and economic costs. *Arch Intern Med.* 1999;159:813-818.
6. Loder E, Brandes JL, Silberstein S, Skobieranda F, Bohidar N, Wang L, Boyle D, Kolodny A, Guerra F, Santanello N, Johnson-Pratt L. The Rizatriptan Protocol 060 Study Group. Preference comparison of rizatriptan ODT 10-mg and sumatriptan 50-mg tablet in migraine. *Headache.* 2001;41:745-753.
7. Pascual J, Bussone G, Hernandez JF, Allen C, Vrijens F, Patel K. Rizatriptan-Sumatriptan Preference Study Group. Comparison of preference for rizatriptan 10-mg wafer versus sumatriptan 50-mg tablet in migraine. *Eur Neurol.* 2001;45:275-283.
8. Young WB, Hopkins MM, Shechter AL, Silberstein SD. Topiramate: A case series study in migraine prophylaxis. *Cephalalgia*. 2002;22:659-663.
9. Sculpher M, Bryan S, Fry P, de Winter P, Payne H, Emberton M. Patients' preferences for the management of non-metastatic prostate cancer: Discrete choice experiment. *BMJ.* 2004;328: 382.
10. Bridges JF. Stated preference methods in health care evaluation: An emerging methodological paradigm in health economics. *Appl Health Econ Health Policy.* 2003;2:213-224.

11. Haughney J, Partridge MR, Vogelmeier C, et al. Exacerbations of COPD: Quantifying the patient's perspective using discrete choice modelling. *Eur Respir J.* 2005;26:623-629.
12. 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):10-73.
13. Silberstein SD, Lipton RB, Sliwinski M. Classification of daily and near-daily headaches: Field trial of revised IHS criteria. *Neurology.* 1996;47:871-875.