Efficacy of Sumatriptan Tablets in Migraineurs Self-Described or Physician-Diagnosed as Having Sinus Headache: A Randomized, Double-Blind, Placebo-Controlled Study

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ABSTRACT

Background: Many patients and physicians interpret episodic headache in the presence or absence of nasal symptoms as "sinus" headache, while ignoring the possible diagnosis of migraine.

Objective: The purpose of this study was to assess the efficacy and tolerability of sumatriptan succinate 50-mg tablets in patients with migraine presenting with "sinus" headache.

Methods: A randomized, double-blind, placebo-controlled, multicenter study was conducted in adult (aged 18–65 years) migraine patients presenting with self-described or physician-diagnosed "sinus" headache. From November 2001 to March 2002, patients meeting International Headache Society criteria for migraine (with ≥2 of the following: unilateral location, pulsating quality, moderate or severe intensity, aggravation by moderate physical activity; and ≥1 of: phonophobia and photophobia, nausea and/or vomiting) and with no evidence of bacterial rhinosinusitis were enrolled and randomized in a 1:1 ratio via computer-generated randomization schedule to receive either 1 sumatriptan 50-mg tablet or matching placebo tablet. The primary efficacy end point was headache response (moderate or severe headache pain reduced to mild or no headache pain) at 2 hours after administration. The presence or absence of migraine-associated symptoms and sinus and nasal symptoms was also measured. Tolerability was assessed through patient-reported adverse events (AEs).

Results: Two hundred sixteen patients with self-described or physician-diagnosed "sinus" headache received a migraine diagnosis and treated 1 migraine attack with sumatriptan 50 mg. The efficacy (intent-to-treat) analysis included 215 patients treated with sumatriptan 50 mg (n = 108; mean [SD] age, 39.6 [12.3] years; mean [SD] weight, 77.7 [17.7] kg; sex, 71% female; race, 69% white) or placebo (n = 107; mean [SD] age, 41.0 [11.3] years; mean [SD] weight 80.7 [20.9] kg; sex, 69% female; race, 64% white). Significantly more patients treated with sumatriptan 50 mg achieved a positive headache response at 2 and 4 hours after administration compared with those treated with placebo (69% vs 43% at 2 hours and 76% vs 49% at 4 hours, respectively; both, $P < 0.001$). Significantly more sumatriptan-treated patients were free from sinus pain compared with placebo recipients at 2 hours (63% vs 49% placebo, $P = 0.049$) and 4 hours (77% vs 55%, $P = 0.001$). All treatments were generally well tolerated. The most common drug-related AEs reported in the sumatriptan and placebo groups, respectively, were dizziness (5% vs <1%), nausea (3% vs 2%), other pressure/tightness (defined as sense of heaviness; heaviness of upper body, upper extremities; jaw tension; neck tension) (4% vs 0%), and temperature sensations (defined as warm feeling of back of neck, or flushing) (2% vs 0%). No patients experienced any serious AEs.

Conclusions: Sumatriptan 50-mg tablets were effective and generally well tolerated in the treatment of these patients presenting with migraine headaches that were self-described or physician-diagnosed as sinus headaches. (*Clin Ther.* 2007;29:99–109)

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INTRODUCTION

In the American Migraine Study II,[1] a population-based survey conducted in 1999 to examine the epidemiology of migraine in the United States, it was estimated that 28 million people suffer from migraine, but 52% of individuals meeting International Headache Society (IHS) criteria for migraine (≥2 of the following: unilateral location, pulsating quality, moderate or severe intensity, aggravation by moderate physical activity; and ≥1 of: phonophobia and photophobia, nausea and/or vomiting)[2] reported that they had not been diagnosed with migraine.

Many people with migraine report that their work/school productivity is reduced by at least half (51%), that they are unable to do household chores (76%), or that they miss family, social, and leisure activities (59%) because of their headaches.[3,4] In addition, because migraine predominantly affects people in midlife, with a peak prevalence around the age of 40 years,[1] many are in their most productive work years. Loss of productive time in the workplace due to migraine entails a large economic burden, estimated at $5.6 to $17 billion annually in the United States.[5] Because of the substantial impact of migraine and the availability of effective treatments, it is important to diagnose and treat migraine headaches appropriately.

If, as the aforementioned estimate suggests, many people with migraine who are substantially impacted by their headaches are not receiving a migraine diagnosis, what diagnoses and treatments are they receiving? Among the people with undiagnosed migraines in the American Migraine Study II, 42% reported a physician diagnosis of "sinus" headache. This suggests that a large proportion of unrecognized migraine might be treated as "sinus" headache.[1] A study conducted by Lipton et al[6] also found that "sinus" headache is one of the terms most commonly used by patients with undiagnosed migraine to identify their headaches, particularly by patients aged ≥40 years. Other studies[7,8] have also suggested that many people with migraine might receive a "sinus" headache diagnosis instead of, or in combination with, a migraine diagnosis.

A 2004 study[9] of 2991 patients with self-described or physician-diagnosed "sinus" headache found that as many as 88% of these patients actually met diagnostic criteria for migraine or migrainous headache as established by the IHS.[2] Eighty-six percent of these patients were significantly impacted by their headaches.[8] Sixty-seven percent of patients expressed some level of dissatisfaction with their current headache treatment, which included nonnarcotic analgesics (86%), NSAIDs (71%), decongestants (56%), and antihistamines (47%). These findings suggest that patients who are significantly impacted by their headaches and dissatisfied with their current treatment should be reassessed for a possibly more accurate diagnosis. If diagnosed with migraine, they might benefit from migraine-specific treatment.

Small (including ~30–50 patients), open-label studies[10,11] have suggested that sumatriptan succinate 50 mg was effective in the treatment of migraine headaches that were patient-described or physician-diagnosed as "sinus" headaches. The efficacy and tolerability profile was similar to that observed when sumatriptan was used to treat other migraine headaches, with a majority of patients preferring sumatriptan to their baseline headache therapy. Therefore, the purpose of this study was to confirm the efficacy of sumatriptan 50-mg tablets versus placebo in the treatment of migraine headaches in patients with self-described or physician-diagnosed "sinus" headaches.

SUBJECTS AND METHODS

This randomized, double-blind, placebo-controlled, single-attack, parallel-group study was conducted at 26 sites in the United States (GlaxoSmithKline Protocol SUM40298) from November 2001 to March 2002. The study protocol, any amendments, the informed consent, and other information that required preapproval were reviewed and approved by a national, regional, or investigational center ethics committee or institutional review board representing each center. The study was conducted in accordance with the guideline of Good Clinical Practice[12] and all applicable regulations, including the 1996 version of the Declaration of Helsinki.[13] All patients provided written informed consent prior to study enrollment. Participating clinicians were compensated on the basis of work performed in the process of implementing a study protocol at their site, including, but not limited to, recruiting, screening, tracking, monitoring, and medically supervising their staff and sub-

jects. Subjects received small honoraria to cover inconveniences associated with participation, such as travel costs and time.

Inclusion and Exclusion Criteria

Patients' typical "sinus" headache symptoms and history were carefully reviewed at screening to determine whether their symptoms and history satisfied IHS diagnostic criteria for migraine with or without aura (1.1 or 1.2).[2] To exclude patients with an existing acute infectious process, those with radiographic evidence of sinus infection within the previous 3 months, fever, and/or purulent or discolored nasal discharge indicative of an infection were not allowed to participate.[14–17]

So that only adults with episodic migraine were enrolled, patients were required to meet the following criteria: age 18 to 65 years; ≥6 self-described or physician-diagnosed "sinus" headaches in the 6 months prior to screening; no previous diagnosis of migraine; and no previous use of migraine-specific medications, such as 5-hydroxytryptamine 1 agonists (5-$HT_{1B/1D}$), ergotamine, or ergot-like medications. Patients with evidence of chronic daily headaches (>15 headache-days per month), a rebound headache pattern caused by analgesics in the previous 3 months, basilar or hemiplegic migraine, cluster headache, or tension headache were also excluded.

Because the use of sumatriptan is contraindicated in patients with cardiovascular or cerebrovascular disease, patients were excluded from study participation for the following reasons: confirmed or suspected ischemic heart disease, Prinzmetal's angina, ischemic abdominal syndromes, peripheral vascular disease, Raynaud's disease, cardiac arrhythmias requiring medication, clinically significant electrocardiogram abnormalities, history of cerebrovascular pathology (eg, cerebrovascular accident), congenital heart disease, or inadequately controlled hypertension (sitting systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥95 mm Hg). The use of sumatriptan concurrently with monoamine oxidase inhibitors is also contraindicated, and patients using these medications within 2 weeks of screening were excluded.

This study sought to assess the efficacy of sumatriptan for the relief of traditional migraine symptoms as well as sinus symptoms. Therefore, patients were instructed not to use any acute analgesics, antiemetic treatment, other acute headache medications, or sinus/nasal medications (eg, antihistamines, nasal sprays, decongestants) within 24 hours before or 2 hours after using the study medication. The patients were also instructed not to use ergotamine or ergot-type medications (eg, dihydroergotamine and methysergide) and other 5-$HT_{1B/1D}$ agonists within 24 hours before or after using study medication.

Lastly, patients were excluded for the presence of other factors that might have compromised the safety of the patient or the interpretation of the data, such as the following: history of epilepsy; impaired renal or hepatic function; pregnancy, attempt to become pregnant, breastfeeding, or use of unapproved methods of birth control; evidence of alcohol or substance abuse within 1 year of screening; and participation in an investigational drug trial within 4 weeks of screening.

Study Design

Two study visits were conducted: visit 1 at screening and visit 2 at study exit. At visit 1, patients provided headache and medical histories and demographic information and received a physical examination, including measurement of vital signs. Vital signs included sitting heart rate and blood pressure measurements (systolic and phase V diastolic) following 5 to 10 minutes of rest. Female patients received a urine pregnancy test. Patients also completed a baseline Headache Impact Test 6-item questionnaire (HIT-6™, Quality Metric, Inc., Lincoln, Rhode Island).[18–20]

Patients who met inclusion/exclusion criteria and gave informed written consent were randomized in a 1:1 ratio to receive either 1 sumatriptan 50-mg tablet or a matching placebo tablet. Randomization schedules were computer-generated (SAS Version 8.2; SAS Institute Inc., Cary, North Carolina), and treatment assignments were sealed and remained intact throughout the study. Enrolled patients were required to treat their next headache, previously defined as a "sinus" headache, with the study medication and record their headache symptoms in a diary. Patients were instructed to wait until moderate or severe head pain was experienced before administering study medication. Any patient who had not treated a headache within 6 weeks of screening was withdrawn from the study.

After the patients treated 1 attack, they returned for a follow-up assessment within 24 hours after treatment. At visit 2 (study exit), urine pregnancy tests were performed for patients of childbearing potential, and menstruating female patients were required to

provide the date of the first day of their most recent menstrual period. Diary and follow-up assessments were collected and patients were queried regarding adverse events (AEs) they might have experienced during the study.

Measures

Headache *response* (a reduction in headache pain severity from moderate or severe to mild or no pain with no use of additional migraine or sinus/nasal medication) was patient-rated using a 4-point pain scale (0 = no pain, 1 = mild pain, 2 = moderate pain, 3 = severe pain) and recorded at baseline (study drug administration) 30 minutes, 1 hour, 2 hours, and 4 hours after administration. The primary efficacy end point of this study was defined as the percentage of patients with moderate or severe headache pain who experienced headache response (reduction to mild or no pain) 2 hours after treatment.

The percentage of patients who experienced headache response and the percentage of patients who were *pain-free* (a reduction from moderate or severe predose pain to no pain) at 30 minutes, 1 hour, and 4 hours after administration were secondary end points. The presence of nausea, vomiting, photophobia, or phonophobia was reported at baseline and recorded as secondary efficacy end points at 30 minutes, 1 hour, 2 hours, and 4 hours after administration. The presence of sinus and nasal symptoms was also reported at baseline and recorded as secondary efficacy end points at 30 minutes, 1 hour, 2 hours, and 4 hours after administration. Sinus and nasal symptoms included runny nose, nasal congestion, sinus pain, sinus pressure, watery eyes, itchy nose, postnasal drip, and sneezing. The percentage of patients using additional migraine or sinus/nasal medication within 2 to 24 hours after administration was also assessed.

Health Outcomes

Patients completed the HIT-6 questionnaire at screening. The HIT-6 is a validated 6-item questionnaire developed to quantify the degree to which headache impacts a patient's life.[18–20] Results of the HIT-6 questionnaire are presented as a total score. In general, scores of ≥60 indicate very severe impact of the headache on the patient's life; 56 to 59, substantial impact; 50 to 55, some impact; and <50, little to no impact. The reliability and validity of the HIT-6 have been established.[18–21]

Tolerability

During the study exit visit, patients were asked about the occurrence of AEs. Overall assessments of tolerability were based on the prevalence of AEs, medical and headache history, physical examination, vital sign changes from screening, or electrocardiograms (when clinically indicated).

Statistical Analysis

Assuming percentages of patients with headache response at 2 hours of 60% for sumatriptan 50 mg and 30% for placebo, ~75 patients per group were required to detect a statistically significant difference between groups with a power of 95% and significance level of 5%.[22] All tolerability analyses were performed in the safety population, which included all patients who were randomized and treated. All efficacy analyses were performed in the intent-to-treat (ITT) population, which included patients in the safety population who provided an evaluation of their randomized treatment. All statistical tests were conducted using SAS Version 8.2 software with 2-sided alternative hypotheses, using exact analysis methods (eg, Fisher exact test), controlling for center. The last observation carried forward methodology was used for missing data points. Descriptive statistics are presented for patient demographics and tolerability. The HIT-6 was scored according to the algorithm provided by the developers of the instrument.

RESULTS

Patients

Two hundred twenty-six patients were randomized (112 to placebo and 114 to sumatriptan). Ten patients did not experience a migraine attack within the specified time frame. The safety population consisted of 216 patients who self-treated for 1 migraine attack (sumatriptan 50 mg, n = 108; placebo, 108). One patient randomized to the placebo group who used the study medication did not return diary data and was included in the withdrawal group. The ITT population consisted of 215 patients who treated 1 attack and completed diaries (sumatriptan 50 mg, n = 108; placebo, 107). Two patients, both in the placebo group, discontinued from study participation and were lost to follow-up.

Demographics and Baseline Symptoms

The patient characteristics are listed in **Table I.** The treatment groups were similar with respect to age, sex,

Table I. Baseline demographics of patients with migraine headaches previously defined as "sinus" headache.

Characteristics	Sumatriptan 50 mg (n = 108)	Placebo (n = 107)
Age, y		
Mean (SD)	39.6 (12.3)	41.0 (11.3)
Median	41	43
Range	18–70	18–60
Weight, kg		
Mean (SD)	77.7 (17.7)	80.7 (20.9)
Median	75	79
Range	50–146	48–153
Sex, % female	71	69
Race, no. (%)*		
White	74 (69)	69 (64)
Black	20 (19)	22 (21)
Hispanic	11 (10)	13 (12)
Asian	2 (2)	0
Other	1 (1)	3 (3)
Migraine diagnosis, no. (%)*		
Without aura	98 (91)	96 (90)
With aura	2 (2)	4 (4)
Both	8 (7)	7 (7)
Baseline HIT-6 score†		
Mean (SD)	62.0 (5.8)	61.8 (6.2)
Median	62	63
Range	47–78	42–78
Headache symptoms, no. (%)		
Unilateral pain	65/108 (60)	64/107 (60)
Throbbing pain	89/108 (82)	84/107 (79)
Pain worsens w/ physical activity	74/106 (70)	79/106 (75)
Aura prior to treatment	17/108 (16)	12/107 (11)

HIT-6 = Headache Impact Test 6-item questionnaire.
*Percentages may not total 100 due to rounding.
† Scores of ≥60 indicate very severe impact of headache on the patient's life; 56 to 59, substantial impact; 50 to 55, some impact; and <50, little to no impact.[18-20]

and race. The majority of patients were white (64%–69%) and female (69%–71%), had a diagnosis of migraine without aura (90%–91%), and had baseline HIT-6 questionnaire scores ≥60 (median score, 62–63), suggesting that these patients were generally representative of a typical migraine patient population and severely impacted by their headache. Patients' reporting of aura prior to administration was also similar to that seen in other migraine studies (16% in the sumatriptan 50-mg group vs 11% in the placebo group). Migraine pain was moderate or severe at the time of drug administration as required by the protocol (99% in the sumatriptan 50-mg group vs 98% in the placebo group). Unilateral pain was reported by 60% of patients in both treatment groups. Most patients also reported that their pain worsened with physical activity (70% in the sumatriptan 50-mg group vs 75% in the placebo group).

The prevalence of traditional migraine symptoms and sinus/nasal symptoms at baseline is shown in **Tables II** and **III**, respectively. The sinus/nasal symptoms reported most frequently at baseline in the sumatriptan and placebo groups were sinus pain (78% and 81%, respectively) and sinus pressure (91% and 92%,

Table II. Migraine symptoms present at baseline and 2 and 4 hours after treatment with sumatriptan 50 mg in patients with migraine previously defined as "sinus" headache.

Characteristics	Sumatriptan 50 mg (n = 108)	Placebo (n = 107)
Nausea, no. (%)		
Baseline	34 (31)	30 (28)
2 hours	19 (18)	12 (11)
4 hours	10 (9)	14 (13)
Photophobia/ phonophobia, no. (%)		
Baseline	70 (65)	65 (61)
2 hours	21 (19)*	34 (32)
4 hours	12 (11)*	26 (24)
Vomiting, no. (%)†		
Baseline	1 (1)	0
2 hours	1 (1)	0
4 hours	1 (1)	0

*$P < 0.05$ vs placebo.
†The same patient reported vomiting at all 3 time points.

Table III. Sinus and nasal symptoms at baseline and 2 and 4 hours in patients treating migraine previously defined as "sinus" headache with sumatriptan 50 mg or placebo.

Characteristics	Sumatriptan 50 mg (n = 108)	Placebo (n = 107)
Runny nose, no. (%)		
Baseline	39 (36)	23 (21)
2 hours	27 (25)	13 (12)
4 hours	24 (22)	17 (16)
Nasal congestion, no. (%)		
Baseline	79 (73)	66 (62)
2 hours	51 (47)	36 (34)
4 hours	41 (38)	32 (30)
Sinus pain, no. (%)		
Baseline	84 (78)	87 (81)
2 hours	40 (37)*	55 (51)
4 hours	25 (23)*	48 (45)
Sinus pressure, no. (%)		
Baseline	98 (91)	98 (92)
2 hours	51 (47)	60 (56)
4 hours	39 (36)	50 (47)
Watery eyes, no. (%)		
Baseline	32 (30)	43 (40)
2 hours	11 (10)	17 (16)
4 hours	12 (11)	17 (16)
Itchy nose, no. (%)		
Baseline	30 (28)	21 (20)
2 hours	7 (6)	8 (7)
4 hours	11 (10)	10 (9)
Postnasal drip, no. (%)		
Baseline	37 (34)	35 (33)
2 hours	23 (21)	19 (18)
4 hours	25 (23)	22 (21)
Sneezing, no. (%)		
Baseline	25 (23)	15 (14)
2 hours	7 (6)	7 (7)
4 hours	11 (10)	9 (8)

*$P < 0.05$ versus placebo.

respectively). Concomitant medications used by ≥5% of patients are listed in **Table IV.**

Headache Response and Migraine-Associated Symptoms

Significantly more patients treated with sumatriptan 50 mg achieved a positive headache response at 2 hours after administration (primary efficacy end point) compared with those treated with placebo (69% vs 43%, respectively; $P < 0.001$). The percentage of patients who achieved headache response at 2 and 4 hours after administration is shown in **Figure 1.** Patients treated with sumatriptan 50 mg were also significantly more likely to be pain-free at 2 and 4 hours compared with placebo (33% vs 21% at 2 hours, $P = 0.045$; and 56% vs 29% at 4 hours, $P < 0.001$).

Table IV. Summary of concurrent medications used by ≥5% of study patients.

Concurrent Medication	Sumatriptan 50 mg (n = 108)	Placebo (n = 107)
Any concurrent medication, no. (%)	84 (78)	85 (79)
Ibuprofen	21 (19)	34 (32)
Multivitamins	18 (17)	15 (14)
Acetaminophen	14 (13)	7 (7)
Acetaminophen + aspirin	12 (11)	13 (12)
Aspirin	9 (8)	5 (5)
Acetaminophen + pseudoephedrine	8 (7)	6 (6)
Naproxen sodium	4 (4)	10 (9)
Vitamin E	4 (4)	6 (6)

The percentage of patients with associated migraine symptoms at 2 and 4 hours after administration is shown in **Table II.** Significantly fewer patients treated with sumatriptan reported photophobia/phonophobia at 2 hours (19% vs 32%; $P = 0.017$) and 4 hours (11% vs 24%; $P = 0.005$). Few patients experienced nausea at baseline in the sumatriptan or placebo group; thus, no statistically significant difference was observed in the percentage of patients free of nausea at 2 hours after administration (82% vs 89%) and 4 hours after administration (91% vs 87%). Vomiting was experienced by too few patients (<1% in either treatment group) to analyze the effects of any study medication.

Additional medication for headache pain or sinus symptoms was used within 2 to 24 hours by fewer patients treated with sumatriptan 50 mg compared with those treated with placebo (34% vs 43%, respectively), though the difference was not statistically significant. The single most common medication used within 2 to 24 hours was ibuprofen, which was used

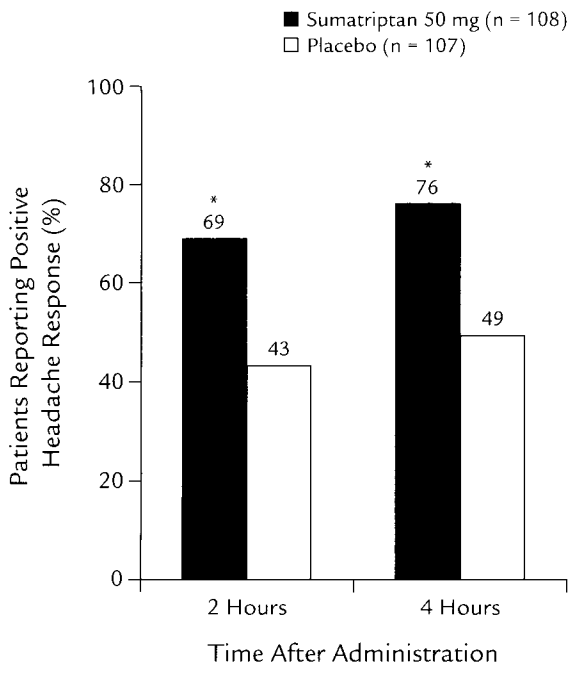

Figure 1. Positive headache response at 2 and 4 hours after administration in patients treating migraine headaches previously recognized as "sinus" headaches. Additional migraine or sinus/nasal medication was allowed from 2 to 24 hours after administration. *$P < 0.001$ versus placebo.

by more patients in the placebo group than in the sumatriptan 50-mg group (16% vs 8%).

Sinus and Nasal Symptoms

The percentage of patients in the total population with sinus and nasal symptoms at 2 and 4 hours after administration is shown in **Table III**. Significantly fewer patients treated with sumatriptan 50 mg reported sinus pain compared with placebo at 2 hours after administration (37% vs 51%, $P = 0.049$) and 4 hours after administration (23% vs 45%, $P = 0.001$). The percentage of patients who were free from sinus and nasal symptoms following treatment did not differ significantly between the 2 groups.

Additionally, the percentage of patients free from sinus pain and pressure was determined for the subanalysis of patients who experienced these symptoms at administration (**Figures 2** and **3**, respectively). Of these patients, significantly more of those treated with sumatriptan 50 mg compared with those who received placebo reported freedom from sinus pain at 2 hours after administration (54% vs 37%; $P = 0.032$) and at 4 hours after administration (70% vs 46%, $P = 0.002$). However, the percentage of patients reporting freedom from sinus pressure at 2 hours after administration (50% vs 39%) and at 4 hours after administration (60% vs 50%) did not differ significantly between the sumatriptan-treated patients and the placebo recipients.

Tolerability

All treatments were generally well tolerated. The overall prevalence of AEs was 19% and 11% in the sumatriptan and placebo groups, respectively. Even fewer AEs were judged by the investigator to be study drug–related (14% vs 6%, respectively). The most common study drug–related AEs in the sumatriptan and placebo groups, respectively, were dizziness (5% vs <1%); nausea (3% vs 2%); other pressure/tightness (defined as sense of heaviness; heaviness of upper body, upper extremities; jaw tension; neck tension) (4% vs 0%); and temperature sensations (defined as warm feeling of back of neck, or flushing) (2% vs 0%). No patients experienced any serious AEs.

DISCUSSION

The results of this study indicate that sumatriptan 50-mg tablets were effective and generally well tolerated in the treatment of migraine in this group of patients with migraine presenting as "sinus" headache. Significantly more patients treated with sumatriptan experienced relief of migraine pain and migraine-associated symptoms. These results support the efficacy of sumatriptan for migraine with sinus features, which has been observed in open-label studies and in clinical practice.[7,10,11]

The demographic characteristics, symptoms, and response of these patients with migraine appear to be similar to those reported elsewhere,[22] except that the baseline prevalence of nausea observed in this single-attack study is lower than that usually reported (73%).[1,2,8] Also, the placebo response is at the high end of rates typically reported in migraine trials.[23] As the study was conducted in a population that had not received a migraine diagnosis, patients in both the sumatriptan and placebo groups might have had high expectations of the efficacy of treatment resulting in a high placebo response rate.

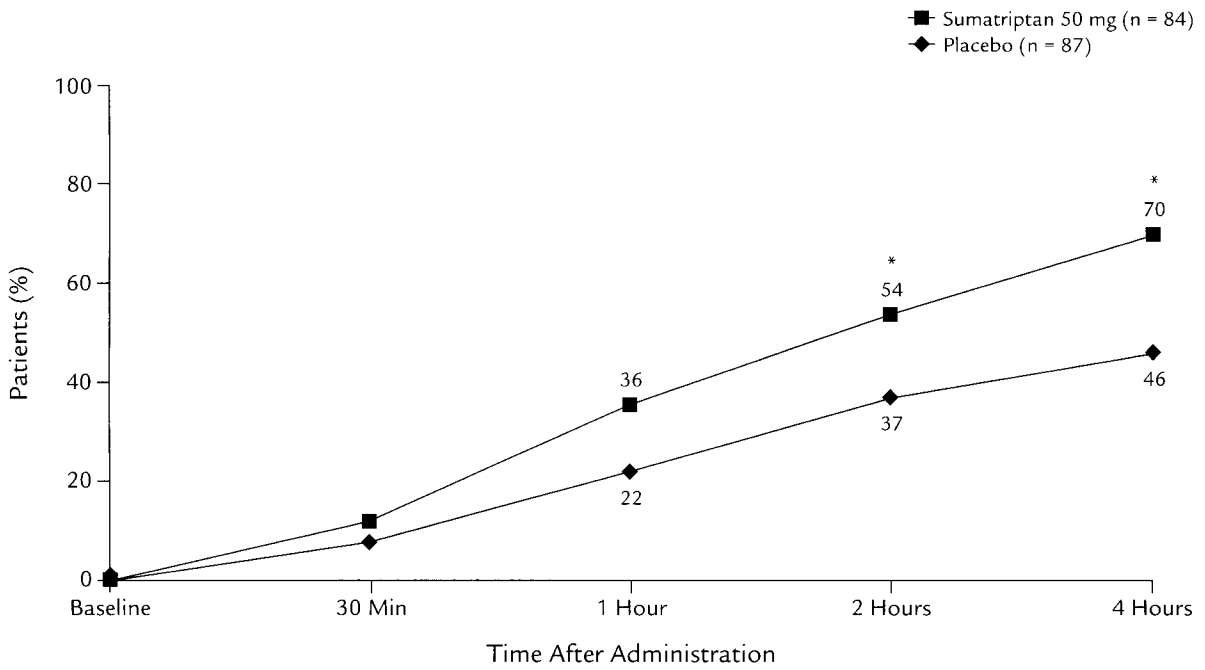

Figure 2. Resolution of sinus pain over time in patients with sinus pain at drug administration (baseline). The presence or absence of sinus pain was recorded at each time point. *Resolution* was defined as the absence of sinus pain. Additional migraine or sinus/nasal medication was allowed from 2 to 24 hours after administration. *$P < 0.05$ versus placebo.

The results of this study, along with other evidence,[9] raise the question of why patients or physicians would confuse the presentation of migraine with "sinus" headache, especially in the absence of infection. Although headache is reported in rhinosinusitis, it is not often the chief complaint, nor is it a good predictor for rhinosinusitis.[24,25] Because the sinuses are also anatomically located in areas of the face where patients commonly experience migraine pain, it is possible that sinus pain and sinus pressure might be misinterpreted. Nasal symptoms (eg, rhinorrhea, congestion) are distinct features of headaches with autonomic features (eg, cluster headaches), but the fact that these symptoms are commonly reported by patients with IHS-defined migraine is not well recognized.[26] It is not surprising that these symptoms are interpreted as "sinusitis" or "sinus" headache.

The understanding of how and why these symptoms might occur in migraine is growing.[27] During migraine, activation of the trigeminal nucleus caudalis (TNC) can cause reflex activation of the parasympathetic nervous system through the superior salivatory nucleus in some patients. Activation of the TNC can produce referred migraine pain along the trigeminovascular network, which can be felt on one or both sides of the head and eyes or sinuses. Reflex activation of the cranial parasympathetic nerves, which innervate the sinus cavities and tear ducts, results in nasal and sinus symptoms like lacrimation, rhinorrhea, and congestion. 5-HT_{1B} receptors have also been observed to be present in the smooth muscle cell layer of human nasal mucosa, suggesting a role for the 5-HT_{1B} receptor in the regulation of vascular tone, glandular secretion, and epithelial functions.[28]

Although sumatriptan effectively treated the migraine symptoms of the majority of these patients, the improvements observed in sinus and nasal symptoms did not reach statistical significance. These symptoms in cluster headache have been suggested to be responsive to sumatriptan injection.[29] A study by Barbanti et al[30] found that patients with migraine who have sinus and nasal symptoms are more responsive than those without these symptoms. As the number of patients with some of these symptoms at baseline was small, this study was not powered to detect differences in these subsets. In addition, this study used inclusion

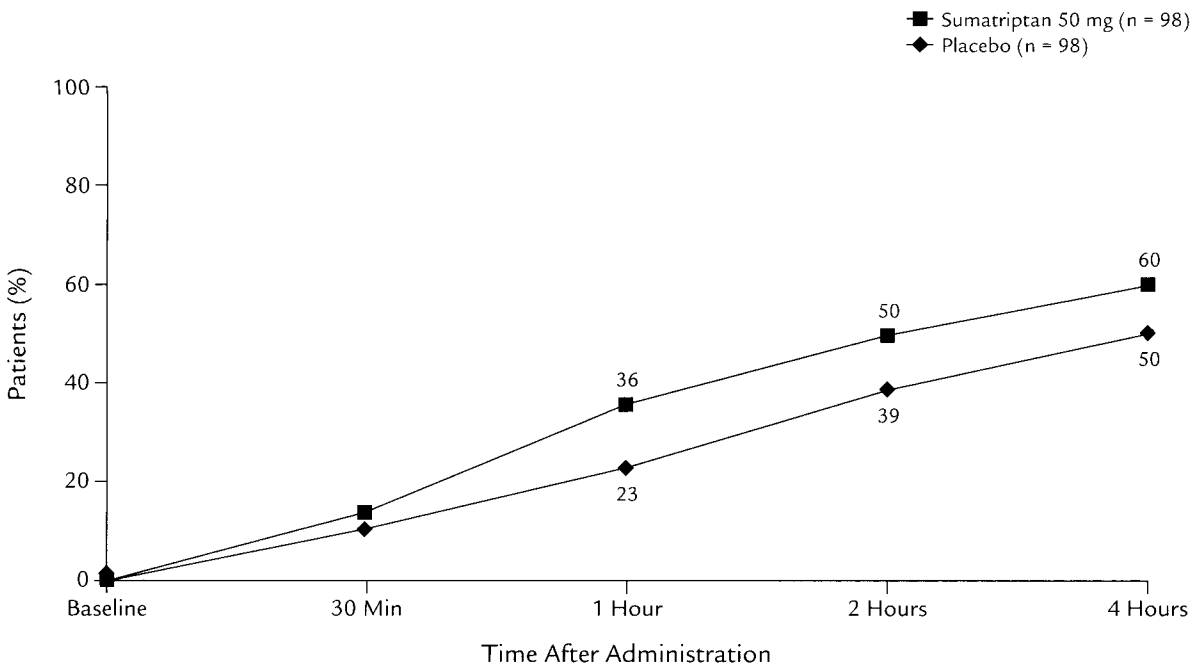

Figure 3. Resolution of sinus pressure over time in patients with sinus pressure at drug administration (baseline). The presence or absence of sinus pressure was recorded at each time point. *Resolution* was defined as the absence of sinus pressure. Additional migraine or sinus/nasal medication was allowed from 2 to 24 hours after administration.

and exclusion criteria to ensure that only patients in the population of interest (ie, those with previously undiagnosed migraine) were enrolled, and to exclude patients with certain comorbidities and those receiving certain medications; this limits the ability to extrapolate to a larger, less strictly selected patient population.

These results, combined with the growing evidence regarding the diagnosis and misdiagnosis of migraine, have important implications for clinical practice. Further investigation of the effect of sumatriptan on the sinus and nasal symptoms present in some patients with migraine is required.

CONCLUSIONS

This study found that patients who were misdiagnosed or had been self-reported as having sinus headaches and subsequently are diagnosed with migraine might respond to sumatriptan 50-mg tablets for their migraine attacks. This study suggests that sumatriptan 50-mg tablets are effective and generally well tolerated in the treatment of migraine in this population.

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