Aspirin Is Efficacious for the Treatment of Acute Migraine

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Background.—More than 50% of migraine sufferers rely on over-the-counter medications for the treatment of migraine. Along with other over-the-counter products, aspirin is considered by the US Headache Consortium to be an option for first-line migraine treatment. This study assessed the efficacy and tolerability of aspirin versus placebo for the acute treatment of a single acute attack of migraine.

Methods.—This prospective, randomized, double-blind, parallel-group, placebo-controlled study evaluated the efficacy of a single, 1000-mg dose of aspirin for the treatment of acute moderate to severe migraine, with or without aura. Subjects recorded all study evaluations in a diary at baseline and at .5, 1, 2, 3, 4, 5, 6, and 24 hours after treatment. Pain was rated on a 4-point ordinal scale from no pain to severe pain. The primary efficacy end point was headache response at 2 hours. Secondary efficacy parameters included reduction of nausea, photophobia and phonophobia, pain intensity difference, and headache recurrence at 24 hours.

Results.—Of 485 subjects enrolled, 409 took study medication and 401 treated a confirmed migraine attack (201 with aspirin and 200 with placebo). Baseline demographic and migraine characteristics were not significantly different between groups. The 2-hour headache response rate was 52% with aspirin versus 34% with placebo ($P < .001$). Aspirin was significantly more effective than placebo for pain reduction beginning 1 hour after dosing ($P < .001$) and continuing throughout the 6-hour evaluation period. Significantly ($P < .05$), more subjects were pain free from the 1-hour evaluation through the 6-hour evaluation. Of the aspirin-treated subjects, 20% were pain free at 2 hours versus only 6% of placebo-treated subjects. At 24 hours, the headache recurrence rate was 21.8% for aspirin (23 of 105 subjects) and 27.7% for placebo (19 of 68 subjects). Only 34% of aspirin-treated subjects needed rescue medication at 24 hours compared with 52% of placebo-treated subjects ($P < .001$). Aspirin was well tolerated, and adverse events were not significantly different between groups.

Conclusions.—This study demonstrates that aspirin is safe and effective for treatment of acute migraine in appropriately selected patients.

Key words: migraine, aspirin, treatment, efficacy, safety

Abbreviations: OTC over the counter, FDA Food and Drug Administration, IHS International Headache Society, PID pain intensity difference, SPID sum of pain intensity differences, ANOVA analysis of variance, ITT intent to treat, PROC CATMOD procedure for categorical data modeling

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Migraine is a common yet debilitating disease that is both underdiagnosed and undertreated.[1] Results from the 1999 American Migraine Study II indicate that 12% of Americans have migraine headache.[2] In an evaluation of outpatient healthcare delivery, the rate of physician visits related to migraine increased almost 100% in 8 years, from 9.4/1000 visits in 1990 to 18/1000 visits in 1998.[3] Over a one decade period, the rate of physician diagnosis for migraine increased by 10%, from 38% in 1989 to 48% in 1999.[4-6] These increases in physician visits and migraine diagnoses

have been attributed to expanding public and physician awareness of migraine and the availability of a wide array of effective prescription drugs, including the triptans.[4,7]

Because half of those with migraine have never received a physician's diagnosis, it is not surprising that 57% of those in the American Migraine Study II relied on over-the-counter (OTC) drugs for the treatment of migraine to the exclusion of prescription drugs.[4] Several OTC products are currently approved by the Food and Drug Association (FDA) for acute migraine attacks, including ibuprofen and combination products containing acetaminophen, aspirin, and caffeine. Other OTC products, including naproxen sodium, aspirin, and acetaminophen, are routinely recommended for migraine and other headache disorders.[8]

The US Headache Consortium guidelines on pharmacologic management of acute migraine attacks[9,10] were developed according to an evidence-based evaluation of literature available at the time. Aspirin, ibuprofen, naproxen sodium, and combination products containing acetaminophen, aspirin, and caffeine were considered by the Consortium to be reasonable options for first-line treatment of mild to moderate migraine or severe migraine that has previously responded to a similar agent.

The current guidelines for acute migraine treatment recommend aspirin, although few published studies have evaluated aspirin use for migraine headache. Aspirin has been evaluated for general headache or tension-type headache.[11-16] The limited data that are available for acute migraine support the efficacy and safety of aspirin in this setting.[17–21] The purpose of this study was to assess the efficacy of a single, 1000-mg dose of aspirin for the management of acute migraine attack of moderate to severe pain intensity with or without aura.

METHODS

This prospective, randomized, double-blind, parallel-group, placebo-controlled study was conducted between March 1999 and January 2000 to evaluate the efficacy of a single, 1000-mg dose of aspirin (Extra Strength Bayer Aspirin Caplets, Bayer Consumer Care Division, Morristown, NJ) for the treatment of acute moderate to severe migraine, with or without aura. The goal was for 400 subjects (200 per treatment group) to complete the study. To achieve this goal, 240 subjects per treatment arm were enrolled. Each subject was trained to identify an eligible migraine attack and to complete a self-reporting diary. Prior to the use of study medication, subjects were asked to complete a migraine qualifying form that included questions regarding drug use within the previous 72-hour period and the headache features used to assign a diagnosis of migraine based on the International Classification of Headache Disorders (ICHD-1) developed by the International Headache Society.[22] In addition, the diary captured the features of the attack. If the headache was qualified as a migraine (with or without aura), the pain was of at least moderate intensity, and the attack was otherwise eligible, subjects were instructed to take the study medication (2 caplets of Extra Strength aspirin, 1000 mg total, or matched placebo). Subjects were instructed to complete all study evaluations in the diary at baseline (just prior to taking medication) and at 30 minutes and 1, 2, 3, 4, 5, 6, and 24 hours after taking the medication. Concomitant medications were recorded; those medications that could have confounded quantification of analgesia were not permitted prior to the attack. Rescue medication was permitted, but subjects were encouraged to wait at least 2 hours before rescue. Subjects were expected to return for a follow-up visit, ideally the next business day, but within 1 week after taking study medication. Subjects who did not treat an acute migraine within 8 weeks of randomization were dropped from the study.

Inclusion/Exclusion Criteria.—Subjects between 18 and 50 years of age who experienced migraine headache with or without aura according to International Headache Society's (IHS) criteria[22] and who had at least moderate pain and at least one, but not more than six, migraines per month for the previous year were eligible for inclusion. Those who experienced vomiting at least 20% of the time during an attack were excluded, as were subjects recently (within the past 3 months) started on preventive medications. Subjects taking prescription drugs for anticoagulation, gout, or arthritis, and subjects taking ergot alkaloids to treat migraine attacks were not eligible to participate. Subjects not previously responsive

to OTC analgesics and/or prescription medications for migraine were excluded. Subjects with headache symptoms caused or aggravated by recent traumatic injury, history of other disease of the head or neck, or severe emotional disorders also were excluded. Eligible subjects could not have allergies or contraindications to aspirin, including ulcer disease, gastrointestinal bleeding, bleeding, or coagulation abnormality, asthma, inflammatory bowel or pancreatic disease, serious cardiac, renal, hepatic, metabolic, or neurologic disease, diabetes, uncontrolled hypertension, or active malignancy. Females were required to be practicing effective birth control methods and could not be pregnant or nursing. Written informed consent was provided by each subject.

Evaluation Parameters.—In this single-dose study, aspirin and placebo were evaluated for the treatment of migraine attack with moderate or severe baseline pain. Pain was rated on a 4-point ordinal scale as follows: 0 = no pain; 1 = mild pain; 2 = moderate pain; and 3 = severe pain. The primary efficacy end point was the percentage of subjects who experienced headache response at 2 hours defined by a change in pain intensity from moderate or severe at baseline to mild or none 2 hours after taking study medication. The percentage of subjects pain free at each time point also was evaluated.

Secondary efficacy parameters included reduction of the symptoms of nausea, photophobia, and phonophobia during the 6-hour study period. These were recorded on the same 4-point scale as pain and evaluated as the reduction of symptoms from baseline. Improvement in functional ability compared with baseline also was assessed. Pain intensity differences (PIDs) at each time point were assessed by subtracting pain at any time from baseline. The sum of pain intensity differences (SPID) was computed as a time-weighted sum of PID scores at 6 hours. Headache recurrence and time to headache recurrence were captured at 24 hours. Recurrence was defined as increased pain intensity to moderate or severe, or the need for rescue medication, within 24 hours after taking study medication in those subjects whose pain was originally reduced to mild or none at 2 hours.

Adverse events were assessed with regard to seriousness, incidence, intensity (mild = 1 to severe = 3), duration, action taken, outcome, and relationship to study medication. Subjects were asked to record all adverse events that occurred within 24 hours of taking study medication.

Statistical Analyses.—All statistical processing was performed using SAS statistical software (versions 6.12 and 7 for Windows; SAS, Cary, NC), except for calculation of the confidence interval computed for the analysis of headache recurrence, which was computed using StatXact (version 2.11; Cytel Statistical Software Corporation, Cambridge, MA). Sample-size calculations were designed to detect differences of 15% between Extra Strength Bayer Aspirin and placebo, with a 2-sided alpha of .05 and power of .85. A 15% difference was considered to be clinically meaningful.

Statistical significance was based on 2-tailed tests of the null hypothesis resulting in P values of .05 or less. Baseline values of demographic and clinical parameters were analyzed to assess the degree to which randomization achieved comparability between the treatment groups. Demographic variables such as age, weight, and height were analyzed with a 2-way analysis of variance (ANOVA) model with factors of treatment and site. Categorical variables such as gender and race, as well as baseline pain intensity score, were assessed by the Cochran-Mantel-Haenszel test.

Each subject who took the study drug was included in the safety and intent-to-treat (ITT) efficacy analyses. Only those subjects who took study medication for a confirmed migraine were included in the confirmed migraine analysis. A repeated-measures ANOVA with factors of treatment, investigator, time, and treatment-time interaction was conducted for the subset of subjects whose migraine attack included the symptom prior to dosing. A significant treatment-by-time interaction or between-subject effects provided evidence of a treatment effect that was subsequently analyzed by an analysis of covariance at each postdosing time point during the 6-hour study period. The factors of treatment and investigator were included in the model, with baseline symptom severity as a covariant. Percentage of responders was analyzed using the Cochran-Mantel-Haenszel test stratified by the investigator. The consistency of the treatment effect on the primary variable (percentage of responders) was investigated for the different race, gender, and

age of the subjects who were enrolled in the study. An SAS procedure for categorical data modeling (PROC CATMOD) analysis was conducted with factors of treatment, gender, and treatment-by-gender interaction. Analyses with race or baseline severity in place of gender were conducted. Race categories (non-white) were combined to ensure sufficient sample size for analysis. The interaction term was used to test for consistency of treatment effect. The subgroup analysis of baseline severity included within-severity comparisons that were conducted using contrast with the PROC CATMOD analysis. Additionally, logistic regression of the primary variable with factors of age, age squared, treatment, and treatment-by-age interaction was conducted, and the interaction term was used to test for consistency. Fisher's exact test was used to compare incidence rates of adverse events.

Subset analyses on the primary variable for the subgroups of race, gender, and baseline severity were analyzed with a PROC CATMOD, as were within-severity comparisons. Subset analysis for age was conducted with a logistic regression. Cochran-Mantel-Haenszel test for row mean scores, stratified by investigator, was conducted to determine if there was a significant difference between treatments in the proportion of subjects who experienced a reduction in symptoms.

RESULTS

Subjects.—A total of 485 subjects were enrolled in the study, with 243 randomized to receive 1000 mg of aspirin and 242 randomized to receive placebo. Of the 76 subjects who could not be assessed, 57 were excluded because of failure to treat a migraine in the 8-week period, 3 voluntarily withdrew, 9 were lost to follow-up, and 7 could not be assessed for other reasons. There were 409 subjects (205 receiving aspirin, 204 receiving placebo) who took study drug and so were included in the safety ITT analysis (Figure 1). Four subjects in each group treated an attack that did not meet IHS criteria for migraine. Excluding these 8 subjects left 401 subjects (201 receiving aspirin, 200 receiving placebo) in the confirmed migraine ITT analysis (Figure 1). Results were analyzed both excluding

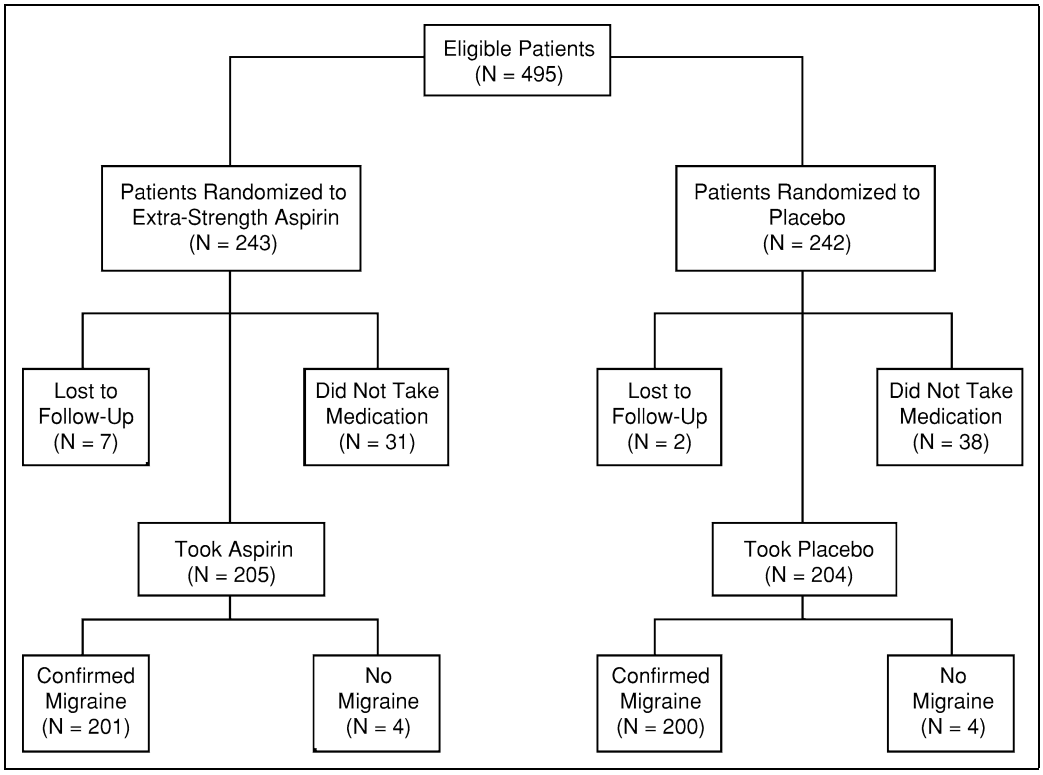

Fig 1.—Summary disposition of all enrolled subjects.

these individuals (per-protocol analysis) and including them. Results did not substantially differ; herein we present the per-protocol analyses.

Baseline demographic characteristics and features of the treated attacks were not significantly different between the aspirin- and placebo-treated groups (Tables 1 and 2). The majority of subjects were white females, with a mean age of 37 years. Baseline migraine pain intensity was moderate in approximately 60% of subjects and severe in approximately 40%. More than 75% of subjects had no nausea or mild nausea at baseline. In contrast, photophobia and phonophobia were noted by 96% of subjects or more, at least half of whom experienced moderate intensity.

Efficacy in Treating Pain.—Headache response rates at each time point from 30 minutes to 6 hours were higher in subjects who received aspirin than in those who received placebo (Figure 2), with a 2-hour response rate of 52% with aspirin versus 34% with placebo. A significant difference ($P < .001$) was noted at all time points from 1 hour onward. For subjects with severe migraine at baseline, the 2-hour headache response with aspirin was 48% versus 26% with placebo ($P = .005$). For those with moderate baseline pain, the 2-hour headache responses were 56% for aspirin and 39% for placebo ($P = .001$). The overall treatment response was not significantly influenced by gender, race, or baseline severity. At 2 hours, 20% of subjects treated with aspirin were pain free versus only 6% of subjects treated with placebo (Figure 3). Again, statistically significant ($P < .05$) improvement with aspirin was noted at all time points except at 30 minutes postdose.

Aspirin was significantly more effective than placebo with regard to pain reduction beginning 1 hour after dosing and continuing through the 6-hour evaluation period, as reflected in the significantly higher PID scores from 1 to 6 hours (Table 3). At the primary 2-hour end point, the PID score with aspirin was 1.03 compared with .61 with placebo ($P < .001$). The 6-hour SPID was 6.94 for the aspirin group versus 4.25 for the placebo group ($P < .001$).

Headache recurrence at the end of the 6-hour evaluation period and at 24 hours did not differ between groups. At 24 hours, headache recurrence was 21.9%

Table 1.—Baseline Demographic Characteristics (Per-Protocol ITT)*

Parameters	Aspirin (1000 mg) (N = 201)	Placebo (N = 200)
Age (years)		
Mean ± SD	37.3 ± 8.7	37.9 ± 9.4
Range		
Race (N, %)	20.0-58.0	19.0-64.0
White	155, 77%	154, 77%
Black	43, 21%	44, 22%
Other	3, 1%	2, 1%
Gender (N, %)		
Male	43, 21%	42, 21%
Female	158, 79%	158, 79%
Weight (lb)		
Mean ± SD	171.9 ± 44.5	167.3 ± 42.2
Range	89.0-342.0	101.0-323.0

*There were no statistically significant differences between groups.
ITT, intent to treat; SD, standard deviation.

Table 2.—Baseline Characteristics of Treated Migraine Attacks (Per-Protocol ITT)*

Parameters	Aspirin (1000 mg) (N = 201) N (%)	Placebo (N = 200) N (%)
Baseline pain intensity		
Moderate	121 (60)	127 (64)
Severe	80 (40)	75 (37)
Baseline nausea		
None	85 (42)	90 (45)
Mild	69 (34)	65 (33)
Moderate	44 (22)	41 (21)
Severe	3 (1)	4 (2)
Baseline photophobia		
None	6 (3)	6 (3)
Mild	39 (19)	35 (18)
Moderate	112 (56)	128 (64)
Severe	44 (22)	31 (16)
Baseline phonophobia		
None	5 (2%)	7 (4%)
Mild	38 (19%)	49 (25%)
Moderate	115 (57%)	101 (51%)
Severe	43 (21%)	43 (22%)

*There were no statistically significant differences between groups.
ITT, intent to treat.

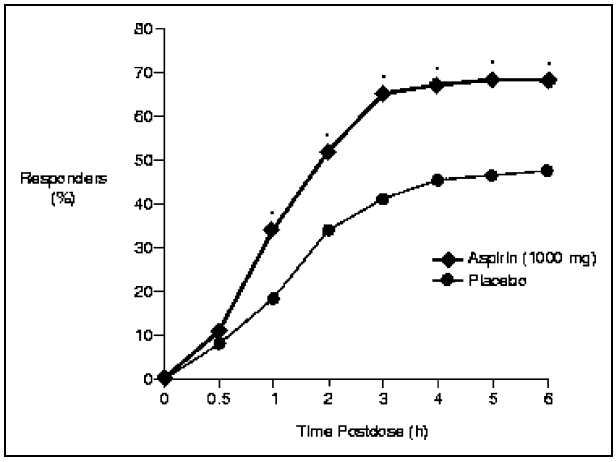

Fig 2.—Headache response rates at 30 minutes to 6 hours postdose with 1000 mg of aspirin (N = 201) or placebo (N = 200) in the per-protocol intent-to-treat population. Responders are those subjects who experienced a change in pain intensity from moderate or severe at baseline to mild or none at the postdose time point. Subjects who used rescue medication are considered nonresponders. *$P < .001$ versus placebo.

for aspirin (23 of 105 subjects) and 27.9% for placebo (19 of 68 subjects).

Treatment of Associated Symptoms and Functional Disability.—Though there were no statistically significant differences between groups, nausea resolved in more subjects treated with aspirin than subjects treated with placebo by 3 hours after treatment (52% vs 43%); this pattern persisted to 6 hours (55% vs 46%). A significant reduction in both photophobia and phonophobia was evident by 1 hour and continued through the 6-hour evaluation with aspirin when compared with placebo. Photophobia resolved in 30% of aspirin-treated subjects versus 14% of placebo-treated subjects at 2 hours ($P < .001$), in 49% versus 34% at 4 hours ($P = .002$), and in 58% versus 39% at 6 hours ($P < .001$), respectively. Similar reductions in phonophobia were noted with symptom resolution in 34% of aspirin-treated subjects versus 17% of placebo-treated subjects at 2 hours, in 53% versus 36% at 4 hours, and in 59% versus 40% at 6 hours ($P < .001$ at all time points), respectively. Significant improvement in functional ability was evident with aspirin versus placebo at 1 hour through the 6-hour evaluation ($P < .001$), with evidence of improvement as early as 30 minutes after treatment ($P = .059$).

Rescue Medication.—Rescue medication was required by more subjects who received placebo than by those who received aspirin starting at 1 hour postdose until the end of the 24-hour evaluation period. Based on Kaplan-Meier analysis, throughout the 24-hour period only 34% of aspirin-treated subjects needed

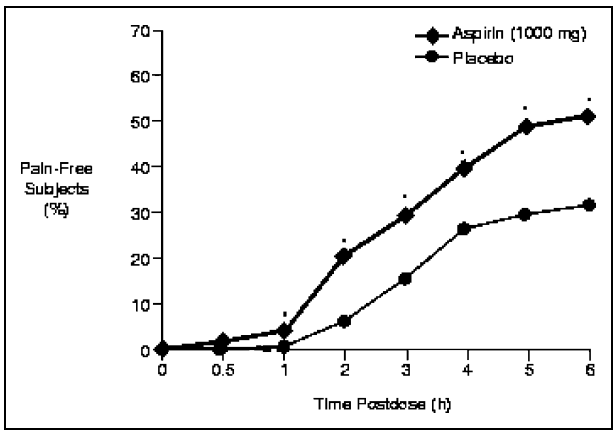

Fig 3.—Percentage of subjects who were pain free at 30 minutes to 6 hours postdose with 1000 mg of aspirin (N = 201) or placebo (N = 200) in the per-protocol intent-to-treat population. *$P <$ .05 versus placebo.

Table 3.—PID from Baseline by Time With 1000 mg of Aspirin or Placebo, and SPID (Per-Protocol ITT)

Parameters	Aspirin (1000 mg) (N = 201)	Placebo (N = 200)	*P* Values*
PID** ± SD			
Hour .5	.22 ± .49	.18 ± .49	.428
Hour 1	.61 ± .70	.38 ± .71	.001
Hour 2	1.03 ± .92	.61 ± .92	<.001
Hour 3	1.23 ± 1.03	.73 ± 1.03	<.001
Hour 4	1.35 ± 1.13	.85 ± 1.14	<.001
Hour 5	1.45 ± 1.17	.88 ± 1.18	<.001
Hour 6	1.47 ± 1.20	.90 ± 1.20	<.001
SPID*** ± SD	6.94 ± 5.43	4.25 ± 5.45	<.001

ANOVA, analysis of variance; ITT, intent to treat; PID, pain intensity difference; SD, standard deviation; SPID, sum of pain intensity differences.
*Least squares means, SDs, and *P* values for comparison of treatments at individual evaluation times are from ANOVA with factors of treatment and investigator.
**The PIDs at each evaluation time are calculated by subtracting the postdose score from the predose score (hour 0).
***SPID is calculated as the time-weighted cumulative 6-hour sum of PIDs.

Table 4.—Adverse Events Reported by Subjects Who Received 1000 mg of Aspirin or Placebo (All ITT)

Adverse Events	Number of Subjects (%)	
	Aspirin (1000 mg) (N = 205) N (%)	Placebo (N = 204) N (%)
Any adverse event	18 (9)*	10 (5)
Abdominal pain	1 (<1)	2 (1)
Asthenia	2 (1)	0
Chills	0	2 (1)
Diarrhea	0	2 (1)
Dizziness	2 (1)	0
Dry mouth	1 (<1)	0
Dyspepsia	0	1 (<1)
Euphoria	1 (<1)	0
Insomnia	1 (<1)	0
Intestinal perforation	0	1 (<1)
Nausea	7 (3)	2 (1)
Nervousness	1 (<1)	0
Paresthesia	1 (<1)	0
Pharyngitis	0	1 (<1)**
Pruritus	1 (<1)	0
Rash	1 (<1)	0
Sleep disorder	1 (<1)	0
Somnolence	2 (1)	1 (<1)
Sweating	0	1 (<1)
Taste perversion	1 (<1)	0
Tooth disorder	1 (<1)†	0
Urticaria	1 (<1)	0

ITT, intent to treat.
*$P = .17$.
**Required treatment.

rescue medication compared with 52% of placebo-treated subjects ($P < .001$).

Tolerability.—All subjects who received study medication were included in the ITT analysis of safety. Overall, 1000 mg of aspirin was well tolerated, with 9% of 205 aspirin-treated subjects reporting a total of 25 adverse events compared with 5% of 204 placebo-treated subjects who reported a total of 14 adverse events (no significant difference between groups) (Table 4). The most common adverse event related to aspirin use was nausea, which occurred in 3% of subjects. One adverse event in each group required treatment: pharyngitis in a placebo-treated subject and a tooth disorder in an aspirin-treated subject.

Most adverse events were mild or moderate in severity. There were two severe adverse events in each group, including pruritus and urticaria in 1 aspirin-treated subject and abdominal pain and intestinal perforation in 2 separate placebo-treated subjects. There was only one serious adverse event, a perforated appendix in a placebo-treated patient, which was not thought to be related to treatment.

COMMENTS

The results of this study support the efficacy of a single, 1000-mg dose of aspirin for the acute treatment of migraine. Use of aspirin resulted in significantly higher headache response rates than placebo at 60 minutes and thereafter, indicating that a 1000-mg dose of aspirin decreased the intensity of pain attributable to acute migraine headache from moderate to severe to mild or no pain. Similarly, the percentage of subjects who were pain free was statistically significantly higher with aspirin versus placebo at all time points except 30 minutes. These results compare favorably with other published studies on the use of aspirin for acute migraine. Headache response at 2 hours in five studies ranged from 48% to 55% with 900 to 1000 mg of aspirin versus 19% to 37% with placebo, 17 to 21, which is similar to our 2-hour response rate.

The benefits of aspirin were not confined only to subjects treated for moderate pain; of the subjects with severe pain at baseline, the 2-hour headache response was higher for aspirin than placebo. Beginning 1 hour after dosing, the aspirin-treated group experienced a significant reduction in pain intensity, photophobia, and phonophobia; there was also an improvement in the ability to function, when compared with the placebo-treated group.

Although the aspirin group had lower rates of nausea than the placebo group at several time points, these differences were not statistically significant. It is not clear why pain, photophobia, and phonophobia were significantly relieved while nausea was not. It is possible that aspirin caused treatment-emergent nausea as a side effect, perhaps through a gastrointestinal mechanism, attenuating benefits on nausea relief. The rate of treatment-emergent nausea (nausea as an adverse event) was higher in the aspirin group (3%) than in the placebo group (1%). Another factor may be the relatively low baseline prevalence of nausea in both

aspirin and placebo groups (58% and 55%) in comparison with pain (100% in both groups), photophobia (97% and 97%), and phonophobia (98% and 96%). Thus, the power to detect relief of nausea was substantially lower than the power to detect relief of other features. The study was powered to detect pain but not nausea relief.

Fewer aspirin-treated subjects required rescue medication, indicating that 1000 mg of aspirin provided sufficient pain relief to significantly decrease the need for supplemental analgesia when compared with placebo. Aspirin was well tolerated in this study, and adverse-event rates were not different from those of placebo.

Similar studies have demonstrated the efficacy of other OTC products for acute migraine.[23-25] The patient populations in this and other studies are difficult to compare. Most recent OTC migraine studies exclude patients who usually require bed rest because of disability due to their migraine and those who vomit more than 20% of the time. Disability due to migraine requiring bed rest is an important exclusion because a significant proportion of those with migraine (up to 50%) may experience severely debilitating attacks.[26] In the present study, we chose not to limit eligibility based on disability, but we did exclude those with a lack of response to previous OTC or prescription medications. Differences in study population make it difficult to directly compare these results with studies of other OTC treatments.[23-25]

Both strategies of migraine patient selection, excluding those who are usually disabled or those who have failed other treatments, are intended to identify an appropriate patient population for OTC treatment. There is evidence that disability predicts treatment needs in the context of randomized trials.[27] Excluding those with migraine who are usually disabled, independent of treatment history, is one patient stratification approach that has been successfully used in OTC migraine trials. In fact, current guidelines for the management of acute migraine recommend stratified care such that the intensity of treatment (eg, triptan vs OTC analgesic) is linked to the level of disability and presence of nausea and vomiting.[10] The favorable results of this study demonstrate that it also is beneficial to select patients based on previous response to OTC analgesics when considering an OTC migraine regimen.

Migraine is a debilitating condition that negatively impacts patients' health-related quality of life.[28,29] The effects of migraine have been estimated to be similar or worse than those of other chronic diseases, including depression and diabetes.[30,31] In addition, headache in general adversely impacts productivity and is one of the most common reasons for lost productive time in U.S. workplace.[32] Because most of those with migraine rely on OTC medications for relief of acute migraine,[4] quality data can support development of evidence-based treatment recommendations, such as the US Headache Consortium guidelines.[9,10] OTC medications have been shown to improve quality of life for those with migraine.[33] This study demonstrates that aspirin is safe and effective for treatment of acute migraine in appropriately selected patients. Aspirin is a rational OTC alternative for patients who have migraine.

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