Almotriptan Versus Rizatriptan in Patients With Migraine in Spain

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Objectives.—To compare patient-reported use of rizatriptan 10 mg with that of almotriptan 12.5 mg per migraine attack (24 hours) in a Spanish population.

Methods.—One hundred twenty Spanish community pharmacies recruited patients with migraine to whom they had dispensed almotriptan and rizatriptan. No other selection criteria were used. Patients kept diaries for baseline pain intensity, the number of triptan tablets used, additional medication taken per attack, and their degree of satisfaction with the medication 2 hours after the initial dose. Patients recorded details for a maximum of 3 attacks. Analysis of variance or the Student *t* test and chi-squared or Fisher exact tests were used for univariate comparisons. A generalized estimating equation method was used to correct for within-subject variability. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated.

Results.—One hundred twenty-six patients (85% women) recorded data for 318 migraine attacks. Rizatriptan was used to treat 122 attacks, almotriptan was used to treat 110 attacks, and a nontriptan medication was used in the initial treatment of 86 attacks. Triptan use (adjusted mean, 95% CI) per attack in this study was lower for rizatriptan (1.19 tablets; 95% CI, 1.06 to 1.32) than for almotriptan (1.43 tablets; 95% CI, 1.30 to 1.56; $P = .003$). The use of a triptan and additional medication per attack increased with baseline pain severity. Rizatriptan was used to treat more attacks with only one tablet (78%) than almotriptan (58%). Treatment of attacks with almotriptan was more than twice as likely to involve the use of more than one tablet per attack (24 hours) than those treated with rizatriptan (adjusted OR, 2.42; 95% CI, 1.37 to 4.30; $P = .003$). Patient satisfaction with treatment response at 2 hours was more than 2-fold greater for rizatriptan (85%) than for almotriptan (68%) (adjusted OR, 2.55; 95% CI, 1.11 to 5.87; $P = .03$).

Conclusions.—In this prescription-selected Spanish population, a significantly lower number of rizatriptan tablets were required to treat migraine attacks compared with almotriptan. Further, patients were more than twice as likely to use more than one tablet or additional medication (or both) for attacks treated with almotriptan than for those treated with rizatriptan. Although these data suggest that rizatriptan may be a more effective treatment for migraine than almotriptan, further randomized studies are required to confirm this conclusion.

Key words: rizatriptan, almotriptan, triptan, consumption survey, migraine

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Migraine is a chronic and highly prevalent condition which imposes a substantial economic burden, an important component of which are prescription costs.[1,2] Triptans are an effective but relatively expensive therapy for the treatment of acute migraine and therefore, optimizing their efficacy is vital for cost containment. The amount of triptan required to treat an attack may be influenced by factors inherent to migraine itself, but the efficacy of oral triptans is also

an important driver of consumption.[3] We designed this "real-world" open-label study to extend a previous consumption survey[4] to include almotriptan which was recently launched in Spain. We again hypothesized that differences in the self-reported use of triptan medication per migraine attack would be apparent due to differences in efficacy.

PATIENTS AND METHODS

One hundred twenty community pharmacies in 4 regions of Spain participated in this study. Pharmacists were asked to recruit all patients with migraine to whom they had dispensed almotriptan or rizatriptan between March 2001 and December 2001. No other selection criteria were used. Prior to entry, patients were informed of the purpose of the study and were asked to provide verbal consent. Patients completed a demographic questionnaire on entry.

When patients suffered a migraine attack, they were asked to record baseline pain intensity (mild, moderate, or severe), the medication taken initially, any additional medication taken, and the total number of tablets of all medications taken over a 24-hour period. Each patient recorded details for a maximum of 3 attacks. Patients also scored their degree of satisfaction with the medication 2 hours after their initial dose using a 7-point scale (from "completely satisfied" to "completely dissatisfied"). Satisfaction scores were grouped in 2 categories: "satisfied" ("completely satisfied," "very satisfied," or "somewhat satisfied") and "dissatisfied" ("completely dissatisfied," "very dissatisfied," or "somewhat dissatisfied"). Scores of "neither satisfied nor dissatisfied" were excluded. Satisfaction scores were also grouped into a more stringent "satisfied" category that included only "completely satisfied" and "very satisfied" responses.

Statistical Analysis.—We estimated that a sample size of 116 attacks per triptan would be needed to detect a difference of 30% between almotriptan and rizatriptan consumption per attack (ß = 80%, $\alpha = .05$, and estimated standard deviation [SD] = 1).

Treatment groups were assigned according to the triptan prescribed. Comparisons between continuous variables, expressed as mean (SD), were performed using the analysis of variance (ANOVA) and Student *t* test. Chi-squared or Fisher exact tests were used for qualitative variables. Bonferroni correction was used for multiple between-group comparisons.[5]

Statistical methods were used to correct for the intra-subject variability in triptan tablet consumption across multiple attacks. A generalized estimating equation method, using a cumulative logit link and multinomial variance, was used to model the self-reported consumption of abortive migraine medication and patient satisfaction (adjusted by patient, number of attacks, and baseline pain intensity). Patient, attack, and baseline intensity variables were included in a multivariate logistic regression analysis. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for the probability of patients using more than one tablet of rizatriptan or almotriptan per attack and the probability of only using one tablet of rizatriptan or almotriptan per attack. Adjusted ORs and 95% CIs were also calculated for the degree of patient satisfaction with rizatriptan versus almotriptan, rizatriptan versus nontriptan, and almotriptan versus nontriptan. The existence of interactions was evaluated. The null hypothesis was rejected in each statistical test if $P < .05$.

Table 1.—Patient Demographics*

Feature	Rizatriptan	Almotriptan	Total
Age, mean (SD), y	42.9 (11.1)	41.6 (12.9)	41.9 (13.2)
Sex			
Female	54 (50.5)	50 (56.7)	107† (85.0)
Male	8 (42.1)	11 (57.9)	19 (15.0)
Migraine attacks			
Frequency/mo			
<3	33 (54.1)	32 (52.5)	65 (53.3)
>3	28 (45.9)	29 (47.5)	57 (36.1)
Duration, h			
<12	12 (19.7)	11 (17.7)	23 (18.7)
1-24	23 (37.7)	21 (33.9)	44 (35.8)
>24	26 (42.6)	30 (48.4)	56 (45.5)
Previous exposure to study drug			
Yes	32 (59.2)	22 (40.7)	54 (44.3)
No	30 (44.1)	38 (55.9)	68 (55.7)

*Values are number (percentage) unless otherwise indicated.
†Information on drug allocation in the demographic questionnaire was missing for 3 female patients.
Note: Although 126 patients participated in the study, not all patients fully completed the demographic questionnaire. As a result, not all of the above figures total 126.

Table 2.—No. (%) of Attacks Grouped by Initial Treatment Used and Baseline Pain Intensity

Headache Characteristic	Rizatriptan	Almotriptan	Nontriptan*	Total
No. (%) of attacks	122 (38.4)	110 (34.6)	86 (27.0)	318 (100)
Attacks/patient, mean (SD)	2.38 (0.81)	2.63 (0.67)	2.59 (0.68)	2.53 (0.72)
Baseline pain intensity				
Mild	9 (7.4)	8 (7.3)	15 (17.4)	31 (10.1)
Moderate	58 (47.5)	62 (56.4)	42 (48.8)	162 (50.9)
Severe	54 (44.3)	39 (35.4)	29 (33.7)	122 (38.4)
Unknown	1 (0.8)	1 (0.9)	0 (0.0)	2 (0.6)

*These patients had been prescribed a triptan but used a nontriptan as initial treatment.

Missing values were always below 10%. All analyses were conducted using Statistical Analysis Systems (SAS) 8.2 software.[6]

The definitions used in the analysis have been described elsewhere.[4]

RESULTS

Patient Population and Migraine Attacks.—Of the 188 patients who consented to participate in this study, 126 (85% women) completed diaries for 318 migraine attacks (Tables 1 and 2). Analysis was by attack rather than by patient, therefore, multiple data are presented in the results for individuals who suffered 2 or 3 attacks. Most of the attacks occurred between 6 AM and 12 noon (56%) or 6 PM and 6 AM (33%). Not all patients prescribed a triptan chose to treat their attacks with the prescribed drug and as a result, a nontriptan medication was used in the initial treatment of 86 attacks (27%). Rizatriptan was used to treat 122 attacks (38%) and almotriptan was used to treat 110 attacks (35%). All 126 patients who completed diaries treated at least one attack, 108 (61%) treated 2 attacks, and 84 (26%) treated 3 attacks. The average number of migraine attacks per patient was 2.53 (SD, 0.72) with no difference in frequency noted for patients who treated attacks with rizatriptan or almotriptan ($P = .74$). Men treated a higher percentage of their attacks with almotriptan (41%) than with rizatriptan (22%). No other demographic differences were observed between groups (Table 1).

Most of the treated attacks (89%) were of moderate (51%) or severe (38%) intensity. Nontriptan medications were used to treat 47% of mild attacks, whereas triptans were used to treat 75% of the moderate and

Table 3.—Triptan and Additional Medication Tablets per Attack (24 Hours) and Adjusted Mean (95% Confidence Interval)

		Total No. of Triptan Tablets per Attack*					Adjusted Average No. of Tablets per Attack (95% CI)	
Treatment	Total No. of Attacks	0	1	2	3	4	Triptan	AdMet†
Rizatriptan	122	0	95 (77.9)	24 (19.7)	2 (1.6)	1 (0.8)	1.19‡ (1.06-1.32)	0.27§ (0.11-0.43)
Almotriptan	110	0	64 (58.2)	38 (34.5)	8 (7.3)	0 (0.0)	1.43 (1.30-1.56)	0.42 (0.25-0.59)
Nontriptan	86	16 (18.6)	58 (67.4)	7 (8.1)	4 (4.7)	1 (1.2)	0.97 (0.83-1.11)	1.93 (1.75-2.11)

*Values are number (percentage) unless otherwise indicated.
†AdMet indicates additional nontriptan medication.
‡$P = .0003$ rizatriptan versus almotriptan.
§$P < .05$ rizatriptan versus nontriptan and almotriptan versus nontriptan.

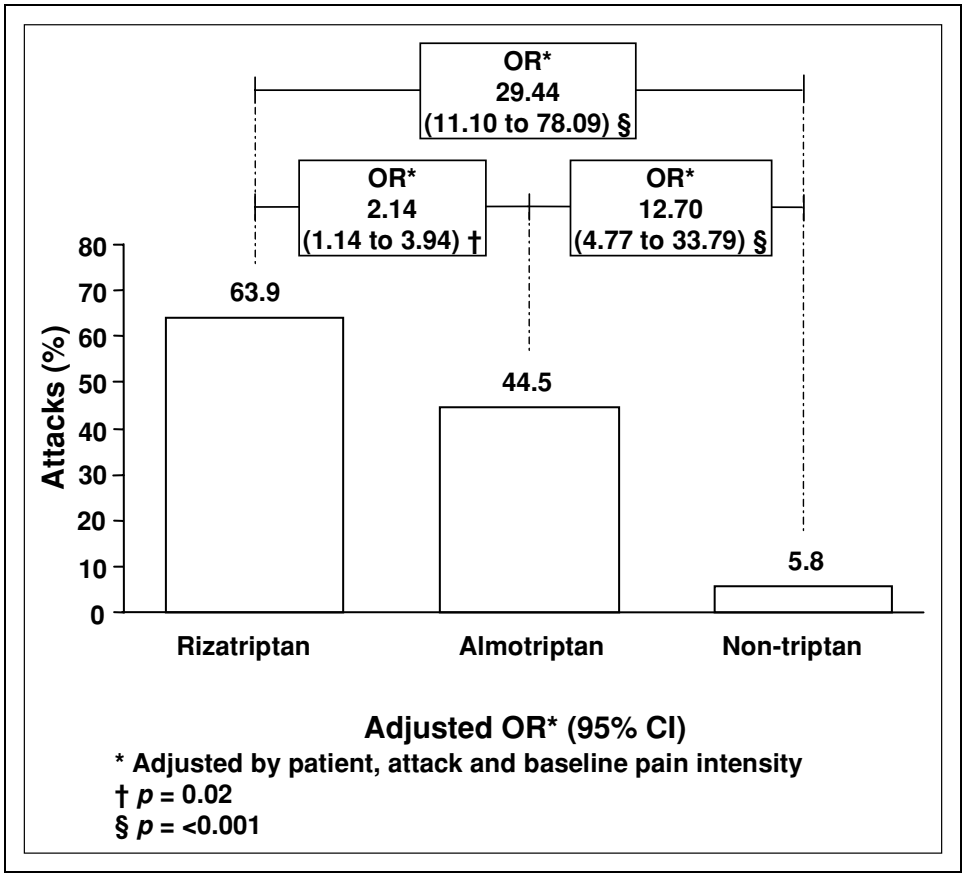

Fig 1.—Percentage of attacks treated with one tablet only and no additional medication in 24 hours. The corresponding probabilities (adjusted odds ratios [OR] [by patient, attack, and baseline pain intensity] and 95% confidence intervals) of using more than one tablet of triptan or additional medication (or both) are also shown. $^{*}P < .001$, $^{\dagger}P = .02$.

severe attacks. A greater number of severe attacks were treated with rizatriptan (44%) than with almotriptan (32%).

There was no statistically significant difference in the proportion of patients previously exposed to either rizatriptan or almotriptan. At the time of entry into the study, 30 patients (44.1%) prescribed rizatriptan were naive to the drug and 38 patients (55.9%) prescribed almotriptan were naive to the drug ($P = .10$).

Medication (Triptan and Nontriptan) Use per Attack (24 Hours).—Triptan use (adjusted mean, 95% CI) per attack in this study was lower for attacks initially treated with rizatriptan (1.19 tablets; 95% CI, 1.06 to 1.32) than with almotriptan (1.43 tablets; 95% CI, 1.30 to 1.56; $P = .003$) (Table 3). The use of additional nontriptan medication in attacks initially treated with rizatriptan (0.27 tablets; 95% CI, 0.11 to 0.43 tablets) was also lower than for almotriptan (0.42 tablets; 95% CI, 0.25 to 0.59) but did not reach statistical significance ($P = .21$). Previous exposure to rizatriptan or almotriptan resulted in no statistically significant differences in triptan or additional medication consumption ($P = .58$). Initial treatment of attacks with a nontriptan medication (0.97 tablets; 95% CI, 0.83 to 1.11) was associated with lower triptan use but with a higher use of additional medication (1.93 tablets; 95% CI, 1.75 to 2.11) and the overall highest consumption of medication. Independently of the use of additional nontriptan medication, rizatriptan was used to treat more attacks with a single tablet (78%) than almotriptan (58%). Of the attacks treated with rizatriptan, 2 tablets were used for 20% of attacks, compared with 35% of attacks treated with almotriptan. Only a small number of attacks were treated with more than 2 tablets of either rizatriptan or almotriptan.

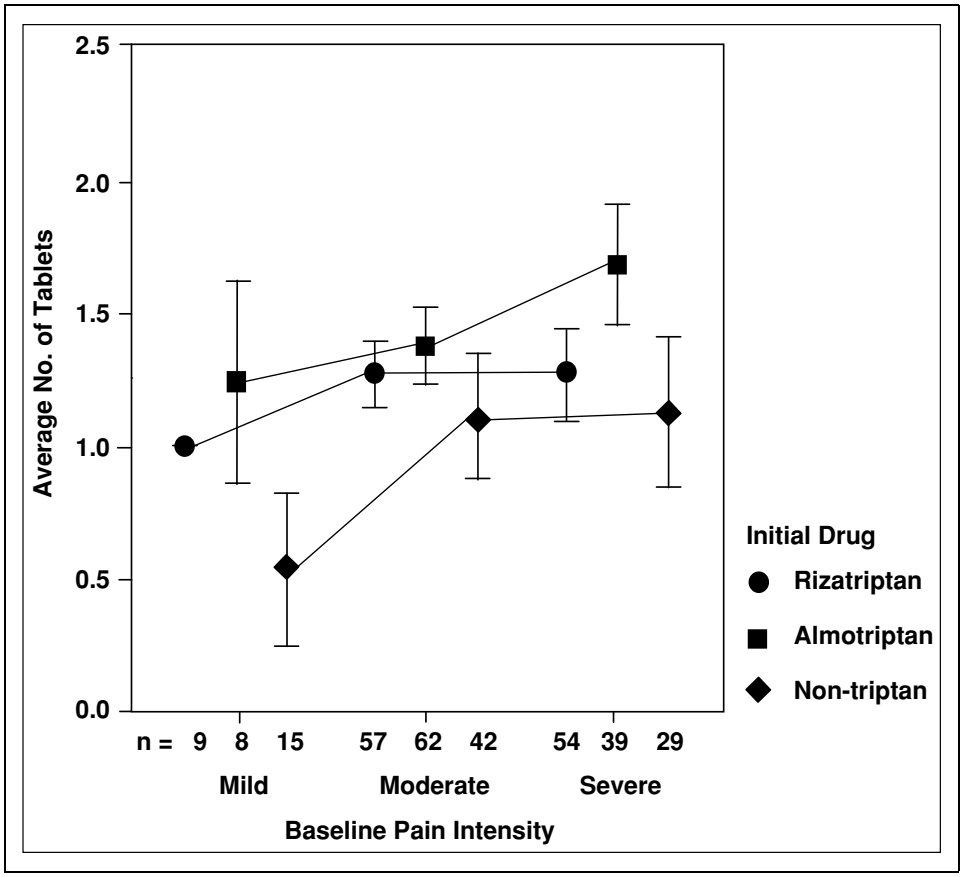

Fig 2.—Mean (± 95% confidence intervals) triptan tablet usage according to baseline pain intensity and initial medication taken.

We calculated the probability (adjusted OR, 95% CI) of a patient using more than one tablet of rizatriptan or almotriptan per attack (24 hours). Initial treatment of attacks with rizatriptan was less likely to involve using more than one tablet per attack than those treated with almotriptan (adjusted OR, 2.42; 95% CI, 1.37 to 4.30; $P = .003$).

Number of Attacks Treated With Only One Tablet and No Additional Medication (24 Hours).—Single tablet treatment (with no additional triptan or nontriptan medication) occurred in a higher proportion of attacks initially treated with rizatriptan (64%) than with almotriptan (45%) or nontriptan medication (6%) (Figure 1). Attacks initially treated with rizatriptan were less likely to involve additional tablets or nontriptan medication (or both) than those treated with almotriptan (adjusted OR, 2.14; 95% CI, 1.14 to 3.94; $P = .02$). Attacks initially treated with a nontriptan were more likely to involve using additional triptan or nontriptan medication per attack than those treated with rizatriptan (adjusted OR, 29.44; 95% CI, 11.1 to 78.09; $P < .001$).

Effect of Baseline Pain Intensity on Medication Usage.—The use of triptan (Figure 2) and additional nontriptan medication (Figure 3) per attack increased with baseline pain severity. Average rizatriptan use was 1.00 tablets (SD, 0) in mild attacks, 1.28 tablets (SD, 0.45) in moderate attacks, and 1.28 tablets (SD, 0.63) in severe attacks ($P = .31$ moderate versus severe). This compared with higher almotriptan use of 1.25 tablets (SD, 0.46) in mild attacks, 1.39 tablets (SD, 0.58) in moderate attacks, and 1.69 tablets (SD, 0.69) in severe attacks ($P < .05$ moderate versus severe). For severe attacks, the use of additional nontriptan drugs was also lower for rizatriptan (0.37 tablets, [SD, 0.71]) than for almotriptan (0.72 tablets [SD, 0.97]). Attacks initially treated with a nontriptan medication were associated with lower triptan use of 1.12 tablets (SD, 0.77) in moderate attacks and 1.14 tablets (SD, 0.74) in severe attacks. However, in this case, the use of

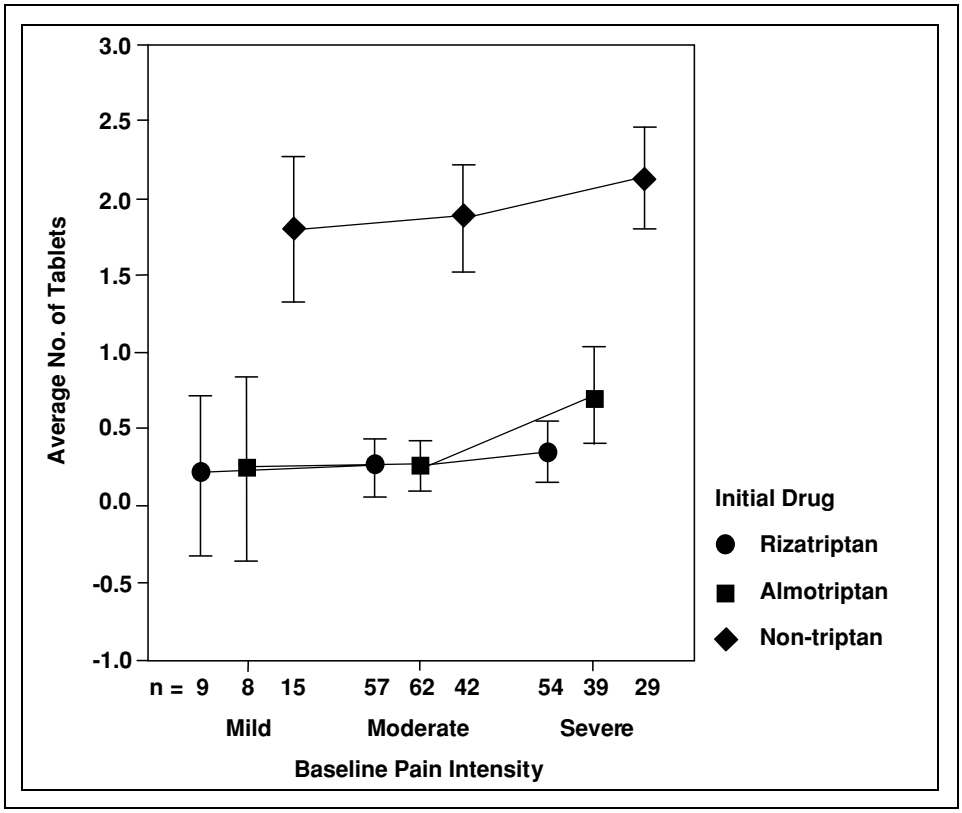

Fig 3.—Mean (±95% confidence intervals) use of additional medication according to baseline pain intensity and initial medication taken.

additional medication was higher than for the triptans in both moderate attacks (1.88 tablets [SD, 1.15]) and severe attacks (2.14 tablets [SD, 0.89]).

Patient Satisfaction With Medication 2 Hours After Treatment.—For all attacks, patient satisfaction with the initial treatment used was assessed 2 hours after medication was first taken. Patient satisfaction (satisfied = completely + highly + somewhat) (Figure 4) was greater for rizatriptan (85%) than for almotriptan (68%) or for nontriptans (64%). The adjusted ORs were 2.55 (95% CI, 1.11 to 5.87; $P = .03$) for rizatriptan versus almotriptan and 3.20 (95% CI, 1.35 to 7.59; $P = .03$) for rizatriptan versus nontriptan. For almotriptan versus nontriptan, the adjusted OR was 1.24 (95% CI, 0.61 to 2.54; $P = .56$).

When using the more stringent grouping of completely and highly satisfied (Figure 5), patient satisfaction was again greater for rizatriptan (55%) than for almotriptan (35%) or for nontriptans (33%). The adjusted ORs were 2.28 (95% CI, 1.14 to 4.58; $P = .02$) for rizatriptan versus almotriptan and 2.69 (95% CI, 1.27 to 5.70; $P = .01$) for rizatriptan versus nontriptan. For almotriptan versus nontriptan, the adjusted OR was 1.02 (95% CI, 0.48 to 2.20; $P = .95$).

COMMENTS

Triptan tablet use per migraine attack over a 24-hour period, as reported by the patients in this study, was significantly lower for rizatriptan than for almotriptan. Further, the use of rizatriptan per attack was consistent with that in our previous study where patients reported significantly lower use of rizatriptan than of sumatriptan, naratriptan, and zolmitriptan per migraine attack over a 24-hour period.[4] No direct head-to-head comparison has been conducted between rizatriptan and almotriptan. However, the results of recent meta-analyses of triptan medications suggested that rizatriptan 10 mg offered greater efficacy and more consistent reliability than almotriptan and other triptans for pain-free and pain relief at 2 hours.[7,8] In particular, placebo-subtracted figures

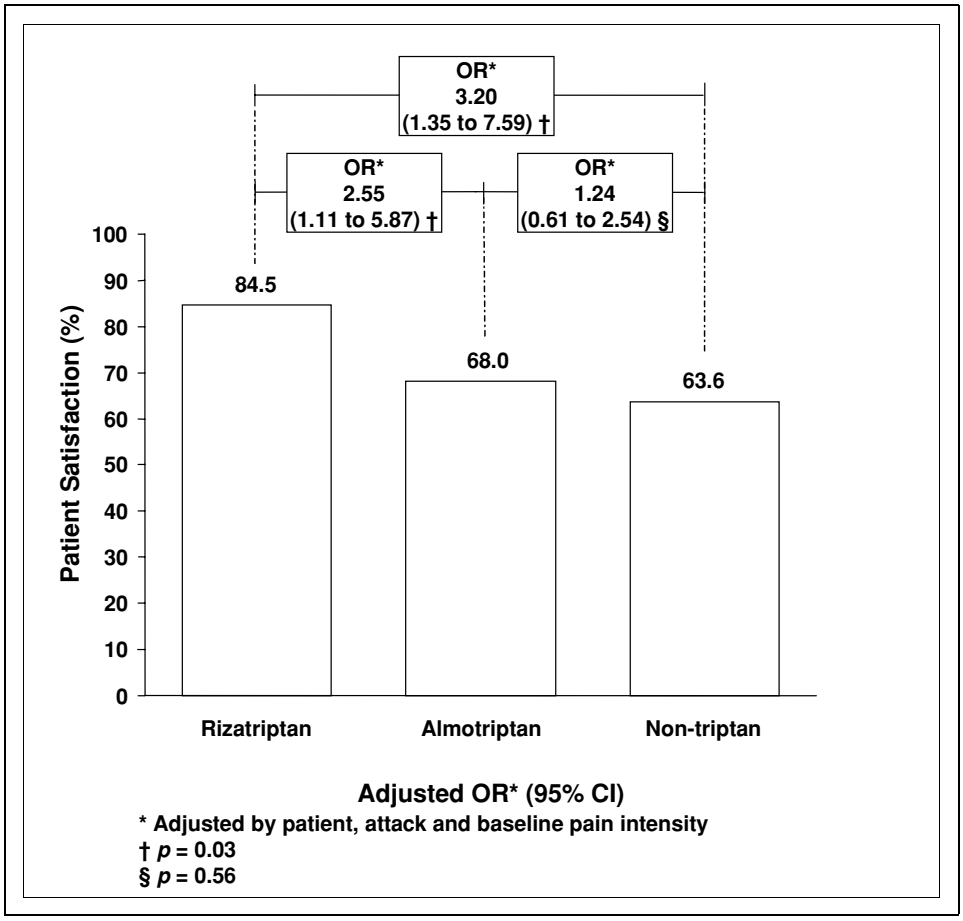

Fig 4.—Patient satisfaction (completely, highly, and somewhat satisfied) 2 hours after medication was first taken. The corresponding adjusted odds ratios (OR) (by patient, attack, and baseline pain intensity) and 95% confidence intervals for patient satisfaction for rizatriptan versus almotriptan, rizatriptan versus nontriptan, and almotriptan versus nontriptan are also shown. $^{*}P = .03$, $^{\dagger}P = .56$.

clearly favored rizatriptan over almotriptan. Although our present investigation did not assess efficacy, patients who initially used almotriptan for acute migraine attacks were more than twice as likely to use more than one tablet per attack than those who used rizatriptan. In addition, patient satisfaction with treatment response at 2 hours was more than 2-fold greater with rizatriptan than with almotriptan. Although prescribed a triptan, a number of patients initially treated their attacks with a nontriptan medication. However, in 81% of these cases a triptan was used later as additional medication. Consumption of additional medication was higher and patient satisfaction lower in these cases than for attacks initially treated with a triptan (particularly rizatriptan). No difference in patient satisfaction at 2 hours between almotriptan and nontriptan medication was found.

Baseline pain intensity affected triptan consumption. There was a significant difference in rizatriptan consumption between mild and moderate attacks, but the difference between moderate and severe attacks did not reach statistical significance. In contrast, almotriptan consumption increased with attack intensity from mild to moderate and from moderate to severe. Further, when almotriptan was initially used to treat a severe attack, the consumption of additional nontriptan medication was also higher than for rizatriptan.

Although our study suggests lower consumption per attack and greater patient satisfaction with rizatriptan than with almotriptan, our study has limitations. This was not a randomized study and therefore, not a true head-to-head comparison. Selection bias introduced by prescribing physicians or patient self-selection (patients requesting a triptan to which they

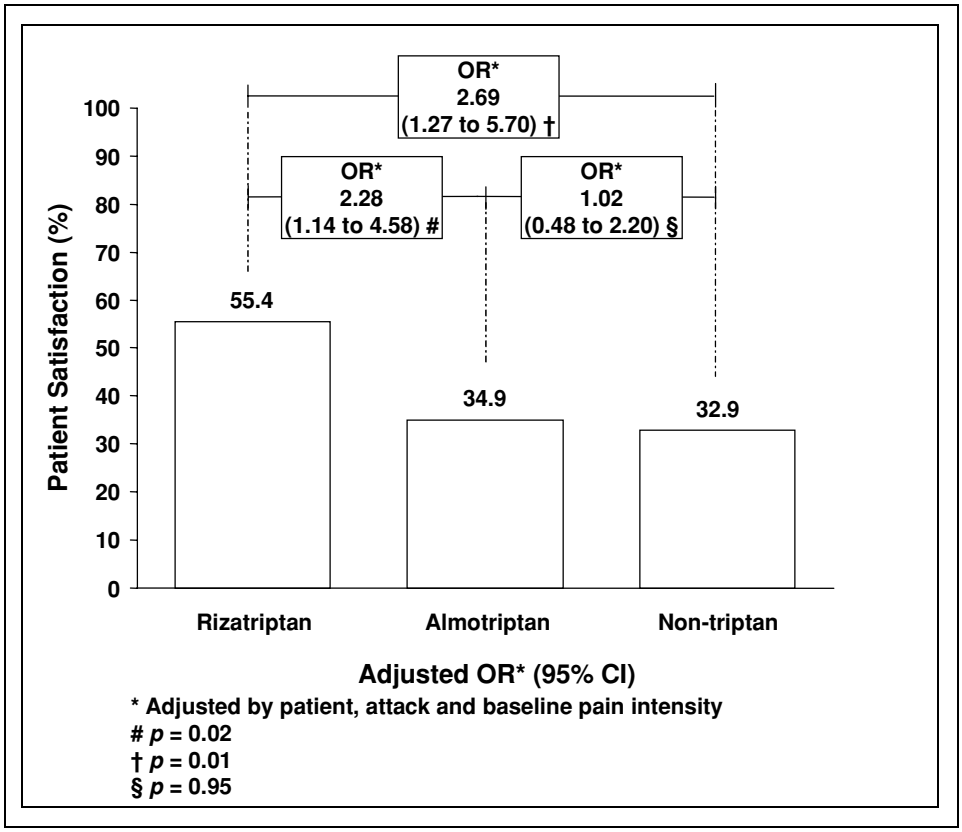

Fig 5.—Patient satisfaction (completely and highly satisfied) 2 hours after medication was first taken. The corresponding adjusted odds ratios (OR) (by patient, attack, and baseline pain intensity) and 95% confidence intervals are also shown for rizatriptan versus almotriptan, rizatriptan versus nontriptan, and almotriptan versus nontriptan. *$P = .01$, †$P = .02$, ‡$P = .95$.

previously responded) is a possibility. As a result, the conclusions drawn require randomized studies for confirmation. However, we also established that previous exposure to rizatriptan or almotriptan resulted in no statistically significant differences in triptan or additional medication consumption. This suggests that any bias introduced by patient self-selection was minimal. Our results are consistent with our previous findings and provide supporting evidence for the superiority of rizatriptan compared with other triptans used for acute treatment of migraine.[4] In our studies, rizatriptan had the lowest triptan tablet usage, the lowest probability of using a single tablet to treat an attack, and the highest patient satisfaction.

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