

EFFICACY AND TOLERABILITY OF THE MARKETED DOSES OF RIZATRIPTAN IN CHILDREN AND ADOLESCENTS: A RETROSPECTIVE REVIEW

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INTRODUCTION

An estimated 6% of boys and 3% of girls experience headaches as early as age 4 to 5 years. Headaches can disrupt school and play activities and negatively affect the quality of life of children and adolescents.¹ Thus the need for safe and effective therapies to treat headaches in this patient population is well recognized. However, studies of migraine therapies approved for use in adults are needed to more fully elucidate appropriate doses for children and adolescents.

The triptans represent an important therapeutic option for adult migraineurs and there are some data regarding their use to treat headaches in children and adolescents.² Rizatriptan (Maxalt®, Merck & Co., Inc.) is a selective 5-HT_{1B/1D} receptor agonist indicated for acute treatment of migraine in adults. The recommended dose is 5 or 10 mg; there is evidence that the 10-mg dose may provide a greater effect.

OBJECTIVES

- To assess the efficacy of rizatriptan in the treatment of migraine in children and adolescents.
- To evaluate the adverse experiences of children and adolescents treated with rizatriptan.

METHODS

Medical records and headache diaries of 64 children (less than 18 years of age) were reviewed retrospectively. Subjects were treated with rizatriptan in a tertiary headache center between 7/1998 and 7/2000. Adequate response to medication was determined from diary entries, progress notes, and patient willingness to use the medication for subsequent attacks. The review included an assessment of reported adverse events.

RESULTS

Demographics

Sixty-four children were given rizatriptan tablets to be self-administered (orally) for acute abortive care of migraine attacks. There were 43 females and 21 males. All patients suffered from IHS migraine with or without aura. Their

TABLE 1. Demographic Characteristics of All Subjects

Characteristics	Average (range) (n = 64)
Age, years	13 (6–17)
Body weight, pounds	117 (51–271)
Length of time since first migraine attack, years	3.5 (1–11)

average age was 13 years (range, 6 to 17 years) and the average body weight was 117 pounds (range, 51 to 271 pounds). The average length of time since first migraine attack for all patients was 3.5 yrs (range, 1 to 11).

Of the 64 patients, 48 received 10 mg and 16 were treated with 5-mg doses of rizatriptan.

TABLE 2. Patients Initially Treated with 10 mg Rizatriptan

Characteristics	Average (n = 48)
Age, years	14
Body weight, pounds	129

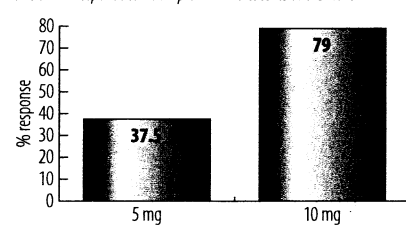
TABLE 3. Patients Initially Treated with 5 mg Rizatriptan

Characteristics	Average (n = 16)
Age, years	11
Body weight, pounds	89

Efficacy

Acceptable or good efficacy was reported in 6 of the 16 (37.5%) subjects treated with 5 mg rizatriptan and 38 of the 48 (79%) subjects treated with 10 mg rizatriptan.

FIGURE. Response to Rizatriptan in Adolescents and Children



Six of the ten patients who did not improve with the 5-mg dose of rizatriptan were then treated with the 10-mg dose. Four of these six subjects (67%) reported good efficacy with the 10-mg dose.

Side Effects Profile

There were only three adverse events reported, all of which occurred in patients treated with 10 mg rizatriptan (3/48; 6.25%). The three adverse events included two patients who experienced drowsiness and one who experienced a warm sensation.

There were no reports of chest pain, palpitations, or gastrointestinal symptoms such as nausea in this series of patients.

DISCUSSION

The response and patient satisfaction with the 10-mg dose of rizatriptan was quite robust (79%) in the studied patient population. These results are commensurate with previously published data from controlled trials in adults.

In contrast, the efficacy in the patients treated with 5-mg tablets (37.5%) was lower than expected based on the available published data. According to the product labeling, the headache response rates at 2 hours were 66% for 5 mg rizatriptan and 56% for placebo in a single study of adolescents (n = 291).

The 5-mg dose of rizatriptan was apparently used to treat the younger (11 vs 14 years) and smaller (89 vs 129 pounds) patients. Although 6 of these 16 patients had acceptable or good efficacy, 10 subjects failed to reach this defined level of efficacy. Nonetheless, four of the six patients (67%) who initially failed at the 5-mg dose were subsequently successfully treated with the higher dose (10 mg) of rizatriptan.

Pharmacokinetic studies suggest that the 5-mg dose of rizatriptan in an adolescent population achieves similar blood concentrations to the 10-mg dose in adults.³ However, in a recently conducted controlled trial of 5 mg rizatriptan in an adolescent population, a clear, statistical distinction between active treatment and placebo was difficult to prove.⁴ Our data suggest that attaining rizatriptan blood concentrations known to be effective in adults may

not induce a clinically acceptable response in children and adolescents. Adequate, well controlled trials using the 10-mg dose of rizatriptan in children and adolescents are warranted.

Both doses of rizatriptan were generally well tolerated. There were no reports of chest pain or palpitations. It is important to monitor for these side effects due to the association between the use of triptans and the potential for cardiac effects.

CONCLUSIONS

This retrospective chart review of data from 64 patients less than 18 years of age showed:

- The 10-mg dose of rizatriptan was associated with a robust response rate (38/48; 79%) and patient satisfaction in a population of children and adolescents.
- Sixteen of the younger and smaller patients were initially treated with the 5-mg dose of rizatriptan; however, the efficacy (6/16; 37.5%) was less than observed with the 10-mg dose.
- Most subjects (4/6; 67%) who failed to show adequate response with the 5-mg dose were subsequently successfully treated with the 10-mg dose of rizatriptan.
- Both studied doses of rizatriptan (5 and 10 mg) were generally well tolerated.

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