

# FREQUENT ELETRIPTAN USE: OBSERVATIONS ON SAFETY

## ISSUES

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## INTRODUCTION

Many patients with chronic migraine (CM) are refractory to the usual preventives. One previous study of patients with CM indicated that, over the long term, only 46% would respond adequately to preventives.(1) These usual preventives include: anticonvulsants, beta-adrenergic blocking agents, calcium channel antagonists, antidepressants, and muscle relaxants. The medication choices for refractory patients are limited, and include: monoamine oxidase inhibitors, botulinum toxin injections, stimulants, opioids, or a combination of preventives.(2)

Certain patients only respond to triptan medications. There have been several studies outlining the use of frequent triptans.(3,4,5) In the current study, the patients were not instructed to utilize triptans on a daily basis. They had 'self-discovered' that a triptan would effectively alleviate the headache for much of the day. Most of the patients had been using the triptans through their primary care physician.

Since rebound headache is an important consideration with any migraine abortive, an effort was made in these patients to withdraw off of the eletriptan. The only patients allowed to continue on frequent triptans were those who: (1) who were truly refractory to other medication/non-medication approaches, (2) experienced minimal side effects, (3) signed a 'Frequent Triptan Informed Consent' form, and (4) had rebound headaches excluded.

The goal of this retrospective study was to evaluate safety issues relating to the frequent use of eletriptan over at least 4 months.

## PATIENTS AND METHODS

Patients.- Twenty-two patients (20 women and 2 men), ages 30 to 59 years (average 45), were evaluated. Inclusion criteria were: (1) the patient had used eletriptan for a minimum of 4 days per week, for at least 4 months; (2) all patients would occasionally go days without any triptan. Exclusion criteria included: (1) not utilizing eletriptan for at least 4 days weekly on a consistent basis, (2) presence of significant rebound headache, and (3) patients who had not had adequate trials of at least 3 preventive approaches. All patients signed a 'Frequent Triptan Informed Consent' form.



Previous Medications.- All study participants were long-term patients at the Robbins Headache Clinic. The patients had been refractory to at least 3 of the usual daily preventive medications. The average number of migraine medications(preventive plus abortive) utilized prior to the eletriptan was 27. Most of the patients had been on 6 or more daily preventives. These included calcium channel antagonists, antidepressants, beta-adrenergic blocking agents, muscle relaxants, anticonvulsants, and others. Most patients were on, in addition to the eletriptan, daily preventive medication.

Type of Headache.- The headache classification was based upon the classifications of the International Headache Society.(6) All 22 patients in this study were diagnosed as having chronic migraine headaches, for a long period of time(see results section).

Rebound Headache.- Patients were screened for the presence of possible rebound headache. Attempts to withdraw the patients from the triptan were undertaken, for a limited period of time, to help exclude the possibility of rebound.

Patients Assessment.- Patients were evaluated by the treating neurologist at the Robbins Headache Clinic, via interviews and chart reviews. Hematologic tests were performed regularly on all patients.

Amount of Eletriptan.- During the course of treatment, eight patients switched from one triptan to another, due to tolerance and insurance issues. The patients in this study had taken the eletriptan for at least 4 months, at least 4 days per week on average.

## RESULTS

Efficacy.- Due to the retrospective nature of this study, the patients would be expected to judge the medication efficacious for their chronic migraine. That indeed was the case; if patients suffered from declining efficacy, they discontinued the eletriptan. 17/22 patients were utilizing daily preventive medication, in addition to the eletriptan, and all patients did use other abortive agents as well. This polypharmacy regimen reflects the refractory nature of this chronic migraine population.

Laboratory(Hematologic) Tests.- Routine blood chemistries and blood counts were performed regularly on all patients, typically every 6 to 9 months. 5 patients had an increased cholesterol, 2 had an increase in ggtp(liver), 1 was anemic, 1 with an increased thyroid test(T4), and one had hypokalemia. None of the abnormalities was felt to be due to the eletriptan.

Durations of Eletriptan Use.- The patients utilized the eletriptan for an average of 12 months. 4 to 8 months=10 pts. 9 to 12 months=2 pts. 13 to 16 months= 1 pt. 17 to 20 months=4 pts. 21 to 24 months=2 pts. 25 to 30 months =3 pts.

Other Clinical Exams.- The patients did not undergo specific testing because of the eletriptan; however, during the course of the study, 6 patients had electrocardiograms, all



of which were normal; 2 patients had cardiac echocardiography, which were normal, and 2 underwent stress testing, both of which were normal.

**Tolerability and Adverse Events.**- Overall the eletriptan was well tolerated. Three patients felt that the eletriptan contributed to fatigue. Two patients had mild pressure sensations that were transient.

Because these patients had decided on their own to utilize eletriptan on a frequent basis, adverse events would naturally be expected to be low. If the patient had not tolerated the eletriptan well, the medication would (presumably) have been discontinued.

## COMMENTS

In this current study, frequent triptan (eletriptan) use did not result in any adverse consequences over a period of time. Twenty-two patients had 'self-selected' eletriptan as the primary beneficial therapy for their frequent migraines. Due to the short time period of this study (4 to 30 months), we cannot state definitively that long-term triptan use is safe.

Several previous studies have examined the safety of frequent triptan use over a period of time.<sup>(3,4,5)</sup> Our previous retrospective study assessed 118 patients over a period of 6 months to over 4 years.<sup>(3)</sup> Hematologic tests were performed in all patients, as well as electrocardiograms in almost all of the subjects. Cardiac echocardiography was also done in 57 patients, as well as stress tests in 20 patients. None of the tests revealed problems relating to the use of the triptan. Adverse events were minimal; 9 patients described fatigue, while 5 had mild chest tightness.

An older study of 59 patients evaluated the long-term use of frequent triptans.<sup>(4)</sup> These patients had found daily triptans to be beneficial after years of failing various preventive regimens. As with the current study, side effects were minimal; however, with the older studies the patients had also 'self-selected' the triptan as the treatment of choice; those who suffered adverse events usually discontinued the medication, or used it sparingly.

Another prospective study of 22 patients with chronic migraine utilized naratriptan for preventive treatment. The conclusions were that "Daily use of naratriptan provided good preventive efficacy in an important subset of subjects with transformed migraine refractory to other preventive treatments, the tolerability of this treatment was excellent, and over a short period of time (3 months) no serious adverse events were reported."<sup>(5)</sup>

Adverse events are common with triptan use. These include paresthesias, fatigue, jaw or neck pressure, chest heaviness, etc.<sup>(7)</sup> Chest symptoms are usually not of cardiac origin. Cardiac ischemia due to triptan use is not commonly encountered.<sup>(8)</sup> While triptans do constrict coronary vessels, it is usually a mild and short-lived effect. Despite tens of millions of patients having used triptans, the number of adverse cardiac events has been fairly limited.<sup>(8)</sup> Electrocardiography and echocardiography have generally been normal after triptan use, even in the presence of chest symptoms.<sup>(9,10)</sup>

The frequency of long-term adverse consequences are unknown from daily triptan use. Theoretical considerations include chronic ischemic changes, valvular abnormalities, or fibrosis. There has not been evidence of these, to date. The number of patients throughout the world who have utilized near-daily triptans is unknown. Until many more



patients have been studied, it is reasonable and prudent to monitor hematologic and cardiac status in these patients.

While adverse effects from long-term triptan use are not known, the other medications that these patients often ingest may lead to various adverse consequences. Many patients with chronic migraine are overusing analgesics, which have well-known adverse events. These include gastrointestinal bleeding, addiction, and renal insufficiency.

Many patients' headache have been refractory to preventive medications. The frequent use of triptans, such as eletriptan, may help a small number of these patients. We must evaluate these patients for long-term adverse consequences.

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