

OPTIMIZING MIGRAINE MANAGEMENT

THE IMPORTANCE OF STRATIFIED CARE
AND EARLY INTERVENTION



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OPTIMIZING MIGRAINE MANAGEMENT

OVERVIEW

ACTIVITY OVERVIEW

Despite the advances of recent years, approximately half of all people with migraine have never received a medical diagnosis and most treat their headaches exclusively with nonspecific, over-the-counter medications. In addition, many patients are treated with less than optimal treatment strategies, mostly variants of step care, despite the compelling evidence for the superiority of stratified care. This new CD-ROM program from the National Headache Foundation and Primary Care Network provides a comprehensive review of the evidence supporting the stratified care approach to acute treatment of migraine, the importance of early intervention during the mild-pain phase of migraine, and a practical, hands-on video case study of a young woman with a high rate of migraine recurrence. The monograph is in the form of PDFs, which may be printed from your computer to provide an enduring resource.

LEARNING OBJECTIVES

After viewing the video and reading the monograph, participating physicians should be better able to:

- Describe the different approaches to acute treatment of migraine: step care within attacks, step care across attacks, and stratified care.
- Evaluate the evidence supporting the stratified-care approach to acute migraine treatment.
- Describe the physiologic rationale supporting early intervention with migraine-specific agents.

ACCREDITATION STATEMENT

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FACULTY DISCLOSURE

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The importance of stratified care and early intervention

More than a decade after the introduction of migraine-specific agents — the triptans — approximately half of all patients have never received a medical diagnosis for their headaches, and most treat their headaches with nonprescription analgesics. In the *American Migraine Study II*, only 48% of survey participants who met IHS criteria for migraine received a physician diagnosis of migraine. [Lipton, 2001] Of these undiagnosed migraineurs, 57% used nonprescription medications exclusively to treat their headaches and 45% experienced at least a 50% reduction in productivity at work or school. At least some degree of functional impairment was experienced by 85.5%. The authors conclude that, “. . . migraine remains an underdiagnosed condition that produces substantial disability.” It is reasonable to conclude that the first, and perhaps most important, step in optimizing patient care should be a public health campaign urging headache sufferers to seek professional medical care.

The first step in evaluating a headache patient is to exclude secondary causes for the headache, based on the patient’s history and a general medical and neurological examination. [Silberstein 1998] After secondary headaches are ruled out, the clinician’s task is to diagnose one or more of the primary headache disorders. Table 1 summarizes the diagnostic features of selected headache disorders.

Migraine is a heterogenous disorder, with considerable variability in the frequency, duration, and intensity of symptoms. [Stewart 1994] Optimal management should therefore be tailored to the individual patient’s headache characteristics. There are two major approaches to the acute treatment of migraine: traditional step care, and the stratified-care approach. In the step-care approach, all patients, regardless of their headache characteristics, are started at the bottom of a therapeutic pyramid, usually with simple analgesics. If treatment fails at this level, therapy is escalated to more potent medications, such as combination analgesics. If this level fails, the patient would move to the next level of potency, typically the triptans. There are two approaches to step care: step care within

attacks and step care across attacks. In step care within attacks, patients initially treat a migraine with a simple, nonspecific analgesic. Response is assessed at a specific time after treatment, usually two hours. If the head pain persists, the patient takes a migraine-specific medication, such as a triptan. In step care across attacks, patients treat several attacks with a simple or combination analgesic. If treatment is unsuccessful, the patient contacts the physician for treatment escalation. [Lipton 2000]

In stratified care, the initial treatment choice is based on the patient’s specific therapeutic needs. There are several variants of the stratified-care approach. Lipton recommends headache-related disability as the basis for stratification, because it is a useful means for assessing the severity and impact of migraine. [Lipton 1998; Goadsby 2002] Mathew suggests that care can also be stratified according to headache severity, time-to-peak pain, or associated symptoms, such as early-onset nausea. [Mathew 1999] When care is stratified by headache severity, for example, patients with severe headaches would be prescribed highly effective, migraine-specific medications early in therapy. Patients with mild attacks might require simple NSAIDs. When migraine attacks are stratified according to time-to-peak pain, patients whose attacks intensify rapidly might be prescribed an injectable triptan or triptan nasal spray.

The Disability in Strategies of Care (DISC) study was a randomized, parallel-group, open-label trial designed to compare the clinical benefits of three migraine strategies across six attacks: stratified care, step care within attacks, and step care across attacks. [Lipton 2000] This study was the first rigorous comparison of acute treatment strategies for migraine. The Migraine Disability Assessment Scale (MIDAS) was used to establish baseline disability. MIDAS measures disability due to headaches based on answers to questions about time lost from the workplace, housework, and family leisure activities, as well as pain frequency and severity. The utility of MIDAS has been well validated. [Stewart 1999]

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TABLE 1. Differential diagnosis of selected headache disorders [Silberstein 1998]

Headache type	Age of onset (yrs)	Location	Duration	Frequency/timing	Severity	Quality	Associated features
Migraine	10-40	Hemicranial	Several hours to 3 days	Variable	Moderate-severe	Throbbing > steady ache	Nausea, vomiting, photo/phono/osmophobia, scotoma, neurological deficits
Tension type	20-50	Bilateral	30 min to 7 days +	Variable	Dull ache may wax/wane	Vise-like band-like pressure	Generally none
Cluster	15-40	Unilateral peri/retro-orbital	30-120 min	1-8 times per day, nocturnal attacks	Excruciating	Boring, piercing	Ipsilateral conjunctival injection, lacrimation, nasal congestion, rhinorrhea, miosis, facial sweating
Mass lesion	Any	Any	Variable	Intermittent, nocturnal, upon arising	Moderate	Dull steady/throbbing	Vomiting, nuchal rigidity, neurological deficits
Subarachnoid hemorrhage	Adult	Global, often occipitnuchal	Variable	Not applicable	Excruciating	Explosive	Nausea, vomiting, nuchal rigidity, loss of consciousness, neurological deficits
Trigeminal neuralgia	50-70	2nd-3rd > 1st division's trigeminal nerve	Seconds, occur in volleys	Paroxysmal	Excruciating	Electric shock-like	Facial trigger points, spasm of muscles ipsilaterally (tics)
Giant cell arteritis	>55	Temporal, any region	Intermittent, then continuous	Constant, ? worse at night	Variable	Variable	Tender scalp arteries, polymyalgia rheumatica, jaw claudication



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A disability grade was assigned to each patient (grade I [little or infrequent disability, score 0-5]; grade II [mild or infrequent disability, score 6-10]; grade III [moderate disability, score 11-20]; and grade IV [severe disability, score ≥ 21]). MIDAS grade I usually indicates a low medical need; simple over-the-counter medications may be effective in the acute treatment of these patients. Grade I patients with infrequent but severe attacks may benefit from using a triptan. MIDAS grade II patients usually have moderate medical needs; patients may qualify for triptans if their headaches are severe. MIDAS grade III and IV patients have high medical needs; triptans are usually the most appropriate therapy and prophylaxis should be considered for some patients.

Patients with grade I disability were excluded from the trial because the majority of patients in this category do not require a triptan to treat their headaches. A total of 835 eligible adult patients with a MIDAS grade II, III, or IV were randomized to one of three treatment groups. Patients were instructed to treat only moderate or severe migraine attacks. The safety analysis included 930 patients.

1. Stratified care. Patients with grade II headaches received aspirin, 800 to 1000 mg, plus metoclopramide, 10 mg, as their acute treatment across all six attacks studied. Patients with grade III or IV headaches received zolmitriptan, 2.5 mg, as their acute treatment for all attacks. Patients were asked not to take rescue medication within the first four hours of the attacks.

2. Step care across attacks. Patients treated the first three attacks with aspirin, 800 to 1000 mg, plus metoclopramide, 10 mg. Those who did not have a satisfactory headache response (defined as a reduction in pain intensity from severe or moderate at baseline to mild or no pain at two hours in at least two of the three attacks) were instructed to escalate therapy to zolmitriptan, 2.5 mg, for the next three attacks. The remaining patients continued using aspirin plus metoclopramide for the remaining three attacks.

3. Step care within attacks. Patients initiated treatment with aspirin, 800 to 1000 mg, plus metoclopramide, 10 mg, for all attacks. After two hours, if a satisfactory headache response was not achieved, patients were instructed to escalate therapy and take zolmitriptan, 2.5 mg.

Enrolled patients ranged in age from 18 to 65 years, met IHS criteria for migraine with or without aura, had migraine onset before age 50, had from one to eight attacks per month for the previous three months, and had not taken a triptan within the last three months. The primary outcome measures were headache response at two hours and disability time per treated attack at four hours.

RESULTS

The proportion of all attacks responding at two hours was significantly greater for stratified care than for step care across attacks for all six attacks (OR: 1.67; CI=1.31-2.12; $p<0.001$; Figure 1). Similar results were seen for headache response at one hour ($p<0.001$ favoring stratified care).

Disability time averaged across all six attacks was significantly lower for stratified care than step care across attacks. The difference was explained by a significantly greater disability time for attacks 1-3 in the step care across attacks group ($p<0.001$).

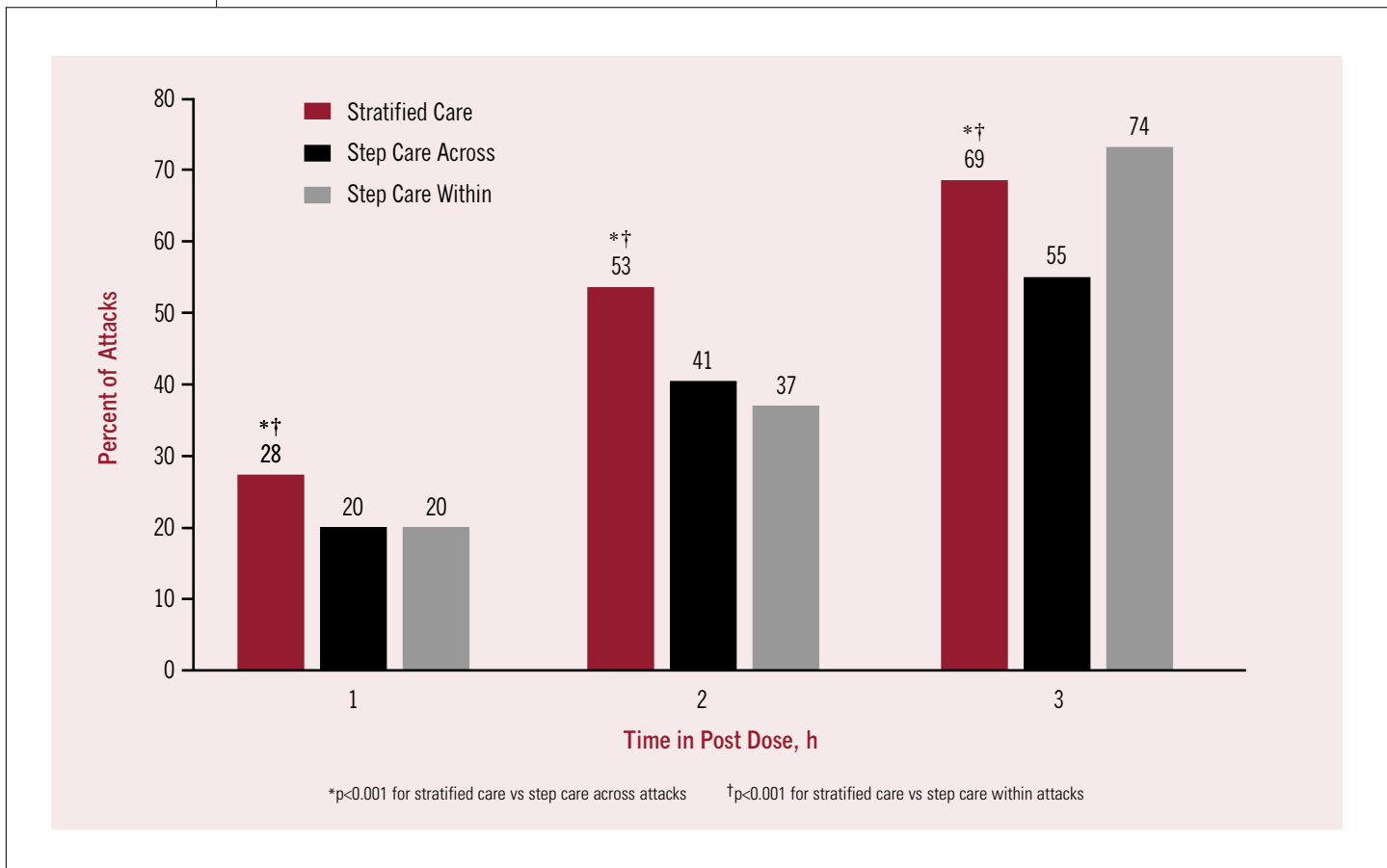
In the step care across attacks group, the proportion of patients who needed to escalate treatment because of lack of response to aspirin plus metoclopramide significantly increased with increases in MIDAS grade, from 56% for patients with grade II to 74% for patients with grade IV headaches.

The proportion of attacks with a headache response at two hours was significantly higher for the stratified-care group than for the step care within attacks group (OR: 2.14; CI: 1.66-2.77; $p<0.001$; Figure 1).



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FIGURE 1. Stratified care vs step care across attacks and within attacks for up to six attacks



Note that the difference between stratified care and step care within attacks is not significant at four hours because patients escalated to zolmitriptan 2.5 mg if they did not have a response at two hours. Disability time was significantly lower in the stratified-care group compared with the step care within attacks group ($p<0.001$). Separation between the two groups was most apparent at two hours prior to rescue with zolmitriptan.

Adverse events (AEs) occurred in 697 attacks; they were generally mild to moderate and consistent with the AEs seen with triptan treatment. AEs leading to withdrawal from the trial were similar across the three treatment groups.

This randomized clinical trial demonstrated the superiority of stratified care over step care within attacks and step care across attacks. Step care can work well

(and may be cost effective), but only if the patient responds to first-line therapy. Step care across attacks is often recommended in managed-care guidelines [Lipton 2000], and many undiagnosed migraineurs employ step care within attacks to treat their headaches. In practice, both step-care approaches have a number of disadvantages:

1. Successful treatment may be delayed, resulting in unnecessary suffering.
2. Resources may be wasted on follow-up visits and failed prescriptions.
3. Patients and physicians may become discouraged and the patient may lapse from care.
4. Overuse of medications (OTC or prescription) may lead to chronic daily headache or medication-overuse (rebound) headache.



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The investigators conclude that their results generally support recommendations regarding the use of stratified care as the more effective treatment strategy.

EARLY INTERVENTION IMPROVES HEADACHE OUTCOMES

One of the disadvantages of step care noted above is that patients may be deprived of early pain relief if their first line of therapy fails. A series of recent studies have underscored the importance of early intervention during a migraine attack. The protocols of early triptan trials instructed patients to wait until head pain was moderate to severe before taking the investigational drug. [IHS Committee 1991] This seemed to be a reasonable approach, since the presence of moderate to severe head pain is one of the IHS criteria for migraine. However, the results seen in protocol violators, who treated their migraines when pain was mild, suggested that this wasn't the best approach. In 1998, the first report was published that suggested that headache outcomes could be improved if patients treated their headaches before the pain progressed to the moderate stage. [International 311C90 Long-Term Study Group 1998] This was a large-scale, nonrandomized study, during which almost 30,000 attacks were treated over a 12-month period. Pain-free response rates more than doubled (80% vs 35%) when mild pain was treated with zolmitriptan 5 mg compared with severe pain. Subsequently, *Cady et al* conducted a post-hoc analysis of the *Spectrum* study, which was a randomized, double-blind, placebo-controlled, crossover study of sumatriptan 50 mg in patients with disabling migraine. [Cady, Lipton 2000] Unexpectedly, study diaries revealed that 46 of the 1156 documented headaches had been treated while pain was mild, a protocol violation. These headaches were removed from the original analysis and subjected to a separate analysis to examine the effect of early intervention with sumatriptan. Across all headaches (migraine, migrainous, and episodic tension-type) treated when pain was mild, pain-free responses were higher for sumatriptan than placebo at four hours (85% vs 17%) and two hours (50% vs 0%) postdose. When the same patients treated headaches while pain was moderate or severe, pain-free rates were lower than those reported for treatment during mild pain. At two hours, the therapeutic gain over placebo was 50% when patients treated mild pain and

21% when patients treated moderate or severe pain. In addition, there was a trend toward lower headache recurrence rates when headaches were treated when pain was mild. Similar results were seen in a retrospective analysis of three other studies that treated migraine with sumatriptan 50- and 100-mg tablets: treatment during mild pain produced higher pain-free response rates and reduced the need for redosing. [Cady, Sheftell 2000]

An additional prospective study evaluated the effect of early treatment in a subgroup of migraineurs with severely disabling headaches (MIDAS grade III or IV). [Klapper, Charlesworth 2002; Klapper, Rosjo 2002] In this study, a total of 302 patients from 24 centers in the U.S., France, and Norway were randomized to zolmitriptan 2.5 mg (n=138) or placebo (n=142). After treatment of one mild migraine attack, significantly more patients in the zolmitriptan group were pain-free at two hours compared with placebo (43% vs 18%; $p < 0.0001$). The majority of patients in this study chose to treat their mild migraine attacks early. In the ITT population, 38.4% of the zolmitriptan group and 39.4% of the placebo group treated their attacks within 15 minutes, while 54% of the zolmitriptan group and 56% of the placebo group treated their attacks within 30 minutes. The pain-free rate increased to 57% in the zolmitriptan group and 20% in the placebo group (an increase of 33%) when the attack of mild pain was treated within the first 15 minutes. The investigators also found that early intervention reduced the impact on normal activities in patients with significant migraine-related disability.

The work of *Burstein et al* on cutaneous allodynia in migraine may provide an explanation for the superior efficacy of early intervention. [Burstein 2000] They observed that initiation of central sensitization appears to depend on impulses from peripheral nociceptors. These nociceptors contain numerous 5-HT_{1D} receptors, the stimulation of which causes a reduction in the release of vasoactive neuropeptides responsible for neurogenic inflammation. [Longmore 1997] The 5-HT_{1D} receptors in trigeminal nerves project peripherally to the dural vasculature and centrally to the brain stem trigeminal nuclei. Peripherally, these receptors are ideally placed to inhibit activated trigeminal nerves and prevent the release of vasoactive peptides. Centrally, they are ideally placed to inhibit pain transmission from the blood vessels to second-order sen-



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sory neurons in the brain stem. [Goadsby 1998] The 5-HT_{1B} receptors occur in large numbers on the smooth muscle of meningeal blood vessels that mediate vasoconstriction; thus, they are ideally placed to reverse the meningeal vasodilation that occurs during a migraine attack. [Longmore 1997; Nilsson 1999; Razzaque 1999; Hargreaves 1999] The triptans are selective 5-HT_{1B/1D} agonists; they target the peripheral nociceptors and are thought to have no effect on second- and third-order neurons. Therefore, the triptans (and other drugs that target peripheral nociceptors) should be most effective in aborting the headache when used early in the pain phase, before the development of central sensitization and cutaneous allodynia. [Burstein 2000]

Will a triptan be effective if it is administered still earlier, during the aura phase of migraine? The study by *Burstein et al* suggests that administering a triptan during the aura, prior to the activation of peripheral nociceptors, would not be effective in preventing the headache phase. [Burstein 2000] *Bates et al* conducted a double-blind, placebo-controlled, multicenter, parallel-group study to determine whether subcutaneous sumatriptan 6 mg administered during the migraine aura would prolong or modify the aura and prevent or delay the headache. [Bates 1994] Patients were randomized to receive either subcutaneous sumatriptan 6 mg (n=88) or placebo (n=83). They treated a single attack of migraine at home, during the aura phase, by self-injection. The median duration of aura following the first injection was 25 minutes for the sumatriptan group and 30 minutes for the placebo group; the difference was not statistically significant. The percentage of patients who developed a moderate or severe headache within six hours after dosing was also similar between the two groups: 68% for those receiving sumatriptan and 75% for those receiving placebo; the difference was not statistically significant. The investigators concluded that sumatriptan given during the aura phase of migraine does not prolong or alter the nature of the aura and does not prevent or delay the development of headache.

The primary goals of acute migraine treatment are to: (1) Treat attacks rapidly and consistently without recurrence, (2) Achieve a pain-free response by two hours, (3) Restore the patient's ability to function, (4) Minimize the use of back-up and rescue medications, (5) Optimize self-care and reduce subsequent

use of resources, be cost-effective for overall management, and (6) Have minimal or no adverse events. [Silberstein 2000] Clearly, early intervention during the mild pain phase of migraine using a stratified-care approach can make major, positive contributions to at least the first five of these goals.

THE PROBLEM OF MIGRAINE RECURRENCE WITH THE TRIPTANS

The evaluation of efficacy in the acute treatment of migraine includes not only initial improvement, but the absence of headache recurrence after initial improvement. Surveys have shown that patients place a high value on low recurrence, rating it more important than good tolerability (Table 2). [Silberstein 1995; Davies 1998] Conversely, headache recurrence is frequently cited as a principal reason for patient dissatisfaction with treatment. [Geraud 2003]

How should headache recurrence be defined? Should recurrence be limited to patients who initially become headache free or should it include headaches that worsen from mild to moderate or severe within a given time period? Is a migraine that returns at 48 hours a recurrence or a new headache? Are worsening and recurrence different physiological phenomena? There are no definitive answers to these questions, although Goadsby argues that, from a clinical point of view, it is reasonable to consider recurrence as a headache that initially improves and then worsens within a 24-hour period. [Goadsby 2000]

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TABLE 2. Features of migraine medication ranked by importance [Silberstein 1995]

Feature	Mean rating*
Provides quick headache relief	9.91
Decreases head pain	9.87
Decreases likelihood of recurrence	9.81
Does not cause nausea	9.14
Decreases nausea	8.75
Decreases vomiting	8.37
Decreases sensitivity to light	8.28
Orally administered	7.97
Decreases visual problems	7.77
Does not cause drowsiness	7.66

*Based on a 10-point scale (1 = not at all important; 10 = extremely important)

Headache recurrence is a problem common to all acute migraine medications, including the triptans and NSAIDs. [Ferrari 2000] Among current therapies, dihydroergotamine appears to have the lowest recurrence rates. [Goadsby 2000] The headache recurrence rates among the triptans differ widely and there have been several attempts to measure these rates. [Goadsby 2000; Ferrari 2000] Methodological problems render the results somewhat suspect, but certain trends have emerged. (One of the problems with a few studies is that recurrence rates were reported as a percentage of the total number of patients treated, including nonresponders.) Table 3 shows a comparison of pain-free response rates and recurrence rates compiled from a variety of triptan trials. A similar comparison was conducted by Gawel and Tepper; they found a clear association between a drug's half-life and the rate of headache recurrence.

Sumatriptan and rizatriptan, which have half-lives of approximately 2 hours, had recurrence rates of approximately 34%. By comparison, frovatriptan, which has a half-life of approximately 26 hours, had a recurrence rate of 9-14% in this series. [Gawel 1998] Naratriptan, which has a half-life of approximately 6 hours, was also shown to have a lower recurrence rate than sumatriptan in a double-blind crossover study of patients with frequent recurrence of their headaches. [Gobel 1999] Another direct, comparative study showed naratriptan to have a lower recurrence rate than rizatriptan. [Bomhof 1999] However, debate exists regarding recurrence rates of the triptans being solely dependent on drug half-life, since longer half-life triptans generally have lower pain-free rates at two hours, and consequently have smaller populations in which pain can recur.



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TABLE 3. Pain-free response at 2 hours and recurrence rates in triptan trials [adapted from Ferrari 2000]

Drug	mg	N	Pain-free at 2 hrs: %(CI)	Recurrence: %(CI)
Sumatriptan	25	361	21 (17-25)	34 (27-41)
	50	367	28 (23-32)	34 (27-40)
	100	962	27 (24-30)	34 (25-42)
Zolmitriptan	2.5	438	25 (21-29)	31 (26-37)
	5	936	32 (29-35)	28 (24-32)
Naratriptan	2.5	799	23 (20-26)	25 (22-29)
Rizatriptan	5	1682	30 (28-32)	39 (36-42)
	10	2485	40 (38-42)	37 (34-39)
Eletriptan	40	1870	27 (25-29)	21 (19-24)
	80	1393	33 (31-35)	20 (17-23)
Almotriptan	12.5	719	36 (32-39)	26 (22-30)
Frovatriptan	2.5	1862	NA*	20 (18-23)

*NA = not available

Triptan half-lives appear to affect recurrence rates, but is this the whole story? *Geraud et al* studied the relationship of the clinical, pharmacological, and pharmacokinetic properties of the triptans to headache recurrence. [Geraud 2003] They evaluated activity at the 5-HT_{1B} and 5-HT_{1D} receptors, elimination half-lives, and clinical efficacy of each triptan. Clinical data were derived from 31 placebo-controlled major efficacy studies. Mean headache response and therapeutic gain were calculated at the time points used to define recurrence in each study. Data for binding affinity and potency were derived from an *in vitro* pharmacologic study, while half-lives were derived from each product's package insert. Rank correlation with recurrence rate was calculated for each test parameter. Results showed that elimination half-life and headache recurrence were inversely correlated ($r = -1.0$; $p = .0016$). There was also a significant inverse correlation between potency at the 5-HT_{1B} receptor ($r = -0.68$; $p = .034$), but not at the 5-HT_{1D}

receptor ($r = -0.20$; $p = .54$). Binding affinities for the 5-HT_{1B} and 5-HT_{1D} receptors were not correlated with recurrence, nor was initial clinical response. The investigators concluded that the triptans with long half-lives and greater potency at the 5-HT_{1B} receptor had the lowest rates of headache recurrence. Goadsby suggests that lipophilicity, which was not studied by *Geraud et al*, might also be associated with a low recurrence rate. [Goadsby 2000] He noted that eletriptan, the most lipophilic of the triptans, has a low rate of recurrence.

Can the relatively high recurrence rates associated with the triptans be reduced? *Ferrari et al* found that administering a second tablet of sumatriptan at 2 hours after an attack did not increase initial efficacy and neither prevented nor delayed migraine recurrence. [Ferrari 1994] However, in two studies *Krymchantowski et al* found that the concomitant administration of an NSAID with sumatriptan sig-



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While the triptans have certainly revolutionized the treatment of migraine, the problem of headache recurrence remains.

nificantly reduced the headache recurrence rate. [Krymchantowski 1999; Krymchantowski 2000] In the first study, the subjects were 50 migraineurs who had treated at least 10 attacks with 100 mg PO sumatriptan, which was effective in at least eight attacks. [Krymchantowski 1999] The subjects also experienced recurrence within 24 hours in at least five of the treated attacks. They were then treated with sumatriptan 100 mg plus tolfenamic acid 200 mg PO during the first 60 minutes of an attack. A total of 240 migraine attacks were treated, with a recurrence rate of 23.8%, compared with a baseline recurrence rate of 62.5% on sumatriptan alone.

The second study included 67 subjects who had treated eight migraine attacks successfully with 100 mg sumatriptan, but had experienced recurrence in at least five attacks (62.5%). [Krymchantowski 2000] The subjects received sumatriptan 100 mg and naproxen sodium 550 mg to treat four consecutive moderate or severe migraine attacks. With the combination therapy, the recurrence rate decreased to 14.2% (38 out of 268 attacks; $p < 0.0001$). The investigators then studied two randomly selected groups of 13 patients each from the 67 subjects evaluated initially. They were given sumatriptan 100 mg plus naproxen sodium 550 mg or placebo in a double-blind design to treat three consecutive migraine attacks. Each group treated 39 attacks. The recurrence rate among subjects taking sumatriptan plus placebo was 59% (23 out of 39 attacks), while the recurrence rate in the group taking sumatriptan plus naproxen was 25.5% (10 out of 39 attacks; $p < 0.0003$). The investigators concluded that sumatriptan plus naproxen sodium significantly decreases migraine recurrence compared with sumatriptan alone.

While the triptans have certainly revolutionized the treatment of migraine, the problem of headache recurrence remains. It is common to all acute treatments; it may occur in up to one-third of attacks, and is perceived by patients as a treatment failure. [Goadsby 2000] The recurrence rate differs from drug to drug and from patient to patient, yet studies suggest that the rate can be reduced. In particular, achieving pain-free efficacy through early intervention during the mild pain phase has been associated with lower recurrence rates. Additionally, the administration of a triptan with a long half-life may suffice in some patients; in others, the concurrent administration of an NSAID or switching to DHE may be helpful.

- ▶ *References on pages 10 and 11*
- ▶▶ *Post-test on page 12*
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OPTIMIZING MIGRAINE MANAGEMENT

POST~TEST

Eight correct answers are required for credit.

- The study by *Bates et al* demonstrated that treatment with subcutaneous sumatriptan 6 mg during a migraine aura:
 A. Shortened the duration of the aura
 B. Prevented the development of a moderate or severe headache
 C. Does not prolong or alter the nature of the aura or prevent or delay the headache
- The results seen in protocol violators in early triptan trials suggested that triptans might be most effective when used early during the pain phase of a migraine attack.
 A. True B. False
- In the *American Migraine Study II*, 25% of the survey participants who met IHS criteria for migraine had received a diagnosis of migraine.
 A. True B. False
- In the step care across attacks group in the DISC study, the proportion of patients who needed to escalate therapy because of lack of response to the initial therapy increased with increases in MIDAS scores.
 A. True B. False
- Which of the following are disadvantages of step care?
 A. Successful treatment may be delayed, resulting in unnecessary suffering.
 B. Resources may be wasted on follow-up visits and failed prescriptions.
 C. Patients and physicians may become discouraged and the patient may lapse from care.
 D. Overuse of medications (OTC or prescription) may lead to chronic daily headache or medication-overuse (rebound) headache.
 E. All of the above
 F. None of the above
- In the post-hoc analysis of the *Spectrum* study, the therapeutic gain over placebo at two hours was 50% when patients treated mild pain and 21% when patients treated moderate or severe pain.
 A. True B. False
- The blockade of 5-HT_{1D} receptors causes a reduction in the release of vasoactive neuropeptides.
 A. True B. False
- In the *American Migraine Study II*, what percentage of undiagnosed migraineurs used nonprescription drugs exclusively to treat their headaches?
 A. 85.5%
 B. 57%
 C. 45%
- The study by *Burstein et al* suggested that triptans should be most effective when used after the development of central sensitization.
 A. True B. False
- According to Lipton, Goadsby, and Mathew, which of the following might serve as the basis for stratification of migraine care?
 A. The degree of migraine-related disability
 B. Headache severity
 C. Time-to-peak pain
 D. Associated symptoms (e.g., nausea)
 E. A, B, and C above
 F. All of the above
- After administration of a triptan, headache recurrence may occur in what proportion of migraine attacks?
 A. Approximately 10%
 B. Up to one out of four attacks.
 C. Up to one third of attacks.
- The binding affinity of a triptan for the 5-HT_{1B} and 5-HT_{1D} receptors is directly correlated with the probability of headache recurrence.
 A. True B. False

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