



Migraine prevention summit proceedings

Part 4 of a 4-part program

Advances in Preventive Therapies for Migraine



Sponsored by Ortho-McNeil Neurologics, Inc.

The National Headache Foundation (NHF) convened an interdisciplinary panel in Chicago, Illinois, to discuss recent developments in the understanding of migraine and current treatment strategies.

This monograph is the last in a series of proceedings of the MIGRAINE PREVENTION SUMMIT. This issue contains important information about recent advances in migraine preventive therapies, as well as excerpts from the panel discussion and a patient case study.

2 Previous issues include a summary of the MIGRAINE PREVENTION SUMMIT outcomes; information on communicating with patients and evaluating patient disability due to migraine; and a discussion of the impact of migraine and the need for preventive therapy. Visit the NHF online for NHF MIGRAINE PREVENTION SUMMIT proceedings and other educational materials at www.headaches.org.

Faculty

Roger K. Cady, MD **Director**

Headache Care Center

Founder

Primary Care Network
Springfield, MO

Kathleen Cahill, MS, CNS, ARNP **Clinical Instructor**

University of South Florida
College of Nursing

Consultant

Headache/Pain Management Center
Tampa General Hospital
Tampa, FL

Christine M. Lantin, PA-C **Physician Assistant**

Diamond Headache Clinic
Chicago, IL

Richard B. Lipton, MD **Vice Chair and Professor**

The Saul R. Korey Department
of Neurology

Director

Montefiore Headache Center
Albert Einstein College of Medicine
Bronx, NY

Debbie Sacchetti **Migraine Patient**

Mt. Laurel, NJ

Richard G. Wenzel, PharmD **Pharmacist**

Diamond Headache Clinic
Inpatient Unit
St. Joseph Hospital
Resurrection Health Care
Chicago, IL

Identifying Candidates for Preventive Therapy

Recently reported results of the American Migraine Prevalence and Prevention (AMPP) study—a population-based study of more than 162,000 people—demonstrated the high prevalence of migraine, the high level of impairment experienced by individuals with migraine, and the underuse of migraine preventive therapies.¹ The study found that approximately 40% of migraineurs were eligible for migraine prevention, but only 13% were currently receiving it.¹ Nearly half of all individuals with migraine were not aware of preventive medications as a treatment option.⁴

Based on AMPP guidelines, patients for whom migraine prevention is recommended exhibit significantly greater levels of disability compared to those who should be considered for and those who do not require migraine prevention (mean MIDAS score of 22.9 versus 8.2 and 3.6, respectively).² According to AMPP results, 22% of patients with migraine report moderate or severe disability level based on their MIDAS scores. Level of impairment is also high; in fact, 54% of patients are severely impaired or require bed rest during their severe headaches.¹ AMPP results indicate a marked underutilization of preventive migraine therapy.¹

The guidelines for initiating preventive migraine therapy below are dependent on information that patients report to their healthcare professionals. Ineffective communication about headache frequency, disability, and acute medication use may contribute to patterns of undertreatment.

Guidelines for Initiating Preventive Therapy*⁵⁻⁷

- Frequency of headache ≥ 2 per month with disability ≥ 3 days per month†
- Recurring migraines that, in the patient's opinion, significantly interfere with daily routines
- Use of acute (over-the-counter or prescription) medication more than 2 times a week
- Acute medications are contraindicated, not tolerated, or ineffective

* Adapted from the US Headache Consortium Guidelines for the Management of Migraines. Members include the National Headache Foundation, the American Academy of Neurology, the American Academy of Family Physicians, and the American College of Physicians–American Society of Internal Medicine.

† Even patients with < 2 attacks per month may experience disability severe enough to require preventive treatment.

Communicating With Patients About Preventive Therapy

Two recent studies, the American Migraine Communications Study I and II (AMCS I and AMCS II) highlighted the need for improved communication between patients and healthcare professionals. Results showed healthcare professional-patient interactions regarding migraine are often dominated by closed-ended questions, primarily about the frequency of migraine attacks. Only 10% of visits addressed migraine impairment in any way. Further, patient interviews by researchers following the clinician's assessment revealed healthcare professionals' and patients' perceptions of frequency did not agree in 55% of cases, and their perception of severity did not agree in 34% of cases. Disagreement on migraine headache frequency was caused by misunderstandings regarding the number of migraine attacks versus the total number of days with headache. For example, if migraine attacks last 2 days each, 3 attacks per month cause 6 headache days per month.

If healthcare professionals do not fully understand their patients' communications of migraine headache frequency and disability, it is not possible to appropriately follow the guideline-based recommendations for preventive migraine treatment. In AMCS I, preventive therapy was discussed with only 50% of patients who met criteria for initiation of preventive therapy. The study investigators suggested that the use of effective communication techniques, including open-ended questions about headache impact and disability, might improve communication (see boxed text for examples of open-ended questions).⁸

Sample Open-Ended Questions to Evaluate Disability From Migraine^{4,8}

1. "How does migraine impact your daily life?"
2. How does migraine make you feel—even when you aren't having an attack?
3. How does migraine impact your work, family, and social life?
4. What activities have you given up because of your migraine? *(Probe to see if the patient avoids participating in hobbies and/or leisure activities out of worry a migraine attack may occur).*

AMCS II assessed an educational intervention designed to improve healthcare professional-patient communication. Healthcare professionals who had participated in AMCS I (8 primary care physicians, 5 neurologists, and 2 nurse practitioners) joined an interactive, 1.5-hour, Web-based training session. During the session, participants learned to use the ask-tell-ask technique to assess migraine attack frequency and open-ended questions (such as “How does migraine impact your daily life?” and “How does migraine make you feel—even when you are not having an attack?”) to assess impairment during and between migraine attacks.⁸

Results showed the use of open-ended questions improved discussion, yielding narratives in 75% of visits. These narratives were brief, usually lasting less than a minute and a half, and helped the healthcare professional to better understand the patient and the patient to feel understood. In addition, healthcare professional-patient alignment on impairment and headache frequency were improved with the use of open-ended questions compared with AMCS I results (61% vs 49% and 56% vs 45%, respectively) and 45% of the healthcare professionals in AMCS II asked about worry between attacks, compared with none in AMCS I. Importantly, length of office visit was not increased by the use of open-ended questions. In fact, although the median length of impairment discussion was 1 minute, 24 seconds with open-ended questions, compared with 1 minute without, the median total visit length was shorter in AMCS II than in AMCS I (median of 9 minutes, 36 seconds vs 11 minutes).⁸

4

Current Treatment Options for Preventive Migraine Therapy

Treatment plans for individual patients may be based on several factors including headache frequency, symptom severity, and comorbid conditions, as well as patient expectations and treatment goals.⁹ A comprehensive migraine treatment plan includes patient education; avoidance of triggers to help minimize attack frequency; use of nonpharmacologic treatments, such as relaxation and biofeedback techniques; and use of acute and preventive medications. Acute medication aims to relieve the pain associated with an attack and stop progression of an individual attack. Preventive therapies aim to reduce attack frequency and duration. The Table below summarizes FDA-approved acute and preventive medications for the treatment of migraine. Lifestyle modification, including maintaining a regular schedule with adequate sleep, exercising, and smoking cessation, is also a focus of disease management. Periodic re-evaluation of the treatment plan is needed to ensure the patient is receiving the optimal benefit from their available therapies.⁹

FDA-Approved Acute and Preventive Treatments for Migraine

Acute Medications	
Analgesics	
Ergot derivatives	
Triptans	
Preventive Medications	
TOPAMAX®* (topiramate)	
Inderal®*-LA (propranolol)	
Depakote®* (divalproex sodium) Tablets	
Blocadren®* (timolol maleate)	

*TOPAMAX is a registered trademark of Ortho-McNeil Neurologics, Inc. Inderal is a registered trademark of Wyeth Pharmaceuticals Inc. Depakote is a registered trademark of Abbott Laboratories. Blocadren is a registered trademark of Merck & Co., Inc.

FDA-Approved Preventive Medications. FDA-approved preventive medications for migraine include TOPAMAX, Inderal-LA, Depakote, and Blocadren. Two large, randomized trials demonstrated the efficacy of TOPAMAX in migraine prevention, with a significant reduction in headache frequency over 6 months of treatment compared with placebo.¹⁰ (See page 10 for full results.) Two randomized trials showed a significant reduction in headache frequency with Depakote compared with placebo over 12 weeks of treatment.¹¹ Results of a placebo-controlled, dose-finding study showed significantly reduced headache frequency and reduced severity (in a composite measure) with Inderal compared with placebo.¹² Combined results of placebo-controlled trials of Blocadren showed at least 50% reduction in headache frequency in approximately 50% of patients receiving Blocadren, compared with 30% of patients receiving placebo.¹³

Summary

AMPP study results demonstrate a high prevalence of migraine in the general population, as well as a high level of impairment experienced by individuals with migraine and the general underuse of preventive therapies.¹ Results of AMCS II suggest part of this underuse may be corrected by improved communication between healthcare professionals and patients, including the use of open-ended questions, which may be better to help identify patients who are candidates for prevention and help assess migraine impairment during and between attacks.⁸

Further, results of AMCS II demonstrated the use of open-ended questions improved discussion and healthcare professional understanding of migraine impairment during and between attacks, without lengthening the total time of office visits.⁸ Individualized treatment plans for patients with migraine may be designed based on headache frequency, symptom severity, and comorbid conditions.⁹ Treatment includes patient education, avoidance of migraine triggers, lifestyle modifications, and use of nonpharmacologic and pharmacologic migraine therapies. Acute medication aims to relieve pain associated with an attack and stop progression of an attack. Preventive therapies aim to reduce migraine attack frequency.⁹ TOPAMAX is included among the group of 4 medications that are FDA-approved for migraine prevention and currently available in the US.

Indication:

TOPAMAX for Migraine: TOPAMAX® (topiramate) Tablets and TOPAMAX Sprinkle Capsules are indicated for adults for the prophylaxis of migraine headache. The usefulness of TOPAMAX in the acute treatment of migraine headaches has not been studied.

IMPORTANT SAFETY INFORMATION

TOPAMAX has been associated with serious adverse events, including:

- Hyperchloremic, non-anion gap metabolic acidosis—lowering of bicarbonate levels in the blood. Measurement of baseline and periodic serum bicarbonate is recommended.
- Acute myopia and secondary angle-closure glaucoma—patients should be cautioned to seek medical attention if they experience blurred vision or ocular pain.
- Oligohidrosis and hyperthermia—decreased sweating and increased body temperature, especially in hot weather. The majority of reports have been in children.
- Cognitive/psychiatric side effects, including cognitive dysfunction, psychiatric/behavioral disturbances including suicidal thoughts or behavior, and somnolence and fatigue.

Most common adverse events associated with TOPAMAX 100 mg vs placebo were: paresthesia, 51% vs 6%; anorexia, *15% vs 6%; fatigue, 15% vs 11%; nausea, 13% vs 8%; diarrhea, 11% vs 4%; weight decrease, 9% vs 1%; taste alteration, 8% vs 1%.

The possibility of decreased contraceptive efficacy and increased breakthrough bleeding should be considered in patients taking combination oral contraceptive products with TOPAMAX.

Patients should be instructed to maintain an adequate fluid intake in order to minimize the risk of renal stone formation.

*Anorexia is defined as a loss of appetite.

**Preventive Treatment of Migraine:
Panel Discussion Highlights**

Following are excerpts from the MIGRAINE PREVENTION SUMMIT panel discussion, addressing recent advances in migraine prevention and designing treatment plans for patients.

Please see enclosed full US Prescribing Information.

**Communicating With Patients About
Migraine**

MODERATOR: What is migraine and how do you begin educating patients about their disease?

RICHARD B. LIPTON, MD: We think of migraine as a chronic disorder with episodic manifestations which, in some cases, can be progressive. This evolving understanding has important implications for treatment. Migraine is a disorder of brain hyperexcitability, a disorder in which the threshold for headache attacks is lowered, not just on days when attacks take place, but everyday. In this context, using preventive therapy to modulate and reduce brain hyperexcitability makes sense. And trying to devise strategies for identifying people at risk for disease progression and intervening to prevent progression also makes sense.⁴

If you ask migraine sufferers what they most want from their healthcare professional, it's an explanation of their illness.⁴

ROGER K. CADY, MD: Well, I agree 100%. And I've really thought of migraine as more of a pervasive disease of the nervous system, characterized by brain hyperexcitability. And what we see is that, as migraine progresses or worsens, it's not only headache we're dealing with, it's the period between headaches.⁴

KATHLEEN CAHILL, MS, CNS, ARNP: When discussing migraine with patients, I try to contextualize a bit for patients, so that they understand why lifestyle changes have to occur—getting across the idea that the migraine brain is different in order to recruit them and enlist them in participating in the lifestyle changes that have to occur.⁴

ROGER K. CADY, MD: We have to realize that for most people who've had this hypersensitivity of the brain, migraine remains a self-diagnosed and self-managed disease. I start that discussion by pointing out that they came to me, typically, to get rid of their headaches. But what I'm trying to really teach them is how they're going to live with this nervous system that nature gave them.⁴

Migraine is a chronic disorder, with episodic manifestations. It is a disorder of brain hyperexcitability, in which the threshold for headache attacks is lowered, not just on days when attacks take place, but every day. Preventive therapy is an appropriate strategy to modulate brain hyperexcitability and reduce frequency of attacks.

Assessing Impairment

MODERATOR: How do you assess patient impairment due to migraine?

KATHLEEN CAHILL, MS, CNS, ARNP: Because I specialize in headaches, I always do a psychosocial assessment on every patient. But often patients do not volunteer information about impairment. They might volunteer about missing days from work, but they're not going to volunteer the other things, like "I'm not socializing." "I'm not going to my kid's dance recitals." "I'm losing touch with my family."⁴

ROGER K. CADY, MD: Nobody likes to admit they have something that disables them.⁴

I ask people to tell me about the life between migraine attacks, and I hear everything from "Well, everything's fine" to a list of various symptoms. Then I have them go through a day with a migraine attack, starting when they wake up and reviewing what decisions they made to treat the attack. It doesn't take very long to do that. And I do the same thing with a day they didn't wake up with a migraine attack. Patients may say life is perfect, but then they describe a life that really isn't. What they're really doing is making choices and decisions and thinking about what they can and can't do.⁴

6 RICHARD B. LIPTON, MD: One limitation of disability measures is that they very much focus on the burden that migraine produces on days when headache is present. Most days, migraine sufferers do not have headaches. But between attacks, migraine also has an impact on individual headache sufferers and on their families. And that component, the interictal burden, is very substantial and takes several forms.⁴

KATHLEEN CAHILL, MS, CNS, ARNP: One of the things I ask them is, "What have you given up? What are the things that you've had to give up because of your migraine attacks?"⁴

Many physicians are still operating within that framework or paradigm of "Treat the symptoms, treat the symptoms, treat the symptoms" and not prevention. The sequelae or the consequences of the headaches are being treated, but the headache itself is not being treated with preventives. This is a change that is needed in the way we treat headache.⁴

Migraine impairs patients both during and between attacks (the interictal burden). Assessing the impact of migraine during and between attacks is key to identifying patients who may be candidates for preventive therapy.

Identifying Candidates for Preventive Therapy

MODERATOR: How do you identify patients who should consider preventive therapy for migraine?

ROGER K. CADY, MD: The most self-evident thing about migraine is the disability it causes, the impact on a patient's life. This is what you see in the office visit, but there is no mention of it when we teach how to diagnose migraine.⁴

KATHLEEN CAHILL, MS, CNS, ARNP: Finding who is the candidate for prevention is not only finding out the frequency, the number of headaches per month, but also the number of migraine days per month and the degree of impairment. You can't just use frequency as your only measure of deciding if a patient is a candidate for migraine prevention. We discuss prevention and lifestyle changes, approaching it from a positive perspective of what can you do and what can we do to help you get your life back.⁴

RICHARD G. WENZEL, PharmD: I tell patients, if you need your acute drug every day or every other day, you're a candidate for preventive therapy.⁴

RICHARD B. LIPTON, MD: If a patient is taking a triptan more than 2 times a week even if the triptan is pretty effective and they're not disabled by their headache, the concern is that their frequent medication use and their frequent headaches may set them up for headache progression. They may move in a direction where acute therapy stops working, and they make that transition to having headaches almost every day. If you're taking an acute medication 3 times a week, that's probably too much.⁴

Patients with headache days ≥ 2 /month with disability, ≥ 3 days/month or recurring migraines that, in the patient's opinion, significantly interfere with daily routines and patients who use acute medication > 2 times/week may be candidates for preventive therapy.⁵⁻⁷

Patient Education and Preventive Therapy

MODERATOR: How do you counsel patients about migraine prevention?

ROGER K. CADY, MD: Patients may be resistant to taking a medicine every day to prevent a headache that happens a few times a month. On the other hand, if that's framed as building support for your nervous system that makes you stronger and healthier not only to prevent headaches but in between headaches, I think that's a very different thing.⁴

RICHARD B. LIPTON, MD: I also think that some patients are reluctant to take a medication on a daily basis and part of that is the way they view the value proposition. Patients feel, “if I have to take a medication every day, that must mean I’m sick.” So there’s an issue of denial at that level. It’s a matter of articulating the value proposition in a way that’s compelling to the patient.⁴

Clearly, part of the value is that preventive therapy decreases attack frequency. If you prevent the attack, you don’t have to endure headache pain during the 2 hours while you’re waiting for the acute treatment to work. Instead of going from 4 to 6 hours of headache-related disability to 2 hours of headache-related disability while you wait for the acute treatment to work, you can avoid the headache-related disability completely.⁴

KATHLEEN CAHILL, MS, CNS, ARNP: You can negotiate with them also, letting them know they may consider discontinuing preventive therapy after a period of time. I find they’re a lot more receptive if we keep that door open.⁴

Increased understanding of the chronic nature of migraine may help patients accept the need for preventive therapy.

Initiating Preventive Therapy

MODERATOR: What do you tell patients who are initiating migraine preventive therapy?

CHRISTINE LANTIN, PA-C: For most of the patients that I see at the headache clinic, by the time they come to see us, they’ve had headaches for so many years and they’ve been to so many clinics that they’re pretty open to the idea of preventive therapy. But I do spend the time explaining that it takes a while for the medication to work. They have to take it on a consistent basis. I explain the purpose of the medication and side effects to watch out for so that they’ll adhere to the treatment program and that, if something comes up, they don’t abruptly stop the medication. And I give them my contact information should they have any questions and so there’s continuity of care.⁴

KATHLEEN CAHILL, MS, CNS, ARNP: Accepting lifestyle changes and preventive therapy for migraine requires a real cognitive shift for patients. It takes time to process and assimilate everything they’re learning, and that takes a lot of support from treating professionals.⁴

RICHARD G. WENZEL, PharmD: I tell patients with migraine that as they make changes, their lives will improve now. With migraine, the changes they make today will improve

their lives, and that can sometimes motivate patients to follow treatment recommendations.⁴

Patient education and support from healthcare professionals is needed to facilitate patient acceptance of lifestyle changes and preventive therapy. Helping patients realize that changes they make today to help manage their disease may motivate them to follow treatment recommendations.

Managing Expectations With Preventive Therapy

MODERATOR: How do you manage patient expectations regarding preventive therapy?

ROGER K. CADY, MD: Our patients often don’t have appropriate expectations of care. If I have high cholesterol, I know what I expect of the medical system when they treat me. That expectation has never really been defined for our patients with migraine.⁴

It is also important to consider how patients convey expectations to the physician. Patients may have unrealistic expectations from treatment, like, “if I take a pill, I’m never going to have another migraine again.”⁴

DEBBIE SACCHETTI, patient: My physician said that the goal was to greatly reduce the amount of headaches I was getting a month, and I may still get headaches. But in my own mind, I thought, “Well, I want to totally get rid of these headaches.” And that was my expectation. When I went back after starting preventive therapy and I still had a few headaches that month, I thought I was a failure, because I felt like I should have been “cured.” But my doctor told me, “You are being helped, because you are getting fewer attacks each month.” This is the medication working. This is success.⁴

RICHARD B. LIPTON, MD: Part of our challenge is the titration of expectations to mobilize patients to seek available care, but not allow the expectations to become unreasonable so that patients are frustrated by the best available care. But we also have a problem that patients’ expectations are sometimes so low that they suffer needlessly for years.⁴

Setting appropriate treatment expectations for preventive therapy is key. Patients may expect to see a reduction in migraine attack frequency, but should not expect a 100% reduction. Although effects may be seen at 1 month, it may take up to 2 to 3 months of continuous treatment to reach full clinical effectiveness. Patients should be encouraged to give therapy an adequate trial.^{14,15}

Reinitiating Preventive Therapy in Previous Failures

MODERATOR: How do you manage migraine in patients who had inadequate migraine prevention in the past? Do you ever reinitiate preventive therapy?

ROGER K. CADY, MD: In my practice, I see a lot of patients taking inadequate doses of preventive medicines. Sometimes just giving them a proper dose, proper instruction on how to use it, and proper titration is all that's needed.⁴

RICHARD B. LIPTON, MD: Yes, it's not unusual for me to see somebody who's tried and failed 6 preventives and hasn't had an adequate trial of 1. That's a little challenging. Sometimes people start at too high a dose and the patient quits because of side effects. Sometimes people start too low and never escalate the dose. Sometimes people escalate the dose but don't give it long enough to have a chance of working. Sometimes patients aren't educated correctly and they have a minor side effect and a breakthrough headache and that's all it takes to get them to quit.⁴

KATHLEEN CAHILL, MS, CNS, ARNP: We have patients who are labeled treatment failures when they come to us, and I put them right back on preventive therapy. Often patients have started too high, ramped up too fast, doses were not raised up high enough, or analgesic rebound was not being addressed. If you fine-tune the dose, sometimes you can get within that therapeutic window.⁴ If I explain to patients why I would like to try it again and give them a good explanation, then I find that they're very willing to do that.⁴

Patients may be labeled treatment failures with preventive therapy due to an inadequate trial or inappropriate dose titration. In some cases, reinitiating preventive therapy with close attention to dose titration and management of side effects may be effective.

Treatment Decisions: Choosing Preventive Therapies

MODERATOR: How do you choose optimal preventive therapy for individual patients?

RICHARD G. WENZEL, PharmD: Choice of preventive therapy is partially determined by efficacy, but it's also often determined by the adverse effect profiles of agents. Often, I say, "What am I trying to avoid in this patient?" and then try to decide which agent to use.⁴

CHRISTINE M. LANTIN, PA-C: When choosing a preventive medication, I first consider the medications that have the biggest body of evidence—the FDA-approved therapies TOPAMAX, Depakote, and the beta-blockers. I would choose those first and then switch things around, if necessary.⁴

I choose a preventive therapy, in part, by looking at the patient's overall health.

Choice of preventive therapy is based on clinical evidence. Efficacy and tolerability, with particular attention to comorbid conditions and pre-existing tolerability issues, are both important.

Preventive Therapy in Patients With Comorbidities

MODERATOR: How do the presence of comorbid conditions affect your choice of preventive therapy?

RICHARD B. LIPTON, MD: Comorbidity is an important factor to consider in selecting preventive medication. The idea of going for the therapeutic "twofer," treating 2 conditions with a single medication, has a lot of appeal. And mainstream, conventional wisdom on choosing preventive medication for a long time focused on comorbidity. In the face of comorbidity, it is preferable to optimally manage all the disorders that are present rather than going for the therapeutic twofer.⁴

Although the therapeutic twofer is desirable, it's not desirable to suboptimally manage 2 diseases rather than focusing on each disease separately. I think it's a particular concern with migraine and comorbid depression, which is a very common comorbidity. The evidence for SSRIs does not support its use for episodic migraine and tricyclics are not well tolerated and the antimigraine dose of tricyclics that one would normally use is below the recommended dose for managing major depression. Therefore, going for the therapeutic twofer — trying to manage 2 conditions with 1 medication — is not the best choice. It is better to use separate agents to optimally manage each condition.⁴

While it is tempting to strive for the therapeutic twofer (trying to manage 2 conditions with 1 medication), it is preferable to optimally manage comorbidities separately to ensure the best management of each condition.

Patient Case: Preventive Treatment for Frequent Migraine⁴

- 40-year-old woman, married with 2 children (ages 7 and 16), with frequent migraine attacks for previous 10 years.
- Previously treated migraine attacks with triptans and over-the-counter analgesics, but had inadequate symptom control and increasing attack frequency.
- Following evaluation at a headache clinic, patient was considered a candidate for preventive therapy due to frequent headaches, dissatisfaction with current triptan and frequent use of acute medications (> 2 times/week).
- Experienced several days of impairment every month because of migraines and a high degree of concern about when her next attack may strike.
- Preventive treatment with TOPAMAX was initiated, resulting in reduced headache frequency.
- After several weeks of treatment, migraine attacks are less infrequent.
- Treatment is generally well tolerated, with mild side effects



Following evaluation at the headache clinic, it was determined that in addition to an increasing frequency of her migraines, Debbie was possibly starting to experience rebound headaches due to overuse of acute medications. She and her doctor initiated TOPAMAX for migraine prevention in conjunction with scheduled reduction and discontinuation of the overused over-the-counter sinus medications and analgesics. A triptan was used as acute treatment for breakthrough migraine attacks. During the first 12 weeks of her treatment, headache frequency gradually reduced to 3 headache days per month.

With continued treatment, including TOPAMAX for migraine prevention, Debbie experienced further reductions of migraine frequency over the next 12 months to <1 headache day per month.

After 15 months of TOPAMAX treatment, she discontinued preventive therapy. Headaches began to reappear, and preventive therapy was reinitiated, titrating to a maintenance dose of 50 mg bid. Debbie now reports that her headaches are infrequent, experiencing a migraine attack approximately once every 4 months.

Side effects were generally transient and mostly resolved once Debbie reached a full therapeutic dose of TOPAMAX after about 1 month of treatment.

In Her Own Words: Debbie Sacchetti Talks About Her Disease

At the **MIGRAINE PREVENTION SUMMIT**, Debbie spoke about her experience with migraine and the impact of preventive therapy on her life. Below are excerpts of Debbie's comments about her treatment and its effects.

Debbie had difficulty functioning on the days she had headaches and between headaches:

You wake up in the morning and you sit there for a minute and you go, "Okay, is there a headache?" And there is that anxiety about getting a headache. You watch the weather. You anticipate a headache coming. But sometimes you don't know how to treat this disease — you don't know that there is prevention out there. So you allow it to get worse, 'cause you think you're doing the best thing possible.

Debbie self-treated her migraine with over-the-counter and prescription medications:

I had to function every day, so I never spent the day in bed. When I wake up in the morning with a headache, I have to decide what I'm going to take today. Usually, I'd try a cup of coffee first. If that didn't work, then I would take the sinus medication. If that didn't work, then I'd have to go to the triptan. I know the episode is going to continue for a few days, so the next morning, I may even wake up right away

Evaluation for Preventive Therapy

After suffering from chronic migraine for 10 years, Debbie went to a headache clinic for a full evaluation. Although she had previously been diagnosed with migraine and prescribed a triptan for acute treatment, Debbie did not fully recognize the frequency of her migraine attacks. Believing she suffered from sinus headaches, Debbie frequently self-medicated with over-the-counter sinus pain medication, sometimes taking up to 8 to 10 pills a day during headache attacks. Despite use of triptan medications, she experienced 4 migraine attacks per month, each typically lasting for 3 to 4 days, resulting in up to 16 migraine days per month. Debbie often employed an incremental approach to treating each migraine attack, beginning with caffeine and progressing to over-the-counter analgesics or sinus and pain medication and finally to a triptan in attempts to control her headache pain.

Debbie experienced side effects to several triptans, including somnolence and feeling "disconnected," and was unable to drive while taking her acute medication. Side effects and inconsistent efficacy in controlling her migraine symptoms prompted her to change from one triptan to another. In addition, she started to become concerned about her increasing need for acute medication because of an increasing frequency of her attacks.

and take a triptan. I always thought I was taking too much medication, but I didn't discuss it with my primary care physician, even as the frequency of attacks increased. I felt fine treating myself, and figured I could just take a triptan if needed. I felt I had that to fall back on.

Debbie visited a healthcare clinic for a full evaluation:

When I went to the headache clinic, my husband came with me. He said, "I'm going to make sure you don't leave anything out." And that's what he did, he made sure the doctor knew all my symptoms and how migraine affected my life. I would sometimes go up and lay on the bed if we were at a friend's house and my headache would start. I would just be miserable all day.

Debbie initiated preventive therapy with TOPAMAX:

My doctor discussed several possible treatments with me, but said that TOPAMAX would probably be best for me. When I first started taking TOPAMAX, within the first couple of weeks, my migraine episodes were drastically reduced to only about 3 a month. They were just getting less and less frequent, and then it was like 2 a month, 1 a month, and they were only lasting a day. If I would wake up with a headache, I would right away take a triptan, and within 10 or 15 minutes, it would take the headache away and that would be the end of it. I wouldn't get it back anymore that day, and I wouldn't wake up the next day with it.

Treatment was generally well tolerated, and side effects were manageable:

I had some tingling of the fingers and toes, which only lasted a little bit. As I increased the dosage, I had a little more disassociation, a little bit of disconnection, a little bit of memory loss. It's very easy to get dehydrated. Those kind of things started to get better as I started to get a little more adjusted to the medication. Most of the side effects went away once I was on full dosage, after about a month.

Overall, I felt the side effects were just a minor nuisance. They never made me want to get off the medication. My doctor told me about what side effects to expect before starting treatment.

I had to balance the benefits and risks and, for me, this treatment plan worked.

Debbie's life has been improved with preventive therapy:

With fewer migraines, I don't always feel like I'm going to wake up with a migraine any more. I don't feel like everything I do is going to contribute

to a headache. I'm careful of certain things that I know can contribute to them, but I didn't have to be afraid with everything I do. It kind of gives you that peace of mind and there's less anxiety in between headaches worrying about "Ooh, is today going to be the one day I'm going to get the headache?" Every day I know is going to be a good day now.

I'm able to perform 100% when I'm with my family and friends. My family enjoys the change, too, because they don't have to always hear "I have a headache right now, just leave me alone" or "I'm going to go, but I'm not going to have a good time." They are certainly glad not to hear that all the time anymore.

TOPAMAX in Migraine Prevention

Results of 2 large, randomized, multicenter trials demonstrate the efficacy and safety of TOPAMAX in migraine prevention. The trials enrolled patients with a history of migraine (using IHS criteria) for at least 6 months who experienced 3 to 12 headache attacks during a 4-week baseline phase. Patients were randomized to TOPAMAX 50 mg/day, 100 mg/day, or 200 mg/day or placebo and treated for 26 weeks (including an 8-week titration period and an 18-week maintenance period). Efficacy was measured by reduction in headache frequency (change in 4-week headache rate).¹⁰

In the first study, 265 of 469 enrolled patients completed the entire 26-week treatment phase. The mean headache frequency at baseline was approximately 5.5 in 28 days. The mean change in 4-week headache period frequency from baseline was -1.3, -2.1, and -2.2 in the TOPAMAX 50-, 100-, and 200-mg/day groups, respectively, compared with -0.8 in the placebo group. Differences in mean change from baseline between the 100- and 200-mg/day groups versus placebo were significant ($P<.001$).¹⁰

The second study showed similar results, with 255 of 468 enrolled patients completing the entire 26-week treatment phase and a mean headache frequency at baseline of approximately 5.5 in 28 days. The mean change in 4-week headache period frequency from baseline was -1.4, -2.1, and -2.4 in the TOPAMAX 50-, 100-, and 200-mg/day groups, respectively, compared with -1.1 in the placebo group. Again, differences in mean change from baseline between the 100- and 200-mg/day groups versus placebo were significant ($P=.008$ and $P<.001$, respectively).¹⁰

Treatment was generally well tolerated, although side effects appeared to be dose related. The most common adverse events associated with TOPAMAX 100 mg vs placebo were: paresthesia, 51% vs 6%; anorexia (defined as loss of appetite), 15% vs 6%; fatigue, 15% vs 11%; nausea, 13% vs 8%; diarrhea, 11% vs 4%; weight decrease, 9% vs 1%; taste alteration, 8% vs 1%.¹⁰ The majority of adverse events occurred with less frequency during the maintenance phase of treatment compared with titration (the first 3 weeks of therapy).¹⁶

NHF Migraine Prevention Summit Consensus Statement

The interdisciplinary panel developed the following consensus statement highlighting the key findings of the **Migraine Prevention Summit**.

- Migraine is a chronic disorder, rather than an episodic disorder. Healthcare professionals treating patients with migraine must be educated about recent advances in the understanding of migraine and current treatment options.⁴
- Proper use of acute medications is essential to maximize their efficacy. Acute medications should be taken at the first sign of migraine (or during the aura, if present).⁴
- Acute medication is not always adequate to control migraine attacks. Preventive therapy should be considered in patients requiring acute medication more than 2 days per week and in those experiencing frequent disability during and between migraine attacks.^{1,4}
- Healthcare professionals need to determine patient disability and the total level of impairment migraine has on a patient's life, both during and between attacks, to better assess when patients may be appropriate candidates for preventive therapy. In addition, it is important to recognize how migraine affects other aspects of the patient's life, such as family and work life.⁴
- Preventive therapies include both medications and behavioral modifications.⁴ Patients need realistic expectations about treatment outcome, specifically time to response. Preventive therapies may take 6 weeks or longer to reach clinical effect. In addition, patients should be counseled on what side effects to expect and should be titrated slowly to the target dose.¹⁵
- Patients are important partners in the management of migraine. Open communication about treatment options and healthcare professional-patient support is essential to ensure treatment plans are followed. Adherence to treatment regimens, including both lifestyle changes and medications, is necessary to achieve optimal effect.⁴
- Migraine is a manageable disease. With communication and cooperation between patients and healthcare professionals, most patients can achieve greater control of their disease and reduce their disability.⁴

NHF Migraine Prevention Summit Proceedings

Issue 1: Overview of Migraine

Issue 2: The Importance of Communicating With Patients

Issue 3: Impact of Migraine: Evaluating Patient Disability

Issue 4: Advances in Preventive Therapies for Migraine

Learn more about migraine prevention and treatment, download patient education materials, and view all 4 issues in this series at www.headaches.org.

Take full advantage of all the resources of the National Headache Foundation today.

The National Headache Foundation (NHF) is a non-profit organization established in 1970 to promote services to headache sufferers, their families, and the healthcare professionals who treat them. Physician membership in the NHF provides the following benefits:

- *Standards of Care for the Diagnosis and Treatment of Headache and the Therapeutic Guide for the Treatment of Headache*
- Copies of **NHF Head Lines**
- Patient education information
- Listing in the NHF professional membership directory
- Opportunities to speak at public education seminars in your area
- Details on grants available through the NHF
- Toll-free access to the NHF office and information via our Web site
- Assistance in organizing local support groups, and more

To join as a professional member or learn more about the services we offer, call 888-NHF-5552 or visit our Web site at www.headaches.org.



National Headache Foundation
820 N. Orleans, Suite 217
Chicago, Illinois 60610-3132
Toll free 1-888-NHF-5552
www.headaches.org

References

1. Lipton RB, Bigal ME, Diamond M, et al, for the AMPP Advisory Group. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2007;68:343-349.
2. Loder E, Silberstein S, Diamond S, et al. Candidates for preventive migraine therapy in a community sample: results from the American Migraine Prevalence and Prevention (AMPP) study. Abstract P04.091 presented at: 58th Annual Meeting of American Academy of Neurology; April 1-8, 2006; San Diego, CA.
3. Lipton R, Stewart WF, Freitag G, Reed ML. Barriers to migraine prevention medication use in a community sample: results from the American Migraine Prevalence and Prevention (AMPP) study. Abstract S17.002 presented at: 58th Annual Meeting of American Academy of Neurology; April 1-8, 2006; San Diego, CA.
4. Data on file. Titusville, NJ: Ortho-McNeil Neurologics, Inc.; June 2006; September 2006; December 2006; February 2007.
5. Schroeder BM. AAFP/ACP-ASIM release guidelines on the management and prevention of migraines. *Am Fam Physician*. 2003;67:1392,1395-1397.
6. Silberstein SD, for the US Headache Consortium. Practice parameter: evidence-based guidelines for migraine headache (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2000;55:754-762.
7. Ramadan NM, Silberstein SD, Freitag FG, et al. Evidence-based guidelines for migraine headache in the primary care setting: pharmacological management for prevention of migraine. Available online at: <http://www.aan.com/professionals/practice/pdfs/g10090.pdf>. Accessed November 13, 2006.
8. Hahn SR, Nelson M, Lipton RB. The Language of Migraine (LOM) study: frequency, impairment, and prevention in migraine communication. Poster presented at: The Diamond Headache Clinic's 19th Annual Practicing Physician's Approach to the Difficult Headache Patient; February 14-18, 2006; Rancho Mirage, CA.
9. Silberstein SD, Saper JR, Freitag FG. Migraine: diagnosis and treatment. In: Silberstein SD, Lipton RB, Dalessio DJ, eds. *Wolff's Headache and Other Head Pain*. 7th ed. New York, NY: Oxford University Press, Inc.; 2001:9-237.
10. TOPAMAX Prescribing Information. Titusville, NJ: Ortho-McNeil Neurologics, Inc.
11. Depakote® Tablets (divalproex sodium) delayed-release tablets [package insert]. North Chicago, IL: Abbott Laboratories; January 2006.
12. Inderal® (propranolol hydrochloride) Tablets [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals, Inc.; August 2006.
13. Blocadren® (timolol maleate) Tablets. Whitehouse Station, NJ: Merck & Co, Inc.; March 2002.
14. Snow V, Weiss K, Wall EM, Mottur-Pilson C, for the American Academy of Family Physicians and the American College of Physicians—American Society of Internal Medicine. Pharmacologic management of acute attacks of migraine and prevention of migraine headache. *Ann Intern Med*. 2002;137:840-849.
15. Loder E, Biondi D. General principles of migraine management: the changing role of prevention. *Headache*. 2005;45[suppl 1]:S33-S47.
16. Freitag F, Láinez MJA, Neto W, Shi Y. Comparing the incidence of adverse event sin the titration and maintenance phases of placebo-controlled trials of topiramate for migraine prevention. Poster P05.159 presented at: 2005 Annual Meeting of the American Academy of Neurology; April 9-16, 2005; Miami Beach, FL.