

Migraine in the Managed Care Environment

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Abstract

Migraine headache remains a major clinical problem in the managed care environment, incurring a heavy toll in terms of treatment costs, patient disability, and patient quality of life. Abortive treatment with triptans has become the standard of care in patients with acute episodic migraine. However, there is no such consensus about the optimal approach to prophylaxis in patients with frequent or intractable migraine. The agents currently approved in this role are not always effective and may cause systemic side effects. One potential alternative to currently approved treatments may be botulinum toxin. When injected into carefully pinpointed pericranial locations at 3-month intervals, botulinum toxin may offer effective prophylaxis with minimal side effects. However, the evidence available to date has been inconsistent, with benefit seen in some reports but not in others. Consequently, managed care policymakers have been cautious about approval of coverage for this treatment. Specific criteria for the use of botulinum toxin vary among different plans. At present, many plans do not approve coverage for this agent for the treatment of migraine; other plans do allow coverage as needed for patients in whom conventional approaches have been ineffective or intolerable, but not as a first-line approach to prophylaxis.

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Clinical approaches to the treatment of migraine in the managed care setting are consistent with currently accepted standards of care in the community. As with any clinical condition, the goals are ultimately the same—first, to achieve the best possible clinical results for the greatest number of patients within the limits of available resources, and, second, to minimize costs when possible without compromising the first goal.

Migraine is a significant problem in primary care, incurring substantial direct and indirect costs and a heavy toll on quality of life due to pain and lost time at school or

work. These issues have long been recognized as a major challenge in the managed care setting.¹ Migraine treatment is almost always provided on an outpatient basis, and the major cost factor in outpatient management, once the diagnosis has been established, is drug therapy. Where the available clinical evidence is strongly supportive of a given type of pharmacotherapy, managed care protocols typically conform closely to the accepted standards of clinical practice.

For example, there is authoritative evidence documenting the effectiveness, tolerability, and cost effectiveness of the triptans (5-HT₁ agonists) in abortive therapy for acute episodes of migraine, yet there is no compelling evidence to suggest that any particular triptan is clearly and consistently superior or inferior to other agents within this class, and no single agent is reliably effective in all cases. Overall, the response rate to triptans (defined as relief within 2 hours of dosing) approaches 70%, but many patients who do not respond to one triptan will respond to another.² Thus, most managed care protocols recognize the use of triptans as a class for first-line abortive treatment of migraine, but the selection of a specific triptan and dosing regimen is usually considered a matter of clinical judgment in each individual patient.

The other US Food and Drug Administration (FDA)-approved abortive treatment for migraine is the ergot alkaloid class. Although these older agents offer acceptable efficacy and tolerability and are less expensive than the triptans, the trend in the practice setting has been toward use of the triptans as first-line therapy (which indicates that the interest in minimizing costs does not outweigh the interest in achieving optimal clinical outcomes, either within or outside of the managed care environment). Triptans account for more than three

fourths of the \$1.5 billion spent annually in the United States for migraine medications.³

Nonsteroidal anti-inflammatory drugs (NSAIDs) may be effective in aborting an acute episode of migraine (an off-label use), but most specialists regard the triptans as superior.⁴ NSAIDs may be cost-effective in patients with relatively mild cases of migraine,⁵ but there is general agreement that early intervention with adequate doses of a triptan improves clinical outcomes in patients with more severe migraine.

In contrast to the general consensus regarding abortive treatment, the evidence pertaining to migraine prophylaxis is far more tentative. Selected beta blockers (propranolol, timolol) and antiepileptic drugs (divalproex, topiramate) are currently approved for prophylaxis, but there are no strong consensus guidelines on when to initiate prophylaxis based on the frequency of acute migraine attacks. With a highly aggressive approach aimed at preventing transformation to a chronic state, prophylaxis might be considered in patients who suffer 3 or more acute attacks per month; with a more conservative approach aimed at avoiding unnecessary pharmacotherapy, the standard might be as high as 6 or 8 attacks per month. In addition, a number of other drugs have been used off-label for prophylaxis, despite limited published data, with varying degrees of effectiveness. Systemic drugs used off-label for migraine prophylaxis include other beta blockers and antiepileptics, antidepressants, and calcium channel blockers.

Botulinum toxin, a nonsystemic modality, is injected locally at carefully targeted muscles of the pericranial regions, usually at 3-month intervals. Several reviews of clinical trial data suggest that botulinum toxin is a promising approach, offering a relatively high degree of prophylactic effectiveness with minimal side effects and no reliance on daily patient compliance.⁶⁻¹⁰ Other research, however, points out that the results with botulinum toxin have been better in open-label trials than in blinded controlled trials.¹¹⁻¹³

As a consequence of the uncertainty about the optimal approach to migraine prophylaxis, protocols tend to be more varied

and less definitive than those in use for abortive treatment. A recent review of advances in migraine management and their implications for managed care emphasizes the clinical and economic advantages of the triptans in abortive treatment, but merely surveys the wide range of agents that have been used for prophylaxis—approved therapy with beta blockers or antiepileptics, and off-label use of tricyclic antidepressants, selective serotonin reuptake inhibitors, angiotensin-converting enzyme inhibitors, and calcium channel blockers.¹⁴

Consequently, different managed care organizations have different policies for coverage of services where the evidence is not clear on whether the service should be considered investigative or unproven; such is the case for botulinum toxin. However, reflecting the relative paucity of data, these plans are in general agreement that botulinum toxin appears promising, but cannot yet be considered a first-line approach to migraine prophylaxis. Indeed, at our current state of knowledge, it is not clear if or when botulinum toxin will ever be considered first-line prophylaxis. Given the lack of definitive evidence, cost factors may determine whether botulinum toxin will eventually find wide acceptance in a clinical role other than that of salvage therapy for patients in whom conventional pharmacotherapy has been inadequate or intolerable.

Managed Care Policy

In the interests of achieving optimal clinical outcomes while remaining committed to cost effectiveness and minimizing medical-legal risk, managed care policy on the use of any drug must be evidence-based, relying on whatever authoritative information is available at a given time. Policy may change with the emergence of new information relating to drug efficacy, safety, interactions, contraindications, dosages and routes of administration, or FDA approval status, or with the appearance of newer agents aimed at treatment of the same clinical condition.

Botulinum toxin may prove to be a safe and effective preventive approach that can improve the quality of life for patients with migraine while reducing the costs and clinical hazards associated with frequent use of

abortive medication. However, the key questions still lack definitive and consistent evidence-based answers: Is it clinically effective? Is it cost-effective? Can we predict which patients will respond?

Based on currently available information, various criteria have been proposed to identify those migraineurs who would be suitable candidates for prophylaxis with botulinum toxin. For example, Blumenfeld and colleagues¹⁵ suggested that the use of botulinum toxin would be suitable in patients with disabling primary headache who had either inadequate response or unacceptable side effects from conventional treatment, or in whom other prophylactic measures are contraindicated, as well as in patients with concomitant discomfort relating to muscle spasm in the neck or jaw, patients who have been abusing or overusing abortive medication, and patients who prefer this form of treatment.

A proposed model policy recommends botulinum toxin for patients with moderate-to-severe pain due to migraine (with or without aura), chronic daily headache, or chronic tension-type headache, and who meet the following criteria: at least 2 headaches per month causing at least 3 days of disability, abortive medication used at least twice weekly, abortive medication contraindicated or ineffective, contraindication to other preventive therapies, failure of at least 2 other preventive strategies over a 6-month period, or special circumstances, such as hemiplegic migraine, profoundly incapacitating headaches, or headaches deemed to pose a risk of permanent neurologic injury.

Three large Blue Cross plans have contrasting policies relating to coverage of botulinum toxin for migraine which illustrate some of the different approaches that have been followed. In one plan, the diagnosis determines the nature of the coverage; the off-label use of botulinum toxin is considered medically necessary in certain conditions (especially spastic disorders of central origin, such as those manifesting as hemiplegia, paraplegia, or achalasia) but experimental in others (including headache as well as neck pain, back pain, and Tourette's syndrome).

In contrast, another plan has adopted the following policy in which headache may, in

certain carefully defined circumstances, be considered a medically necessary use. When recommended by a neurologist, botulinum toxin may be used off-label in patients with intractable migraine headaches, with or without aura, occurring at least twice monthly and causing disability lasting at least 3 days; or in patients with chronic daily headaches (occurring more than 15 days per month) and causing disability lasting at least 3 days. In either of these circumstances, treatment with botulinum is considered medically necessary if all 3 of the following conditions are met: (1) at least 3 preventive regimens titrated to maximally tolerated doses have failed (or are contraindicated in the patient); (2) abortive medications are used at least twice weekly (or are contraindicated or ineffective even at maximally tolerated doses); and (3) rebound headache from medication overuse has been ruled out. If any of these conditions were not met, the use of botulinum toxin would be considered investigational.

A third plan states its policy more simply, relying on the individual physician's clinical judgment rather than detailed formal criteria. The use of botulinum toxin may be considered medically necessary as a treatment of chronic migraine or chronic tension-type headaches in patients who are refractory to preventive measures and have failed or cannot take headache-aborting medications.

The stringent criteria proposed for the use of botulinum toxin reflect the current state of knowledge: there is evidence suggesting effectiveness and safety, but not enough definitive evidence for this modality to be considered a first-line approach to migraine prophylaxis. Consequently, although the specific criteria governing the coverage of botulinum toxin vary between different plans, there is general concurrence that its use at this time should be restricted to migraineurs in whom conventional measures have been ineffective or intolerable.

Conclusion

Migraine treatment has advanced with the advent of the triptans for abortive treatment. At this time, however, prophylaxis has not yet seen the same type of advance. The agents currently approved for migraine pro-

phylaxis are characterized by inconsistent effectiveness and, in some patients, unacceptable side effects. The interest in botulinum toxin reflects the lack of a proved means of migraine prophylaxis, for this modality appears to offer freedom from systemic side effects and from reliance on patient compliance. Nevertheless, definitive evidence from large-scale, well-designed, controlled trials is still scant. In the future, such research may provide meaningful comparisons between botulinum toxin and currently approved agents with respect to long-term effectiveness and tolerability to the patient. If the evidence proves favorable, showing the safety, clinical effectiveness, and cost effectiveness of botulinum toxin in migraine prophylaxis, managed care policies may be amended to allow coverage as an alternative to currently accepted modalities.

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