The Prevalence and Diagnosis of Migraine in a Primary Care Setting—Insights from the Landmark Study

Based on a poster presented by Dowson A University of London, Kings College Hospital

Migraine affects between 3% and 8% of women and 11% to 18% of men, but most migraine sufferers do not seek medical attention. Furthermore, almost one half of migraine patients are underdiagnosed or misdiagnosed. While population-based studies have established migraine prevalence, studies that estimate the prevalence of migraine patients who present to primary care physicians are limited.

The Landmark Study was a prospective, international study examining the association of headache impact assessed by the Headache Impact Test (HIT-6) and migraine diagnosis among patients presenting to primary care physicians. A total of 1217 patients were enrolled in the study, and 1204 completed the screening consisting of HIT-6 assessment and completion of a headache survey.

Physicians categorized patients as having migraine or nonmigraine headache according to their customary diagnostic practice. Newly diagnosed migraineurs and nonmigraine headache sufferers then completed diary cards for their first 6 headaches or for up to 3 months, whichever came first. Patients diagnosed with secondary headache were withdrawn from the study.

Of the 1204 patients, primary care physicians diagnosed 1017 (85%) with migraine, including 306 with newly diagnosed migraine and 711 who had received a previous migraine diagnosis. Nonmigraine headache was diagnosed in 142 patients (12%), and 45 patients (4%) were initially diagnosed with secondary or other headache disorders.

At the end of the 3-month period, an expert panel of headache specialists reviewed the diary cards and used International Headache Society criteria to determine the final headache diagnosis. The expert panel review revealed that the initial primary care physician diagnosis of migraine was correct 87% of the time. However, about 49% of patients diagnosed with nonmigraine headache were reclassified as migraine sufferers by the expert panel.

Additionally, researchers found that patient self-diagnosis may mislead the primary care physician. In this study, patients correctly diagnosed migraine 88% of the time; they also misdiagnosed nonmigraine headache 60% of the time.

REFERENCES

EMPLOYER BURDEN OF HEADACHE IN THE UNITED STATES: RESULTS FROM THE AMERICAN PRODUCTIVITY AUDIT

Based on a poster presented by Stewart WF, Ricci J Center for Work and Health, Advance PCS, Hunt Valley, Maryland

The American Productivity Audit is an ongoing, week-to-week telephone survey of the US work force used to estimate the work-related cost of headache in terms of lost productive time at work (LPT) and to estimate the social costs of headache in terms of underemployment and unemployment.

The characteristics of LPT used in this study were universally applicable to all jobs, not influenced by inherent differences in performance among workers, and not sensitive to work culture or management practices. The characteristics used were sensitive to the impact of health problems and were easily translated into dollar cost.

Households and individuals in the 48 contiguous states and the District of Columbia were selected through random-digit telephone dialing for the survey. Up to 2 respondents per household were interviewed if they met eligibility requirements of being 18 to 65 years of age and having worked for pay during the previous week. A smaller sample of unemployed respondents were also surveyed.

A total of 24,881 employed and 1,446 unemployed adults completed a telephone interview to determine employment status, occupation, quality of life, lifestyle indicators, demographic characteristics, and the frequency of selected work behaviors. The LPT components included during the interview were absenteeism and reduced performance while at work. Work hours lost were translated into dollar cost by using respondents' self-reported salary or wages, LPT associated with headache was also based on self-reports of headache status. The results were then projected to the entire US work force using a direct adjustment method.

Results revealed that headache costs employers an estimated $23.7 billion annually in LPT and that 75% of LPT is due to headache occurring while employees are at work, not while absent. Workers in high-demand, low-control occupations are most likely to miss workdays due to headache. In addition, a minority (28%) of workers reporting the most severe headache account for the majority (70%) of LPT.

Overall, headache produces a significant and largely invisible financial loss to employers.

The impact of headache-related LPT varied with demographic features, and the most severe impact was found among less educated patients and African Americans. Headache was also most prevalent among the unemployed, suggesting that there are significant social costs.

While the estimates of LPT in this survey are subject to selection bias, unbiased estimates linked to the US Bureau of Labor Statistics' Current Population Survey are being calculated.

CORRELATION STUDY BETWEEN HIT-6 AND QUALITY OF LIFE AND SEVERITY IN MIGRAINE

Based on a poster presented by Nachit-Ouinekh F Laboratoire GlaxoSmithKline, Marly-Le-Roi, France

The Headache Impact Test (HIT-6) is a newer scale designed to measure a wider range of levels of disability and impact of migraine. This study aimed to analyze the correlation between this new instrument and a quality-of-life scale (QVM) and a migraine severity scale (MigSev).

A total of 2,537 patients recruited by 349 general physicians were analyzed according to International Headache Society (IHS) migraine criteria, HIT-6, QVM, and MigSev. Patients included 2,021 women and 516 men with an average age of 43.3 years. A total of 1,324 (52.2%) patients were diagnosed with migraine according to IHS criteria, 855 (33.7%) had a migrainous disorder, and 358 (14.1%) were found to not suffer from migraine.

HIT-6 scores ranged from 36 to 78 and defined 4 migraine impact groups: slight or nil, average, considerable, and severe. The MigSev scale defined 3 levels of severity based on the last migraine attack: not severe, moderately severe, and severe. The QVM calculated a global quality-of-life index and 4 scores representing the functional, psychological, social, and iatrogenic dimensions. The global index and the 4 scores produced values between 0 and 100, with
the lowest values representing the best quality of life. A multiple component factorial analysis was then used to analyze the data for each instrument used, and the association between HIT-6 scores and scores on the other scales was determined with a Pearson's chi-squared test and analysis of variance using a 5% significance level.

The average HIT-6 score among study patients was 61.1, and the mean QVM score was 41.0. The last headache attack was rated as severe on the MigSev scale in 682 (27.4%) of patients, moderately severe in 1012 (40.7%), and not severe in 791 (31.8%).

The impact of headache as determined by the HIT-6 was greatest in patients with migraine (P < .01) and in those whose last attack was rated as severe on the MigSev (P < .01). When QVM scores were examined as a function of HIT-6 scores, quality of life was worse with the higher HIT-6 impact levels for the functional, psychological, social, and iatrogenic dimensions (P < .001). Very close correlations (>0.60) were found between the HIT-6 and QVM scores, specifically for the functional and social dimensions.

Overall, the highest headache impact was found among patients meeting strict IHS migraine criteria, lowest impact was found among nonmigraine sufferers, and an intermediary impact was noted in patients with migrainous disorders.

The researchers concluded that the HIT-6 scale is a good measurement instrument to determine the impact of migraine, particularly in the functional dimension.

REFERENCES


**Levetiracetam, Given Intravenously, to Treat Refractory Migraines**

Based on a poster presented by Krusz JC, Daniel D Anodyne Headache and PainCare, Dallas, Texas

A number of intravenous agents have been employed as acute migraine treatment, including magnesium sulfate, propofol, sodium valproate, droperidol, lidocaine, steroids, dihydroergotamine mesylate (DHE-45), sumatriptan, and methocarbamol. Levetiracetam is an anticonvulsant available in tablet form that has shown efficacy in refractory migraine treatment and in various other chronic neuropathic pain disorders.

Levetiracetam blocks high-voltage calcium channels, a characteristic shared by other agents effective in treating pain and headache disorders. Levetiracetam also is highly soluble in water, enabling preparation of a sterile, preservative-free solution for the open-label study with intractable migraine patients presented here. A concentration of 400 mg/mL was used.

A total of 21 migraine patients, 12 women and 9 men, were treated in a headache clinic setting for intractable migraine refractory to typical acute therapy taken by patients at home. Acute treatments included triptans, intranasal or intramuscular DHE-45, cyclooxygenase-2 inhibitors, opiates, or a combination of these.

Upon arrival at the clinic, an intravenous line was placed, and patients were monitored with pulse oximetry and lead II of electrocardiogram. Patients' blood pressure, pulse, and oxygen saturation were also monitored. Normal saline was given prior and during administration of levetiracetam.

Patients were asked to rate their headache as a 0 to 10 on a numeric rating scale prior to receiving a single test dose of 200 mg or 400 mg levetiracetam. If no side effects occurred after 10 minutes, additional intravenous levetiracetam was given at 400 mg to 800 mg every 10 minutes thereafter. Patients were monitored for any side effects at each dosing point and were asked to rate their headache again.

A total of 26 migraines were treated in the 21 patients. One patient was treated 4 separate times but not on consecutive days, and 1 patient was treated on 3 nonconsecutive days. Four patients had already been treated with oral levetiracetam therapy for migraine or other headache prophylaxis. Two
additional patients were treated with oral levetiracetam for prophylaxis after successful treatment with the intravenous form.

Twenty of the 21 patients reported some degree of reduction in migraine severity. Eleven patients reported total eradication of their headache. The mean reduction in migraine severity was 81.9%, including the patient who did not respond; without the nonresponder, the mean reduction in migraine severity was 85.2%. The average migraine severity prior to intravenous levetiracetam treatment was 8.3 compared with an average severity of 1.6 following treatment. The average time to best response was 58 minutes. The average dose of intravenous levetiracetam given was 4773 mg with a range of 400 mg to 11200 mg.

No side effects were observed other than transient nausea lasting 15 to 20 minutes in 1 patient that did not require treatment.

This is the first reported study using intravenous administration of levetiracetam for intractable migraine treatment. The results demonstrate excellent effectiveness in aborting ongoing intractable migraine with virtually no toxicity. Intravenous levetiracetam appears to act rapidly and can be successfully extracted into a sterile, preservative-free solution. These results indicate that a double-blind, placebo-controlled trial of intravenous levetiracetam for intractable migraine is warranted.

REFERENCES


Oxcarbazepine Prophylaxis for Chronic Migraine and Tension-type Headaches

Based on a poster presented by Krusz JC,* Nett RB†
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Initial observations from a small sample of patients with refractory migraine headache treated with oxcarbazepine suggested that this anticonvulsant may be a useful addition to other neuronal stabilizing medications. Therefore, 85 patients from 2 headache clinics who had refractory migraine and tension-type headaches were treated in an open-label study with oxcarbazepine as an add-on therapy to existing prophylaxis therapy.

Oxcarbazepine was started as initial prophylaxis therapy in 18 patients. The remaining 67 patients had failed at least 1 other prophylactic treatment attempt with neuronal stabilizing agents. At baseline, patients had an average of 7.8 migraines meeting International Headache Society criteria per month with a range of 4 to 20 per month. In addition, an average of 12 tension-type headaches per month were present in 48 patients. Coexistent chronic neuropathic pain, primarily from neck and lower back structural pathology, failed surgeries, or other neuropathic pain syndromes, were present in 38 patients.

All patients were instructed to maintain a headache diary rating severity of headaches on a 0 to 10 numeric scale. At baseline, 30% of patients had migraines that either woke them from sleep or were present upon awakening. Sixty patients reported a less than adequate sleep pattern due to headache.

Oxcarbazepine was initially added with a 150-mg dose in the evening for 3 to 5 days. The dose was titrated in 150-mg increments every 5 days until a target evening dose of 600 mg was reached. A 300-mg morning dose was then added with any further necessary dosage titration being done weekly thereafter. The average daily dose was 1450 mg, with a range of 600 mg to 3600 mg. After titration, total duration of treatment was 3 to 15 months with patients observed monthly in the headache clinic.

Of the 85 patients, 65 were evaluable. A favorable response to oxcarbazepine was reported by 46 (74%) of the 65 patients. A greater than 50% reduction in migraine frequency was reported by 38 (83%)
of the responders with an average frequency reduction of 63%, from 7.8 to 2.9 migraine attacks per month. Eight patients (17% of responders) reported 25% to 50% reductions in migraine frequency. In addition, remaining migraines experienced by all patients were reported as being approximately 30% less severe.

Of the 48 patients with coexistent tension-type headache, 30 were evaluable. Four of these patients reported complete cessation of chronic daily headache pattern, and 21 reported a greater than 50% reduction in tension-type headache frequency per month. The average reduction in this group was 78%, from 12 headaches monthly at baseline to fewer than 3 monthly. Five tension-type headache patients had no response or a less than 25% reduction in frequency or severity.

Of the 46 oxcarbazepine responders, 20 migraineurs on other prophylactic therapy were able to discontinue their prior medication regimen. The remaining 26 patients were able to taper their prior medication dose by 50% to 60%.

A total of 10 patients had no response, and an additional 6 patients dropped out due to side effects. The primary side effects were rash (n = 1), nausea (n = 3), and excessive drowsiness (n = 2). Three patients were lost to follow-up.

Results of this open-label study with oxcarbazepine as prophylaxis for migraine and tension-type headache indicate that efficacy is equal or better than other neuronal stabilizing agents in this difficult patient population. Oxcarbazepine is associated with few side effects and does not require laboratory monitoring. Further investigation of oxcarbazepine therapy with double-blind studies in this population is warranted.

**Botulinum Toxins Types A and B, Given Intradermally, to Treat Cervicogenic Migraines**

Based on a poster presented by Krusz JC
Anodyne Headache and PainCare, Dallas, Texas

Cervicogenic migraine is often seen as a result of neck trauma or prior failed surgery. Often, the pain is unilateral and begins suboccipitally with migraine-like features. Current migraine etiology theories include activation of the trigeminovascular neuroinflammatory cascade with elements of central sensitization and windup. This may be similar in cases of neuropathic pain syndrome specific to structures in and above the neck.

Although there is efficacy data for the use of botulinum toxins in blepharospasm, cervical dystonias, and similar disorders, there has not been consistent data regarding efficacy in headache, including migraine. Furthermore, there has been no consensus as to the best placement for botulinum toxin administration in these patients.

Recent studies suggest that botulinum toxin type A (BTX-A) may inhibit neurotransmitters known to play a role in activation of neurogenic inflammation and that its metabolites may undergo retrograde transport, producing an antinociceptive effect. Some studies have also showed local antinociceptive effects without concomitant weakness, suggesting a mechanism of action beyond simple muscle weakness.

Botulinum toxin type B (BTX-B) alleviates pain in a number of conditions, including headache. However, BTX-A and BTX-B are antigenically different and have different mechanisms of subcellular pharmacologic activity. Therefore, both were studied in cervicogenic migraine patients.

The unique feature of this investigation is that an intradermal route of administration was used for BTX-A and BTX-B so that neither toxin was administered into any muscular structure.

Fourteen patients meeting International Headache Society (IHS) criteria for migraine were treated with BTX-A. Twelve of the patients had prior failed neck surgery, and 10 had primarily unilateral headache, whereas 4 patients had bilateral cervicogenic migraines. All had cervical muscle spasm. BTX-A 100 units was given intradermally at the site of greater and lesser occipital nerve inlets on the side of migraine pain.

An additional 10 patients with IHS-defined migraine with muscles spasm, also unilateral, were treated with intradermal BTX-B. Four patients had failed cervical surgery and all had a known cervical structural pathology upon magnetic resonance imaging. A skin wheal on the side of migraine pain at the level of greater and lesser occipital nerve inlets was raised and either 2500 or 5000 units of BTX-B were delivered.

Nine of the patients receiving BTX-A reported a
decrease in migraine headaches and spasm on the treated side. The average decrease in migraine frequency was more than 70% and the remaining headaches were 50% less severe. The average duration of BTX-A effect was 12 weeks, ranging from 5 to 19 weeks. Three patients were treated more than once, but treatments were more than 4 months apart. Three patients did not respond, although 1 patient reported cessation of muscle spasm. Two patients had just been injected, and results were not included.

Five patients treated with BTX-B reported a significant decrease in both migraine frequency and spasm by 75% or greater. Three of these patients reported a greater than 90% reduction in migraine frequency. The average duration of BTX-B effect was 16 weeks, ranging from 10 to 24 weeks. Two patients did not have a significant change in migraine pattern. Three patients in this group had been recently injected and were not included in this analysis.

Both BTX-A and BTX-B delivered intradermally show dramatic efficacy in reducing frequency and severity of cervicogenic migraine. These results raise speculation concerning the mechanisms of action of these agents via uptake into nociceptive fibers with transport to the dorsal horn of the spinal cord. Blockade of pain transmission at central facilitative sites may occur. Double-blind studies with both BTX-A and BTX-B are needed to determine if these results can be replicated.

Botulinum toxin for refractory chronic daily headaches

Based on a poster presented by Edwards K, Dreyer M Western New England Headache Center, Neurological Research Center, Bennington, Vermont

Chronic daily headache is a pain disorder usually consisting of refractory tension-type headache and often precipitated by transformed migraine or analgesic-rebound migraine. Affected patients are frequently narcotic dependent and tend to be treatment resistant. The objective of this study was to evaluate the safety and efficacy of botulinum toxin in patients with chronic daily headache.

A retrospective chart review of 20 patients treated with intramuscularly delivered botulinum toxin and evaluated 4 weeks postinjection was conducted. All patients had been refractory to multiple other treatment modalities and all reported headaches occurring 6 or 7 days per week.

Botulinum toxin dosages ranged from 20 to 100 units with a mean of 89 units. The average dose was 98 units in responders and 85 units in nonresponders. Botulinum toxin was injected at multiple sites, usually in 25-unit doses in the facial region and 75-unit doses in the cervical region.

Pretreatment headache severity based on an 11-point scale ranged from 3 to 10 with a mean of 8. One month after injection, headache severity ranged from 1 to 10 with a mean of 6.5. Of the 20 patients with chronic daily headache, 13 had a highly significant reduction (P = .0002) in headache frequency from 6.8 days per week to 1.9 days per week. The other 7 patients did not respond.

Botulinum toxin was found to give a significant benefit in headache severity and frequency in this difficult-to-treat, refractory, chronic daily headache population. Therefore, this agent may be an alternative treatment that does not carry risk of drug abuse, drug interactions, sedative effects, or other systemic toxicity. In this series of patients, side effects were limited to transient local injection-site discomfort. No clinical muscle weakness was observed.