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# Tension-type headaches: what they are and how to treat them

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The world of headache diagnosis has always been divided into a kind of dichotomous conundrum or, at worst, coinflip: either it's a migraine or it's not. If not, it is likely a tension-type headache (TTH). First of all, headache as a clinical problem is, in the aggregate, the most common clinical complaint of patients. Overall, 100 million people suffer with some form of headache in the United States, and at least half of these people have TTH. In addition, there are nearly 30 million migraineurs, and 62% of these have some episodic TTH (ETTH) accompanying their migraines [1]. ETTH is defined by the International Headache Society (IHS) classification system [2] as occurring less than 15 days per month, while chronic tension-type headache (CTTH) is reserved for TTH more frequent than 15 days per month. The ultimate expression of this pattern is chronic daily headache (CDH) which occurs in approximately 4% of people with TTH.

TTH can last from a few minutes to many days and can be continuous in a small percentage of patients. These patients would be classified as having CDH—the pain is mild or moderate in intensity and is described as tightness, pressure, or mild or moderate ache. The pain is usually localized as a bilateral "hatband" extending back from the forehead across the sides of the head to the back of the neck. Patients often report that this tight feeling or tension radiates from the skull base to the posterior neck muscles. In its most extensive form, the pain distribution can be "capelike," radiating along the trapezius muscles covering the shoulders, scapular, and interscapular areas [3]. In addition, these characteristics, there most often is an absence of signs of any serious underlying condition [4]. Patients who have TTH do not typically report any visual disturbance, constant generalized pain, fever, stiff neck, recent trauma, or bruxism. Presence of any additional clinical features does not, however, mitigate the diagnosis of TTH.

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Before the current IHC criteria for TTH—which were drafted in 1988 and are summarized in the Appendix—we labeled nonmigraine headaches as *tension* or *muscle contraction* headaches. This was the result of a 1962 Ad Hoc Committee Classification of Headache publication [5], which presumed a clear-cut separation of migraines as a vascular headache and TTH as related to muscle contraction. It was a rough guideline for ordinary, muscle contraction headaches. These were described as having an "...ache or sensation of tightness, pressure or constriction, widely varied in intensity, frequency and duration...associated with sustained contraction of skeletal muscles...usually as part of the individual's reaction during life stress."

Often, vague terminology prevailed in the descriptions: "often," "commonly," and "usually" were barriers to accurate diagnosis, and these kinds of descriptors were not sufficiently powerful to allow for reliable diagnosis of TTH by different clinicians. For that matter, the IHS criteria, after 15 years, are seen as rather arbitrary and better suited for research study purposes than as a useful clinical tool for diagnostic purposes. Therefore, it helps us select a more homogeneous population of headache patients to participate in a research study but does not address real-world issues of headache presentations. One positive feature of the 1988 IHS criteria [2] is that a patient may fulfill criteria for both migraines and TTH, episodic or chronic, and that there may be an overlap in the presenting clinical symptoms. We in the headache treatment community await the next iteration of the IHS criteria, due hopefully this year. It is long overdue.

As seen in the Appendix, the definitions for TTH are straightforward. Although useful for thinking about a "pure" TTH disorder, this rigid type of thinking can rapidly become evanescent. What can become confusing to clinicians are headaches that fit the TTH criteria but may actually be migraines. How is that? Approximately 30% to 40% of migraines are not unilateral, without the qualities of throbbing or pulsatility, nausea, or light and sound sensitivity. Thus each of the two major types of headache pattern can mimic the other. For the purposes of this article, we are focusing on TTH, so it is extremely important for clinicians to know that some migraines can, at times, mimic TTH. They may even respond to medications that are used more typically and specifically for migraines (see later discussion) [6]. These types of issues have been presented very elegantly in two previous studies [7,8]. The first study [7] carefully contrasted migraine and TTH and found more similarities than differences in their presenting symptoms, pathophysiology, and older data regarding successful treatment of both types of headaches using the same medication categories (eg, beta blockers, ergotamine, and tricyclic antidepressants). Similar degrees of success were reported for biofeedback in treating both types of headaches. The second study [8] used the IHS criteria to look for "pure" migraine and TTH patients culled from a large database in the Netherlands. It found that pure TTH patients, like pure migraineurs, were rare and that most people who had headaches had features of both types of headache. They also

concluded that strict application of the IHS criteria (see Appendix) without clinical judgment (as determined solely by computer-based decisions) indicated that pure TTH rarely existed. They noted that there was a discrepancy between theory (as per the IHS criteria) and actual clinical practice, where clinical judgment is always operative.

One of the cardinal older attributes of TTH, increased muscle tension, turns out to be simply not true when tested clinically. For example, in one study [9], when people who had recurrent headaches were questioned regarding their symptoms, two thirds of patients described a unilateral location of head pain, with 50% having nausea. This fit the IHS criteria for migraine; however, 70% also reported muscle tightness with their other features, thus giving a strong correlate of what would ordinarily be termed TTH. More surprising at the time of the study was the finding that recorded electromyographic (EMG) activity in the frontalis muscle in TTH patients was no different from that of controls, either during stressful conditions or completely at rest during times of no headache [10]. One other key study measured facial muscle activity in migraine and tension headache patients and compared them to controls without headache. Here, people with migraines showed more muscle activity, or tension, than their counterparts who had TTH. This was seen both during, and in between, headache episodes. Thus the authors concluded that one could not use tension recorded from muscles as any kind of reliable indicator for differentiating migraines from TTH [11]. To be fair, a recent study has documented increased muscle "hardness" as measured externally in muscles of the scalp in people who have CTTH [12].

OK. Now that we can't use muscle contraction as any kind of arbitrary clinical dividing line for diagnosing TTH, what can we do?

## Pathophysiology

### *Biochemistry*

This is a very interesting part of the potential underpinning of TTH. Years ago there were great fights about what was or wasn't responsible for TTH, or, for that matter, migraine headaches [13]. Were TTH patients all depressed, or were their muscles under more "tension"? Were they somehow predisposed to be unfortunate or were they somehow weak? In the last decade or so, many headache experts acknowledge the possibility, or perhaps likelihood, that TTH and migraines may have a common pathophysiology. It may just be that the clinical presentation of the headache and its accompanying characteristics differ at different times.

Regarding other aspects of TTH biochemistry, research suggests that nitric oxide may be the local mediator of TTH. Infusion of a nitric oxide donor reproduces TTH in patients previously diagnosed with CTTH [14]. Furthermore, blocking nitric oxide production with an investigative agent

(L-NMMA) reduces both muscle hardness and pain associated with TTH [15].

### *Neurotransmitters*

The idea that a neurotransmitter (or two) could somehow be responsible for the phenomenon of a headache seemed far-fetched 25 years ago—or, at least, it was very theoretical at that time. Norepinephrine (NE) and serotonin (5HT) come to mind as two potential culprits or causes. Let's take a look at what the evidence suggests.

There is a confusing body of literature regarding the role of NE in TTH, migraine, and cluster headaches. Some publications conclude that there is sympathetic nervous system hypoactivity in both migraines and TTH [16–20]. Opposing this are papers showing increased NE in the plasma of migraineurs during the migraine headache [21]. One possible explanation for this apparent discrepancy might involve increased synthesis of NE by the locus ceruleus in the brainstem, with consequent overstimulation of postsynaptic NE receptors, leading to down-regulation of the NE system, thus leading to the observations of decreased sympathetic tone [22]. The increased NE during the migraine attack might occur on the basis of relative breakdown of the usual properties of the blood–brain barrier.

Evidence for the involvement of 5HT in the pathophysiology of TTH likewise points to lowered levels of this transmitter in platelets [23]. In analgesic rebound headaches, platelet 5HT levels are diminished compared with normal controls [24]. There is also a body of evidence to think of migraine headache as a state of relative 5HT hypoactivity in the central nervous system [25]. This has been called the central hypothesis and may apply to a sharing of pathophysiologic mechanisms relating to dysfunction in pain processing in the brainstem.

### *Comorbidity*

Let us introduce one more concept into the limelight: cause versus comorbidity. Older articles and reviews on TTH and muscle contraction headache tended to make much of the idea that depression was a cause of the headache itself [13]. While it is true that many people with chronic headaches—of any kind—might become depressed and anxious, that is not the same as saying that one causes the other. The same is true for chronic headaches or pain and the exquisitely common problem of sleep quality.

The term *comorbidity* has many clinical implications. If one condition does not cause the other, and both run on separate railroad tracks, don't both have to be treated? Well, yes, if the patient is to be served in the best way. Will treating one condition necessarily improve the other? Well, no, not really, because they are different clinical entities with perhaps completely different treatment paradigms (see later discussion).

*Analgesic rebound headache and chronic daily headache*

A complete headache history should include questions about the type, amount, effect, and duration of self-treatment strategies. Patients typically self-treat their TTH with what is readily available in their daily environment: over-the-counter analgesics come in hundreds of forms, as do so-called "alternative" therapies. A headache history should probe for lifestyle changes such as interpersonal/work stressors or alcohol/tobacco use that may have preceded or accompanied the headache.

The progression of either migraine or TTH into chronic daily headache can occur spontaneously but often occurs in relation to frequent use of analgesic medication. Repeated use of simple analgesics (eg, acetaminophen, aspirin, ibuprofen, and especially ones containing admixed caffeine, butalbital, or opiates) can lead to analgesic rebound headaches. The likely mechanism is the very short effective half-life of these medications which terminates any (usually brief) pain relief quickly. As each dose wears off, the headache returns and the person then takes another repeat dose of medication. This can occur around the clock and literally traps the headache sufferer in an endless cycle of escalating dose adjustments to try to obtain relief of the TTH or CDH. Common features of chronic daily headache associated with frequent analgesic use are: early morning awakening with headache, poor appetite, nausea, restlessness, irritability, memory or concentration problems, and depression [26].

An important part of the successful therapy of analgesic rebound headaches is the slow withdrawal of the offending agent, often over a few weeks, or longer. Substitution of more appropriate agents (see below) and treatment of coexistent sleep disorders and other comorbidities will often change the pattern of headaches.

## Simple analgesics

Simple analgesics, which are often available over the counter—either alone or in various combinations (eg, acetaminophen, aspirin, ibuprofen, and so forth)—are generally to be avoided as primary therapy for anything more than occasional (1–2 per month) TTH. The problem, often enough, is that people who have TTH will try to out-hero their headaches, or use over-the-counter medications before they reach for their more specific therapies. A survey done by telephone found that 98% of responders who had TTH reported using simple analgesics. The most common agents used were acetaminophen (56%), aspirin (15%), or other agents (17%) [27]. This is also true of migraineurs.

Teaching patients to be appropriately aggressive with more specific medications than simple analgesics is part of successful TTH management. In patients who have chronic TTH, the goals of treatment are to stop the frequent use of analgesics and to initiate effective prophylactic treatment as

well as to manage any residual headaches. Patients with chronic TTH should limit their use of simple analgesics to two times per week or less. The use of opiates will be discussed in a later section of this article.

*Tizanidine*

Tizanidine, an alpha$_2$ adrenergic agonist, has been available in the United States for several years, although it has been used for over 20 years in Europe and Asia [28]. It has a single primary mechanism of action, shared only by clonidine. The alpha$_2$ receptor is found both pre- and post-synaptically at many sites in the spinal cord and central nervous system. Centrally, the agonism of this receptor is associated with reducing the output or release of NE from the locus ceruleus in the brain stem, the principal source of this central nervous system neurotransmitter. Tizanidine has a multitude of clinical effects: myotonolysis (inhibition of spasticity), inhibition of pain transmission, sleep promotion, and reduction of headaches, both TTH and migraine. Because it has one mechanism of action identical to clonidine, it may be helpful to aid in detoxification efforts for patients who are tolerant to opiates.

Open-label studies with tizanidine in over 300 patients who have CTTH and migraines showed comparable efficacy to reduce both headache types to a similar degree [22]. Migraines were reduced 78% in frequency and CTTH were reduced 72%. The severity of remaining migraine headaches were also reduced by 55% on average. Over 90% of headache patients who had a coexistent sleep disorder and neck spasms benefited as well. The bulk of the total daily dose was given before bedtime and overnight to maintain a sound sleep pattern and to avoid daytime sedation. Tizanidine was titrated up to an average of 26 mg/d over a period of 1 month to 6 weeks. Treatment was continued at the optimal dose of tizanidine for at least another 3 months after open-label initial titration. That reductions in migraine severity and frequency paralleled the betterment in other CTTH patterns raises many questions about the role of the adrenergic system in maintaining or promoting headache patterns chronically, either centrally or at the level of the spinal cord. The effect of tizanidine on the alpha$_2$ receptor either centrally or at the spinal cord may modulate sympathetic nervous system activity in recurrent headaches. Our results support the concept of sympathetic overactivity as a mechanism for maintaining chronic headaches, both migrainous and not.

Tizanidine (Zanaflex) was slightly more effective than placebo in a double-blind crossover trial of 37 women. The median values of the visual analog and verbal rating scales for headache were significantly lower in the tizanidine periods, but the 95% confidence values overlapped. Side effects of tizanidine (mostly drowsiness and dry mouth) made the tolerability of this drug bothersome for 38% of the patients [29]. The doses used were 2 to 6 mg three times daily. However, in a second study of (modified release) tizanidine [30], doses of 6 or 12 mg daily were no more effective than placebo in

alleviating chronic TTH. Newer double-blind studies have reconfirmed the results of open-label studies [31].

In short, tizanidine represents a step forward in the treatment of TTH, both episodic and chronic, as well as chronic migraine.

### *Tricyclics*

#### *Episodic tension-type headache*

Preventives may not be needed for ETTH, because its occurrence is, by definition, less than 15 days per month, Furthermore, the intensity is not disabling, and its response to simple analgesics may be satisfactory. However, when this headache pattern intensifies and disturbs a person's activities, particularly with respect to sleep, then a prescription for amitriptyline or a similar tricyclic drug (eg, nortriptyline or protriptyline) should be considered. The more recent above-mentioned data regarding tizanidine should also be kept in mind. Patients should be started on a very low dose of a tricyclic—10 to 25 mg before bedtime. An open study of amitriptyline in episodic and chronic TTH showed no significant betterment of the ETTH [32]. Some of the newer categories of agents, such as tizanidine or neuronal stabilizing agents, may play a role in suppressing ETTH (see previous and later discussion).

#### *Chronic tension-type headache*

Prophylaxis or preventive medications are the main therapy for chronic TTH. Choices in the tricyclic category are quite limited, and often their side effect profile interferes with their use. In general, lower-than-antidepressant doses should be tried. Amitriptyline is the only drug shown by rigorous, clinical trials to ameliorate CTTH. When discussing the potential goals of therapy with patients, it is important to stress to them that while their headache pattern may lessen in frequency, their CTTH will not be eliminated. Those who respond to amitriptyline can have more days without headache and have less severe headache when it is present [33].

Nortriptyline, a metabolite of amitriptyline, can also be effective against chronic TTH when amitriptyline is too sedating or induces too much weight gain, constipation, or sluggishness. The bottom line is the benefit-to-risk ratio for all the tricyclics.

A recent open-label study of protriptyline (10–40 mg in the morning) in women with chronic TTH suggests that this tricyclic drug may be comparable in effectiveness to amitriptyline, with fewer side effects [34].

### *Selective serotonin reuptake inhibitors*

In general, selective serotonin reuptake inhibitors (SSRIs) have not provided a reliable literature in CTTH/TTH treatment strategies, although the common wisdom is that they are effective. Although there is a trend toward betterment of the headache pattern, several studies using this group

of agents have been disappointing. One double-blind study compared citalopram with amitriptyline against placebo in a crossover manner, but citalopram was not statistically effective compared with amitriptyline [35]. While on citalopram, patients did have lower headache scores than when on placebo. In another study, paroxetine at 30 mg/d was compared with an active comparator, sulpiride, a dopaminergic antagonist. There was no placebo arm and each patient was crossed over to the other active medication. In neither group were headache scores significantly different from each other, but were improved over baseline headache scores [35]. A double-blind trial with fluoextine over a 12-week trial seemed to show significant efficacy over placebo. This occurred only in the last 4 weeks of active treatment. The study was entitled "Chronic daily headache" but was actually done for CTTH. Days with no headache were not different with fluoxetine [36]. A third study [37] of CTTH compared desipramine with fluoextine to look at differential effects of these medications on the norepinephrine versus the serotonin system. Again, there was no placebo arm used. Despite a high rate of dropout from the study in both arms, no difference in headache pattern was seen with either medication.

So, in all, the available data is weak at best for efficacy of SSRI medication in treating ETTH and CTTH.

### *Venlafaxine*

Venlafaxine is marketed as an antidepressant with SSRI-like activity in blocking serotonin reuptake and also has an ability to simultaneously block reuptake of norepinephrine. Thus it has been termed a *serotonin-norepinephrine reuptake inhibitor*. Venlafaxine also has marked activity in reducing anxiety and can be used in a wide range of doses (150–450 mg/d). A recent retrospective study found the extended-release formulation to be useful for TTH and migraine prophylaxis [38].

### *Buspirone*

Buspirone has been on the market for anxiety disorders and has been tried at higher dosages for depression. A recent open, randomized, 12-week clinical trial compared buspirone with amitriptyline [39]. The results suggest that buspirone may be an effective preventive medication for some patients. Anecdotally, my experience with this medication suggests that some patients may have less headaches when taking buspirone, particularly if comorbid anxiety is present with TTH or mixed headache patterns.

## Neuronal stabilizing agents

Although a host of medications have been introduced to the marketplace since 1978, primarily as anticonvulsants, physicians who specialize in

headache and pain management have used these agents for many other neuropsychiatric conditions, including TTH, migraine, and mood and movement disorders. I prefer to use the term *neuronal stabilizing agent* (NSA) or *neuromodulator* when describing the use of these medications where seizures are not being treated, either comorbidly or primarily. This more accurate term diffuses the fear and anxiety among physicians who practice general medicine. Unfortunately, there is reluctance in trying these agents because of the perception that these are the "neurologist's drugs." Nothing could be further from the truth, and indeed, most family practitioners and other physicians are familiar with medications such as valproate sodium and gabapentin. They simply have not had the chance to begin treating their patients with newer categories of neuronal stabilizing agents.

Approaches to headache treatment, both acute and prophylaxis, have evolved as our understanding of some of the underlying pathophysiology has deepened. This section speaks to the many cellular actions of NSAs to reduce pain transmission in the spinal cord, in the brainstem, and supraspinally. The similarities between chronic neuropathic pain states and the processes leading to migraine and TTH have used similar nosology such as central sensitization, windup, cortical spreading depression, and multiple orders of neuronal barrage of brainstem structures in the trigeminovascular system from facial, sinus, and neck inputs [40–44]. Many NSA studies are being reported for the treatment of all headache syndromes. Although there are no data to support their use in ETTH, several have been shown in small or open-label studies to have beneficial effects for CDH, some of which are CTTH.

The various NSAs are listed in Box 1. They have all been used anecdotally to treat CDH, which includes CTTH. The agents with published data for use in CDH are noted as well. It is important to keep in mind that none of these agents has been adequately or specifically studied for ETTH

**Box 1. Neuronal stabilizing agents**

Divalproex (Depakote) [45–47][a]
Gabapentin (Neurontin) [48]
Lamotrigine (Lamictal) [49–52]
Topiramate (Topamax) [53,54][a]
Tiagabine (Gabatril) [55]
Oxcarbazepine (Trileptal) [56][a]
Levetiracetam (Keppra) [57–60][a]
Zonisamide (Zonegran) [61,62][a]

[a]Published data for use in CDH exist.

or pure CTTH. However, plans for further study are underway, and additional evidence for or against their use will undoubtedly become available in the future.

*Opioids*

Many physicians consider opioid use as a place they would rather not go, and this is entirely understandable. However, a case for legitimate opioid therapy for CDH and CTTH can be made. Those family practitioners who are comfortable with opiate use for the treatment of chronic headaches will find this section comforting. As we all know, the Joint Commission on Accreditation of Healthcare Organizations and the National Committee for Quality Assurance are trying to develop rational treatment guidelines for opiates. Indeed, pain is considered the fifth vital sign.

Although hardly a mainstay therapeutic option, a recent forum discussed the use of methadone and other long-acting opioid preparations (eg, fentanyl patches) to successfully treat CDH that was otherwise refractory to other modalities [63]. Three headache clinicians presented data from their respective clinics; at best, 25% of their opioid-treated patients benefited from long-term therapy. In absolute numbers, 10 to 25 patients per year were in the "successful" opioid treatment cohort. It is important to note that these were specialty clinicians treating patients who had refractory CDH. It is certain that many headaches experienced by their study subjects were phenotypically consistent with TTH.

However, one should not accept therapy of any kind as treatment for routine ETTH or for most cases of CTTH. It should be reserved for patients that have proven refractory to most or all other treatments and who have had medication overuse headache ruled out. Arguably, this more severe, refractory population may be better served to be referred to an experience specialist for treatment, where those services are available. Certainly, primary care physicians who have a keen interest and experience in the management of chronic opioid therapy can handle such cases; however, this should be done with the utmost diligence with emphasis on prevention of abuse, habituation, and tolerance. Furthermore, in all such cases, a pain management contract and frequent office follow-up is mandatory.

Even when used by experts in the field, chronic opioids are less than optimal therapy for even the most carefully selected patients. A retrospective chart review with patient interviews by a neurologist headache specialist in refractory CDH looked at approximately 300 patients in a clinic. All had been refractory to usual therapy and had been placed on methadone or OxyContin. Thirteen percent continued on opioid therapy long-term (at least 9 months), the remainder reporting lack of efficacy or side effects. A better home and work life was reported by patients who were successful with chronic opioid therapy for headache [64]. While only 39 patients (13%) overall did well long-term, quality of life was considerably enhanced in these people.

After years of incapacitating headaches, frustrated by lack of efficacy of the usual medication regimens, they felt that work, home, and social life were significantly improved. A previous beneficial effect from short-acting opioids was indicative of benefit from longer-acting opioids as well. Patients who had overused short-acting opioids were more likely to abuse methadone or OxyContin. However, a few patients previously treated for addiction to short-acting opiates did well long-term on methadone or OxyContin. The opioids were discontinued in 8% of the patients due to prrescription opiate abuse.

### *Botulinum toxins*

Botulinum toxin injections of both toxin type A and B have been shown to relieve not only wrinkles, contractured muscles, and blepharospasm but also painful symptoms, including headaches. Often the duration of pain relief outlasts the clinical symptoms for which the toxin is primarily used. The pathogenesis of chronic TTH remains unclear, and the role of muscle tension is especially controversial. In addition to vascular and supraspinal influences, contraction of craniofacial muscles or central sensitization processes following continuous nociceptive input of craniofacial muscles may play an important role in the pathogenesis of TTH.

However, in one study, pericranial injections of botulinum toxin type A (Botox) into the scalp and neck of patients who had chronic TTH were not more effective than placebo injections in alleviating CTTH, although the injections do diminish the scalp's EMG (muscle contraction) activity [65]. A randomized placebo-controlled study was performed to examine the effect of 20 U of botulinum toxin injected into frontal and temporal muscles in patients who had chronic TTH; the effect was evaluated with daily records and a pain inventory [66]. Important outcome variables—such as pain intensity, the number of pain-free days, and consumption of analgesics—were not statistically different between the groups. Reasons for these weak effects may include the injection sites, dose of botulinum toxin, duration of treatment, or lack of clinical effect.

Regarding sites of injection of the toxins, it is known that there is a much greater density of nociceptor nerve fibers in the skin, as compared with that in muscles. Intradermal administration of botulinum toxin types A and B has recently been tried for headaches of cervical origin [67–68]. Initial data have shown comparable or better rates of success using this method of administration, and a double-blind placebo-controlled study is underway currently.

In any case, the proper use of botulinum toxin to treat headache and pain disorders is still being defined. It may be an option if more standard treatments fail. It should be noted that the cost of this treatment is quite expensive and is not reimbursable by many insurance plans for headache diagnoses.

## Psychologic and biofeedback therapy

I refer many headache patients to psychologists who have an interest in treating headaches. Patients often gain significant headache relief from psychologic or biofeedback therapy, or a combination of both. A recent study reported the results of a randomized placebo-controlled trial in which four treatment arms were evaluated for response of CTTH to tricyclic antidepressants (amitriptyline or nortriptyline) or stress management therapy, or both [69]. Two hundred and three subjects who had CTTH were recruited; 53 received tricyclic antidepressants, 49 received stress management therapy (three sessions and two telephone follow-ups) plus placebo, 53 were treated with stress management plus antidepressants, and 48 were given placebo. Patients who finished the 6-month study were 44, 34, 40, and 26 subjects, respectively, showing a fair number of dropouts. The outcome measures were monthly headache index scores calculated as the mean of pain ratings (0–10 scale) recorded by participants in a daily diary four times per day; number of days per month with at least moderate pain (pain rating $\geqslant 5$), analgesic medication use, and Headache Disability Inventory scores, compared by intervention group. Tricyclic antidepressant medication and stress management therapy each produced larger reductions in headache activity, analgesic medication use, and headache-related disability than placebo, but antidepressant medication yielded more rapid improvements in headache activity. Combined therapy was more likely to produce clinically significant ($\geqslant 50\%$) reductions in headache index scores (64% of participants) than antidepressant medication (38% of participants; $P = .006$), stress management therapy (35%; $P = .003$), or placebo (29%; $P = .001$). On other measures, the combined therapy and its two component therapies produced similar outcomes. The results indicate that combined therapy may improve outcome relative to monotherapy.

The most frequently used nonpharmacologic treatments for headache are physical therapy, biofeedback, relaxation training, self-hypnosis, and cognitive therapy. All have value in helping reduce severity and frequency of TTH.

The use of traditional physical therapy for headache has been investigated in a randomized controlled trial [70]. Study participants received weekly sessions of education in proper posture and instruction in a home exercise program and used ice packs, massage, and "passive mobilization" of the cervical facets. Both headache frequency and psychologic well-being improved significantly in the group receiving physical therapy at the end of 6 weeks and at the 12-month follow-up.

One study [71] showed improvement in 39% of 94 patients with headache using relaxation training alone. Adding biofeedback increased the portion of patients experiencing improvement to 56%. One small, long-term study [72] of relaxation and EMG biofeedback showed that improvement was maintained at 5-year follow-up.

Numerous small studies have investigated cognitive psychotherapy alone and in combination with other behavioral treatments for CTTH. Among these trials, at least 50% of patients had reduced symptoms when treated with progressive relaxation, cognitive therapy, or a combination of the two. One study compared patients who self-administered treatments at home with patients who received therapy in the office [73]. A trend toward more symptom reduction in patients getting in-office treatment was noted; this difference was not statistically significant.

A recent systematic review of acupuncture treatment for headache found 40 randomized controlled studies, but only one study was categorized as "rigorous." In all of the trials of TTH that were examined, patients who received acupuncture had superior outcomes compared with patients in the control groups. The authors of the review concluded that "overall, the existing evidence suggests that acupuncture has a role in the treatment of recurrent headaches" [74]. Studies have also been conducted investigating the role of spinal manipulation for headache relief [33]. In a trial comparing manipulation with the use of amitriptyline, both modalities showed improvement in headache intensity, frequency, and medication usage. However, headache intensity was significantly less in the amitriptyline group. Four weeks after cessation of therapy, patients in the spinal manipulation group continued to experience benefits from the intervention [75].

## Treatment of TTH comorbidities

Comorbidites are just that; they neither cause nor are necessarily caused by the headache disorder itself. I think of them as two common disorders running on a parallel track, or in the same person at the same time.

### Anxiety

Anxiety disorders are common, and any practitioner treating chronic headaches and pain knows very well that comorbid anxiety exists in the headache sufferer. They fear the next attack that will cost them time away from work and family. The anxiety is similar to a generalized anxiety disorder, and it must be treated.

Brief recommendations for treatment:

1. Venlafaxine (EffexorXR) can be used for more than just adjunctive therapy for comorbid anxiety (and depression). Although the indications are to stop at 300 mg/d, our European colleagues often exceed that dose. In any case, getting to 225–300 mg/d, especially in the morning, is key.
2. Tizanidine can be an excellent choice for comorbid anxiety and for promoting sleep. Of course, it has great effects on the headaches themselves.

3. Buspirone (Buspar) can be administered at 10 to 20 mg twice a day, once in the morning and once in the evening. More can be taken if necessary and if there are no side effects. Bedtime dosing is usually not a good idea.
4. SSRIs are acceptable but are not as helpful for significant anxiety.
5. Nefazodone (Serzone) can help sleep maintenance and daytime anxiety in low doses (25–50 mg three times a day). It is also a highly effective medication for depression and is useful for sleep promotion.
6. Clonazepam in low dosages (0.25–0.5 mg twice a day) may be wonderful for comorbid anxiety.
7. So-called "second generation" antipsychotics (eg, risperidone, olanzapine, quetiapine, ziprasidone) can help sleep and anxiety and can even reduce headache patterns.

## Sleep disorders

This should be relatively easy, because most sleep disorders are of two varieties: either you don't fall asleep well or you don't stay asleep. For the former, the list of sleep induction agents is a short one:

Zolpidem (Ambien)
Zaleplon (Sonata)
Chloral hydrate
Tizanidine

Patients should be in bed when these agents are taken and should be informed that the agents are short-acting with virtually no carryover the following morning. They are also useful if taken at the height of a severe headache along with more abortive medications, particularly tizanidine.

For sleep maintenance, tizanidine is a favorite of mine. Sometimes a "part 2" dose is given between 3 and 4 AM, because by then the first dose has effectively been metabolized. This can be done with one or one and a half tablets. Trazodone is an excellent choice, because it comes without the downsides of the tricyclics (eg, constipation, weight gain, sluggishness). Nefazodone is also excellent for maintaining sleep. Carbamazepine can be a handy agent to help maintain sleep, and, of all the modern neuronal stabilizing agents, oxcarbazepine (Trileptal, an offspring of Tegretol) is also quite useful.

## Depression

I do not recommend tricyclics for the treatment of depression, even though they have been mainstays for many years. But at what pricetag for the patient? This category of medications needs to be retired and replaced with newer agents like trazodone, nefazodone, venlafaxine, SSRIs, and the NSAs (ie, anticonvulsants).

## Bipolar and mood disorders

Consider things much newer than lithium (c. 1960s) with its wicked side effect profile. (No wonder you want to refer this kind of problem to a psychiatrist!) Realistically, all of the modern so-called anticonvulsants (NSAs) have been or are being tried for mood stabilization. Just about all practitioners have tried and use valproate sodium (Depakote) and gabapentin (Neurontin). Why not get your feet wet with one of the newer agents I described above? It doesn't matter which one; they can all be added to, or be a replacement for, the older group of agents. Remember that gabapentin has been on the market for 10 years. Did it take that long for you to try the latest antibiotic?

## Summary

TTH has for years been misnamed and misunderstood. As we come closer to a better understanding of this disorder, the diagnosis and treatment are becoming easier to accomplish. Theories of shared mechanisms with migraine are being explored and present exciting new ways of thinking about this age-old problem. Tricyclic antidepressants have a well-established role in the treatment of TTH, and tizanidine has come to light recently as a useful treatment. The NSAs—otherwise known as anticonvulsants—hold promise as well. Newer research on more controversial treatments such as opioids and botulism toxin may offer new insight in the future. Non-pharmacologic treatments such as relaxation therapy and biofeedback may be some of the best treatments for TTH.

In one or two sentences, it is very much a new millennium in our thinking about TTH and its causes and treatments. Stay tuned, for we are getting nearer to the answers.

## Appendix: International Headache Society criteria

*Episodic tension-type headache*

1. At least 10 previous headache episodes fulfilling the criteria; number of days with the headache less than 180/y or 15/mo
2. Headache lasting from 30 minutes to 7 days
3. At least two of the following pain characteristics:
    - Pressing/tightening (nonpulsating quality)
    - Mild or moderate severity
    - Bilateral location
    - No aggravation by walking stairs or similar routine physical activity
4. Both of the following:
    - No nausea or vomiting (anorexia may occur)
    - Photophobia and phonophobia are absent, one but not the other is present

*Character of pain*

1. Variably described as pressure, soreness, tightness, a band or cap on the head, or weight on the head
2. Occasionally pulsating during severe pain episodes

*Location*

1. 90% bilateral
2. Can be unilateral in the presence of trigger points or oromandibular dysfunction

*Chronic tension-type headache*

1. Average headache frequency is 15 or more d/mo or 180 d/y for 6 months
2. The same pain characteristics as for ETTH
3. Both of the following:
   - No vomiting
   - No more than one of the following: nausea, photophobia, or phonophobia

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