

Learning From Our Treatment Failures

Kenneth A. Holroyd¹

Barton and Blanchard's report that multicomponent behavioral treatment fails to modify chronic daily headaches is discussed with reference to the effectiveness of behavioral and drug treatments for chronic tension-type headache, the distinction between chronic tension-type headache and chronic migraine, and the psychophysiology of episodic vs. persistent pain (K. A. Barton & E. B. Blanchard, 2001). It is suggested that the treatment of chronic daily headache can be improved through research on the benefits of combined behavioral and drug therapy, the psychophysiology of persistent pain, and methods of preventing episodic headaches from evolving to daily headaches.

KEY WORDS: headache; migraine; behavior; biofeedback; pain.

Barton and Blanchard (2001) are to be congratulated for focusing our attention on their failure to modify near daily headaches in 14 of 16 patients with a multi-component behavioral treatment. Near-daily headaches are a leading reason for consultation at headache subspecialty centers in the United States, by some reports accounting for 30–75% of all subspecialty visits and a disproportionate share of the personal and social costs of headache (Mathew, 1997; Mathew, Reuveni, & Perez, 1989; Scher, Stewart, Liberman, & Lipton, 1998; Silberstein, Lipton, Solomon, & Mathew, 1994b). Thus, treatment failure with chronic daily headache (CDH) is no minor concern. It is frustrating for both the patient and the clinician to confront treatment failure, possibly explaining why treatment failures are rarely presented. Fortunately, Barton and Blanchard recognize that it is by understanding treatment failures that we will develop fresh hypotheses that can point us toward more effective treatments.

The authors allude to the use of preventive medication by some patients, suggesting this is a report of nonresponse to the addition of behavior therapy to preventive medication in some cases. It also would be unusual in today's practice environment if none of these patients had used a triptan to treat their severe headaches. When triptans are used as acute therapy during behavioral treatment, behavioral treatment may interact with triptan therapy in a number of ways. For example, the potent vasoconstrictive effects of the triptans might reduce the effectiveness of behavioral interventions such as thermal biofeedback, or changes in the timing or frequency of triptan use induced by behavioral treatment may alter global measures such as the headache index obscuring the effects of behavioral treatment. These

¹Department of Psychology, Ohio University, Athens, Ohio 45701-2979; e-mail: holroyd@ohio.edu.

methodological concerns clearly do not account for the treatment failures described here. However, if we are to identify the circumstances where treatments succeed or fail, we will need to control and manipulate interactions between drug and behavioral treatments, rather than leave them as uncontrolled “error” variance.

TCTH TRIAL RESULTS

The Treatment of Chronic Tension-Type Headache (TCTH; Holroyd et al., 2001) trial provides additional information about the effectiveness of behavior therapy for one subgroup of patients with CDH. This randomized placebo controlled trial evaluated the effectiveness of cognitive-behavioral stress-management therapy, tricyclic antidepressant medication and their combination in 203 patients with chronic (mean 26 headache days per month) tension-type headaches. Modest, but clinically significant improvements were observed with cognitive-behavior therapy in this trial, but these improvements were not fully evident until months after patients completed treatment, probably because headache management skills needed to be applied for a number of months before they affected near daily tension-type headaches. Thus, cognitive-behavior therapy yielded statistically significant but modest improvements in headache activity at the time point Barton & Blanchard assessed improvements in headache activity (12 weeks after initiating treatment); however, 6-months after completing cognitive-behavior therapy results were somewhat better, with approximately a third of patients treated with either cognitive-behavior therapy or with antidepressant medication, and almost two thirds of patients treated with the combined treatment showed clinically significant reductions ($\geq 50\%$) in headache index. Might the similarities and differences in outcome in these two reports tell us something about the treatment of daily headaches?

CHRONIC MIGRAINE VS. CHRONIC TENSION-TYPE HEADACHE

Chronic daily headache is, of course, not a diagnostic category but a pattern of headache activity. Chronic tension-type headaches are one reasonably well-defined subtype of chronic daily headache. However, chronic migraine, which might logically be expected also to be a second subtype of chronic daily headache, is not addressed by the current International Headache Society classification system (Olesen, 1988). Nonetheless, efforts have been made to develop diagnostic criteria for chronic migraine or “transformed” migraine (Manzoni et al., 1995; Silberstein et al., 1994b; Silberstein, Lipton, & Sliwinski, 1996; Silberstein, Lipton, Solomon, & Mathew, 1994a) and some version of this diagnosis is likely to be included in the forthcoming revision of International Headache Society classification system. Intuitively, we would expect chronic migraines, unlike chronic tension-type headaches, to evolve from episodic migraines, and to meet most diagnostic criteria for migraine (duration of 3–72 hr a likely exception). Recent findings further indicate that in individuals with frequent migraines, but not in individuals who experience *only* tension-type headaches, headaches that meet tension-type headache diagnostic criteria respond to sumatriptan (Lipton et al., 2000). This raises the possibility that in some individuals with chronic daily headaches, headaches with a range of phenotypes are migrainous in nature, and thus are best understood as chronic migraines.

The distinction between chronic migraine and chronic tension-type headache is important, because there is no reason to expect these two disorders to respond to the same therapies. Chronic migraines may be more refractory to standard nonpharmacological interventions and may respond to different drug therapies than chronic tension-type headaches. Results from the TCTH trial, where care was taken to exclude patients with transformed or chronic migraine, suggest that chronic tension-type headaches are modestly responsive to behavior therapy, although the full effects of behavior therapy may not be observed for months following treatment. Results further suggest that behavior therapy alone may not be the treatment of choice for chronic tension-type headaches. Even if, as it appears, behavioral interventions are not the treatment of choice for CDH diagnostic distinctions within the general rubric of CDH may encourage investigators to focus on identifying subtypes of CDH where behavior therapy enhances the effectiveness of specific drug therapies.

EPISODIC VS. PERSISTENT HEADACHE

The psychophysiology of episodic and persistent headache probably differ in important ways. Neuroplastic changes in trigeminal pain transmission circuits and possibly deficits in supraspinal pain modulation appear to play a more important role in persistent headache than in episodic headache. For example, the sequential sensitization of spinal and supraspinal nociceptive neurons observed during the migraine attack (Burnstein & Cutrer, 2000; Burstein & Yamamura, 1998) may not abate following severe headache attacks in chronic migraine, as it does in episodic migraine, producing a persistent headache between migraine attacks. Also, sensitization of second order neurons at the nucleus caudalis may play a more important role in chronic than in episodic tension-type headaches (Bendtsen & Ashina, 2000; Bendtsen, Jensen, & Olesen, 1996; Lipchik et al., 2000). In general as pain becomes continuous or nearly continuous there are likely to be qualitative changes in the variables that control pain.

To the extent that the variables that control episodic and persistent pain differ, the methods of treating episodic and persistent headaches may need to differ as well. Behavioral interventions that enable patients to prevent or abort episodic migraines may be ineffective in dampening the central sensitization that underlies chronic migraines. On the other hand, anticonvulsant medication may dampen this central sensitization and thus play a role in the treatment of chronic migraines but have little role in the treatment of infrequent episodic migraines (Rothrock, Kelly, Brody, & Golbeck, 1994). Similarly, amitriptyline may dampen the central sensitization that underlies persistent tension-type headache (Wantanabe, Saito, & Abe, 1993) via its indirect effects on NMDA receptors, helping to "break up" continuous headaches, so that behavioral headache management skills can be used effectively.

NEEDED RESEARCH

If the above, admittedly speculative notions have any validity, they suggest three lines of research that might lead to more effective treatments for CDH. First, we need to determine if behavior therapy can enhance the effectiveness of drug therapies that have shown promise in managing different subtypes of chronic daily headache, and, if behavior therapy increases the probability patients can successfully discontinue drug therapy (Holroyd, in press). Unpublished findings from the TCTH trial indicated that patients who received

both cognitive-behavior therapy and tricyclic antidepressant medication were significantly more likely to have successfully discontinued antidepressant medication at a 12-month evaluation than were patients who received antidepressant medication alone. The combination of cognitive-behavior therapy and antidepressant drug therapy also yielded more rapid improvement than behavior therapy alone, greater changes in psychological variables than drug therapy alone, and was more likely to yield clinically significant reductions in headache activity than either drug or behavior therapy alone. Similar studies that examine the separate and combined benefits of behavioral and drug therapies for chronic migraine are needed.

Second, we need a better understanding of the psychophysiology of persistent headache. The psychophysiological correlates of neural sensitization or other central nervous system changes that underlie persistent pain deserve the attention of applied psychophysiologicalists. Pericranial electromyographic activity and peripheral finger temperature may be inappropriate targets for behavioral treatment in chronic migraine. We may simply be using these interventions because they are handy, not because they are the appropriate tools for the job. A better understanding of the psychophysiology of persistent headache might then lead us to other more effective interventions.

Third, we need to determine if early intervention in individuals who are at high risk for developing chronic headaches can prevent episodic headaches from progressing to chronic headaches, thereby preventing the considerable personal and societal costs associated with daily headaches. A first step would be to identify risk factors for the transformation of episodic headaches to chronic headaches. If risk factors were identified in longitudinal clinical or epidemiological studies, subsequent studies to evaluate interventions to prevent the development of persistent headaches in high-risk individuals would be feasible. Hopefully, progress in our understanding of the psychophysiology of persistent pain would also influence the type of interventions that would be evaluated in such prevention trials.

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