Behavioral Sleep Modification May Revert Transformed Migraine to Episodic Migraine

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Background.—Sleep problems have been linked with headaches for more than a century, but whether the headaches are the cause or the result of the disrupted sleep is unknown.

Objectives.—We previously reported that nonrestorative sleep and poor sleep habits are almost universal in a referral population of women with transformed migraine (TM). Since cognitive behavioral therapy is effective in improving sleep quality in individuals with poor sleep hygiene, we designed a randomized, placebo-controlled study to assess the impact of such treatment on TM. We hypothesized that behavioral sleep modification (BSM) would be associated with improvement in headache frequency and intensity and with reversion to episodic migraine.

Methods.—Subjects were 43 women with TM referred to an academic headache center. After obtaining informed consent, patients were randomized to receive either behavioral sleep instructions or placebo behavioral instructions in addition to usual medical care. Subjects recorded headaches in standardized diaries. The first postintervention visit was scheduled at 6 weeks. At that visit, the blind was broken and all subjects received BSM instructions. A final visit was scheduled 6 weeks later.

Results.—Compared to the placebo behavioral group, the BSM group reported statistically significant reduction in headache frequency \(F(1, 33 = 12.42, P = .001)\) and headache intensity \(F(1, 33 = 14.39, P = .01)\). They were more likely to revert to episodic migraine \(\chi^2(2, n = 43) = 7.06, P = .029\). No member of the control group reverted to episodic migraine by the first postintervention visit. By the final visit, 48.5% of those who had received BSM instructions had reverted to episodic migraine.

Conclusions.—In this pilot study of women with TM, we found that a targeted behavioral sleep invention was associated with improvement in headache frequency, headache index, and with reversion to episodic migraine.

Key words: migraine, sleep, behavioral therapy, insomnia, chronic daily headache, transformed migraine

(Headache 2007;47:1178-1183)
initiating and maintaining sleep. Ohayon described a strong association between sleep problems—including insomnia, circadian rhythm disorder and sleep-related breathing disorder—and chronic morning headaches, and Scher found habitual snoring to be more prevalent in patients with CDH than in those with episodic headache.

Moldovsky reported that in migraineurs who awaken frequently with early morning headaches, sleep disorders are prevalent and exert significant effects on headache and fatigue. Paiva identified primary sleep disorders in the majority of patients whose headaches regularly awakened them from sleep. In those subjects, specific treatment of the identified sleep disorders resulted in improvement or resolution of headache in all cases.

Many of these studies have focused on primary sleep disorders; however, the most prominent factor in poor sleep quality is insomnia—a subjective, complaint-driven diagnosis which is defined by difficulty falling asleep or remaining asleep, early morning awakening or nonrestorative sleep, along with the daytime consequences of such difficulties. These complaints may evolve secondary to a variety of environmental, behavioral, physical or emotional factors, or may reflect an underlying sleep disorder. Regardless of its etiology, insomnia responds to behavioral sleep modification (BSM) in the majority of patients, but information is lacking on the effect of this intervention on chronic headaches.

A meticulous search of the literature failed to reveal a single report of the use of BSM for TM, alone or in combination with standard medical care. One report of BSM in a pediatric population of episodic migraineurs described reduction in headache frequency and intensity. In that study, however, subjects were preselected based on the presence of sleep complaints. The extent to which these findings can be generalized to adults with TM is uncertain.

Objectives.—We previously found that nonrestorative sleep and poor sleep habits are almost universally prevalent in a referral population of women with TM. Since behavioral approaches have proven effective in improving sleep quality in individuals with poor sleep hygiene, we designed a small randomized, single-blind, placebo-controlled pilot study to assess the impact of such treatment on TM. We hypothesized that BSM would be associated with improvement in headache frequency and intensity (as measured by headache index) and with reversion to episodic migraine.

METHODS

Participants.—Study inclusion was offered to 45 consecutive new patients referred to an academic medical center who met inclusion criteria: nonpregnant, nonlactating adult females with TM diagnosed in accordance with criteria proposed by Silberstein et al and no diagnosis of a primary sleep disorder. Headache diagnosis was established or confirmed by a headache specialist at our facility. Two patients declined to participate due to concern that they would receive placebo treatment; 43 were enrolled.

Measures.—Subjects completed a packet of inventories given to all new patients in the clinic. Baseline self-report information on headache frequency, headache severity, headache chronicity, sleep characteristics, demographics, body mass index, and medication use was collected. Fidelity to the intervention was assessed by patient report. There were no missing data from study completers.

Headache Diary Measures.—Subjects recorded their headaches in a standardized diary which was reviewed at each visit. Headache frequency was calculated by counting the number of the preceding 28 days on which any headache was recorded. Headache index was calculated by multiplying the number of days with severe headache by 3; the days with moderate by 2; the days with mild by 1, and summating.

A subject was considered to have reverted to episodic migraine when her diary recorded 13 or fewer headaches in the preceding 28 days, and she registered 4 or more consecutive headache-free days.

Procedures.—After obtaining informed consent, 23 patients were randomized using random number tables; to receive BSM instructions (Table 1); 20 received sham instructions (placebo behavioral group) (Table 2). All behavioral interventions were administered by the same instructor who was not blinded to the intervention. Equal time (approximately
Table 1.—BSM Instructions

1. Schedule consistent bedtime that allows 8 hours time in bed
2. Eliminate TV, reading, music in bed
3. Use visualization technique to shorten time to sleep onset
4. Move supper ≥4 hours before bedtime; limit fluids within 2 hours of bedtime
5. Discontinue naps

20 minutes) was devoted to a detailed explanation and rationale for each element of the behavioral treatment. Subjects were not contacted between visits, but each was provided a list of the 5 study instructions for reference.

All received usual medical care for migraine in addition to the behavioral intervention. Usual care included instruction to discontinue overused medications (when present) while bridge therapy was provided for 2 weeks to all subjects in the form of a naratriptan taper.

The first postintervention visit was scheduled at 6 weeks. After recording study data, the single blind was broken, and all subjects then received BSM instructions. A third and final visit was scheduled 6 weeks later (Fig. 1).

Six subjects were found to have symptoms consistent with restless legs syndrome—4 in the BSM group and 2 in the placebo behavioral group. No medical therapy was offered at the time of the first visit, but all 6 were prescribed medical treatment with ropinirole after the second visit.

This study was approved by the university’s institutional review board.

Statistical Analyses.—A one-sample chi-square test was conducted to determine whether the BSM group was more likely to revert to episodic migraine than the placebo behavioral group. Analyses of variances (ANOVA) were conducted to explore baseline factors that differentiated reverters from nonreverters.

Table 2.—Sham Instructions

1. Schedule consistent suppertime that varies <1 hr from day to day
2. Perform acupressure as instructed for 2 minutes twice daily
3. Record liquid consumption for 3 consecutive days
4. Do 5 minutes of gentle range of motion exercises every morning
5. Have 1 protein serving at breakfast

Study Design

Fig 1.—Study design.

Table 3.—Baseline Demographic and Psychometric Characteristics of the Two Treatment Arms

<table>
<thead>
<tr>
<th></th>
<th>BSM Group (n = 23)</th>
<th>Placebo Group (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>33.5</td>
<td>35.0</td>
</tr>
<tr>
<td>BMI</td>
<td>24.6</td>
<td>25.9</td>
</tr>
<tr>
<td>Chronicity (mos)</td>
<td>140.7</td>
<td>116.4</td>
</tr>
<tr>
<td>HA frequency</td>
<td>24.2</td>
<td>23.2</td>
</tr>
<tr>
<td>HA index</td>
<td>46.7</td>
<td>50.2</td>
</tr>
<tr>
<td>Med. overuse (%)</td>
<td>78.3</td>
<td>70.0</td>
</tr>
<tr>
<td>HIT-6</td>
<td>63.6</td>
<td>64.2</td>
</tr>
<tr>
<td>BDI</td>
<td>10.9</td>
<td>9.1</td>
</tr>
<tr>
<td>State Anx.² Total</td>
<td>44.3</td>
<td>44.1</td>
</tr>
<tr>
<td>Trait Anx.³ Total</td>
<td>48.0</td>
<td>44.7</td>
</tr>
<tr>
<td>HSE⁴ Total</td>
<td>101.8</td>
<td>93.0</td>
</tr>
<tr>
<td>Pain catastrophizing</td>
<td>20.3</td>
<td>25.0</td>
</tr>
<tr>
<td>MHLOC⁶</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal</td>
<td>16.7</td>
<td>15.5</td>
</tr>
<tr>
<td>Chance</td>
<td>14.8</td>
<td>15.2</td>
</tr>
<tr>
<td>Powerful other</td>
<td>19.5</td>
<td>18.2</td>
</tr>
<tr>
<td>Hlth Care Prov</td>
<td>11.8</td>
<td>10.1</td>
</tr>
<tr>
<td>Other</td>
<td>7.7</td>
<td>8.2</td>
</tr>
</tbody>
</table>

¹Headache Impact Test-6, ²Beck Depression Inventory, ³State Trait Anxiety Inventory, ⁴Headache Self-Efficacy, ⁵Pain Catastrophizing Scale, ⁶Multidimensional Health Locus of Control. There were no significant differences in these baseline characteristics between the 2 treatment arms.
RESULTS

Baseline demographics, psychological status, sleep and headache characteristics were equivalent between the treatment arms with one exception (Tables 3 and 4). The BSM group reported being less likely than the control group to get enough sleep to feel rested in the morning F (1, 33 = 7.53, $P = .01$). Additionally, there was a trend toward the BSM group endorsing slightly higher baseline levels of trait anxiety than the placebo behavioral group F (1, 28 = 4.00, $P = .06$). Baseline sleep onset latency, average hours of sleep, and the perception of adequate sleep was equivalent between groups.

A clinical diagnosis of depression and/or anxiety was present in 39.5% of the subjects: 39.1% of the BSM group and 40% of the control group. Two additional subjects—one in each treatment arm—reported either chronic fatigue or fibromyalgia.

Seven women were lost to follow-up before the second visit, leaving 36 evaluable subjects. Those lost to follow-up had similar sleep and headache characteristics as the total group. Although their mean duration of chronicity was shorter, and fewer of them overused acute medications, the only statistically significant demographic factor that differentiated those lost to follow-up was age: they were younger than all randomized subjects [25.7 years vs 34.2 years, F (1, 34 = 5.32, $P = .027$)].

By the second visit, the BSM group reported a statistically significant reduction in headache frequency F (1, 33 = 12.42, $P = .001$) and headache intensity F (1, 33 = 14.39, $P = .01$) when compared to the placebo behavioral group (Fig. 2). They were more likely to have reverted to episodic migraine $\chi^2 (2, n = 43) = 7.06, P = .029$. No member of the placebo behavioral group reverted to episodic.

Once the study blind was broken, all subjects received BSM instructions. By the third visit, 48.5% of those who had received sleep instructions (at the first and/or second visit) had reverted to episodic migraine.

Adherence to study instructions did not statistically differ between treatment arms. Adherence to sham instructions was not related with headache improvement; adherence to BSM instructions was strongly related with improvement: among participants who adhered to all 5 BSM instructions, only one did not revert to episodic migraine. Among those who were nonadherent with 3 or more instructions, none reverted (Table 5).

Table 4.—Baseline Sleep Characteristics of the 2 Treatment Arms—As Well as of Those Who Eventually Reverted and Nonreverters

<table>
<thead>
<tr>
<th>“In the past 4 weeks....”7</th>
<th>BSM Group (n = 23)</th>
<th>Placebo Group (n = 20)</th>
<th>Reverters (n =16)</th>
<th>Nonreverters (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>How long did it usually take to fall asleep?</td>
<td>2.1</td>
<td>2.5</td>
<td>2.2</td>
<td>2.2</td>
</tr>
<tr>
<td>1 = 0-15 minutes</td>
<td>2 = 16-30 minutes</td>
<td>3 = 31-45 minutes</td>
<td>4 = 46-60 minutes</td>
<td>5 = &gt;60 minutes</td>
</tr>
<tr>
<td>On average, how many hours did you sleep each night?</td>
<td>7.2</td>
<td>7.0</td>
<td>7.2</td>
<td>6.9</td>
</tr>
<tr>
<td>1 = always; 6 = never</td>
<td>4.6*</td>
<td>3.4</td>
<td>3.9</td>
<td>4.7</td>
</tr>
<tr>
<td>How often did you get enough sleep to feel rested upon waking in the morning?</td>
<td>3.7</td>
<td>3.2</td>
<td>3.5</td>
<td>3.5</td>
</tr>
<tr>
<td>How often did you get the amount of sleep you needed? (1 = always; 6 = never)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

7Items taken from sleep scale in Medical Outcomes Study.

*P = .01 compared with placebo group.
Table 5.—Adherence to BSM Correlates with Reversion to Episodic Migraine

<table>
<thead>
<tr>
<th># of Persistent Detrimental Habits</th>
<th>Reverted to Episodic</th>
<th>No Reversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

All subjects were instructed to taper or discontinue overused medications, when present. At baseline 74.4% of the subjects were overusing acute agents. By the final visit (12 weeks), medication overuse was eliminated in all subjects who reverted to episodic migraine, as well as in 60% of the nonreverters.

Despite the fact that subjects were not preselected for sleep problems, the items most frequently endorsed on baseline self-report inventories related to tiredness/fatigue, energy levels, or sleep. Two-thirds of responders reported that they were experiencing changes in sleeping pattern; 69% reported that they were more tired or fatigued than usual, and 81% reported a decrease in energy.

** F (1, 33 = 12.42, p = .001)
* F (1, 33 = 14.39, p = .01)

Fig 2.—Compared to the placebo behavioral group, the BSM group reported greater reduction in headache frequency and intensity.

CONCLUSIONS

Transformed migraine is a painful, disabling disorder which accounts for personal suffering, impaired function, lost work, and heavy utilization of medical resources. Conventional treatments are variably effective, expensive, symptom-directed, and occasionally limited by side effects.

Nonrestorative sleep and poor sleep habits are almost universally prevalent in women with TM. This randomized, placebo-controlled behavioral trial suggests that BSM may be an effective, noninvasive adjunctive treatment for TM.

Transformation is most commonly attributed to medication overuse. This factor is accepted as instrumental because (1) it exhibits very high prevalence in patients with TM and (2) withdrawal from the overused medications can result in clinical improvement, which suggests a causal relationship between overuse and headache chronicity. However, it is recognized that one-third of individuals who develop CDH are not overusing medication; this would imply that this single factor, though important, is not the sole determinant of chronicity.

Clues to other factors that engender chronicity may be found in TM’s earliest presentation—in childhood or adolescence. Here, medication overuse is less
commonly present, suggesting that other factors may predominate in these age groups. A comparison of children with CDH and healthy controls revealed that chronicity in children was associated with decreased nocturnal sleep duration and increased frequency of poor sleep hygiene.

Limitations of this study include its single-blinded design, which permits the possibility that demand characteristics from unblinded staff may have been conveyed to the subjects and influenced outcome. Future studies would benefit from double-blind methodology.

If these pilot results are replicated in larger, well-designed studies, additional investigation would be warranted to explore possible mechanisms by which nonrestorative sleep might influence migraine transformation.

Studies are also warranted to identify hindrances to patient compliance in following BSM instructions. Identifying such hindrances is particularly important in this setting, since advocating sleep changes to benefit chronic headaches is analogous to advising emphysema patients to quit smoking: the plan is simple, but not easy. Future studies should identify psychological factors in subjects who fail to comply, fail to reconvert, or fail to follow-up in the treatment plan; such information would enable these individuals to be recognized early and—with issues successfully addressed—could effect better outcomes.

Acknowledgment: The authors acknowledge the National Headache Foundation for financial support of this project.

Conflict of Interest: Dr. Calhoun has worked for the Speakers Bureau of GlaxoSmithKline.

REFERENCES
