Headache
© 2014 American Headache Society
ISSN 0017-8748
doi: 10.1111/head.12420
Published by Wiley Periodicals, Inc.

Research Submission

Meditation for Migraines: A Pilot Randomized Controlled Trial

Rebecca Erwin Wells, MD, MPH*; Rebecca Burch, MD; Randall H. Paulsen, MD; Peter M. Wayne, PhD; Timothy T. Houle, PhD; Elizabeth Loder, MD, MPH

Objective.—Our objective was to assess the safety, feasibility, and effects of the standardized 8-week mindfulness-based stress reduction (MBSR) course in adults with migraines.

Background.—Stress is a well-known trigger for headaches. Research supports the general benefits of mind/body interventions for migraines, but there are few rigorous studies supporting the use of specific standardized interventions. MBSR is a standardized 8-week mind/body intervention that teaches mindfulness meditation/yoga. Preliminary research has shown MBSR to be effective for chronic pain syndromes, but it has not been evaluated for migraines.

Methods.—We conducted a randomized controlled trial with 19 episodic migraineurs randomized to either MBSR (n = 10) or usual care (n = 9). Our primary outcome was change in migraine frequency from baseline to initial follow-up. Secondary outcomes included change in headache severity, duration, self-efficacy, perceived stress, migraine-related disability/impact, anxiety, depression, mindfulness, and quality of life from baseline to initial follow-up.

Results.—MBSR was safe (no adverse events), with 0% dropout and excellent adherence (daily meditation average: 34 ± 11 minutes, range 16-50 minutes/day). Median class attendance from 9 classes (including retreat day) was 8 (range [3, 9]); average class attendance was 6.7 ± 2.5. MBSR participants had 1.4 fewer migraines/month (MBSR: 3.5 to 1.0 vs control: 1.2 to 0 migraines/month, 95% confidence interval CI [–4.6, 1.8], *P* = .38), an effect that did not reach statistical significance in this pilot sample. Headaches were less severe, although not significantly so (–1.3 points/headache on 0-10 scale, [–2.3, 0.09], *P* = .053) and shorter (–2.9 hours/headache, [–4.6, –0.02], *P* = .043) vs control. Migraine Disability Assessment and Headache Impact Test-6 dropped in MBSR vs control (–12.6, [–22.0, –1.0], *P* = .017 and –4.8, [–11.0, –1.0], *P* = .043, respectively). Self-efficacy and mindfulness improved in MBSR vs control (13.2 [1.0, 30.0], *P* = .035 and 13.1 [3.0, 26.0], *P* = .035 respectively).

Conclusions.—MBSR is safe and feasible for adults with migraines. Although the small sample size of this pilot trial did not provide power to detect statistically significant changes in migraine frequency or severity, secondary outcomes demonstrated this intervention had a beneficial effect on headache duration, disability, self-efficacy, and mindfulness. Future studies with larger sample sizes are warranted to further evaluate this intervention for adults with migraines. This study was prospectively registered (ClinicalTrials.gov identifier NCT01545466).

Key words: mindfulness, meditation, migraine, yoga, randomized controlled trial

Abbreviations: CAM complementary and alternative medicine, HIT-6 Headache Impact Test-6, MOH medication overuse headache, MIDAS Migraine Disability Assessment, MBSR mindfulness based stress reduction, PHQ-9 Patient Health Questionnaire-depression module, REDCap Research Electronic Data Capture system

(*Headache* 2014;54:1484-1495)

From the Wake Forest School of Medicine, Wake Forest Baptist Medical Center, Winston-Salem, NC, USA (R.E. Wells and T.T. Houle); Division of Headache and Pain, Brigham and Women's Faulkner Hospital, Harvard Medical School, Boston, MA, USA (R. Burch and E. Loder); Osher Center for Integrative Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA (R.H. Paulsen and P.M. Wayne).

Address all correspondence to R.E. Wells, Medical Center Boulevard, 6th floor, Janeway Tower, Winston-Salem, NC 27157, USA, email: rewells@wakehealth.edu

Accepted for publication May 22, 2014.

Traditionally, medications are first-line treatment for migraine therapy. However, only about half of migraineurs have clinically meaningful responses to preventive drug treatments, more than 10% discontinue due to adverse events,[1] and half report dissatisfaction with their current treatment strategies.[2] When preventive treatments are ineffective, migraineurs may overuse symptomatic relief medications with a consequent worsening of their headache burden. Excessive use of abortive medications can cause the challenging and often refractory condition of medication overuse headache (MOH). These shortcomings of existing treatment options substantiate the great need for additional migraine treatment strategies.

Non-pharmacological options are believed to have few serious side effects, can be used concurrently with medications or when medication use must be limited or avoided due to side effects or contraindications, and reduce overall medication reliance and the possibility of MOH. Such therapies may be more congruent with patients' beliefs about health and life,[3] can be taken concurrently with pharmacological therapies, and may have therapeutic effects on other factors contributing to headache burden such as stress or anxiety.[4] Stress is widely believed to be a significant trigger for headaches.[5-10] The US Headache Consortium's treatment guidelines for prevention of migraines recommends the behavioral interventions of electromyographic biofeedback, relaxation training, thermal biofeedback combined with relaxation training, and cognitive behavioral therapy with Grade A evidence (based on evidence from 39 controlled trials).[11]

In addition to these evidence-based behavioral interventions, many patients are using less-well researched non-pharmacological options such as complementary and alternative medicine (CAM) modalities in the treatment of headache.[12] Approximately half of US adults with migraines report using CAM, especially mind/body therapies such as meditation and yoga.[13] Many view CAM therapies as more helpful than conventional headache treatment.[14] Both the evidenced-based behavioral interventions and CAM interventions may have many similar active ingredients (such as relaxation and stress management), and mindfulness meditation has the distinct purpose of teaching individuals how to maintain focus on a stimulus while simultaneously allowing intruding thoughts/feelings to be acknowledged but not judged. Mindfulness-based stress reduction (MBSR) is a mind/body intervention that follows a standardized 8-week protocol involving group instruction by certified instructors.[15] It teaches mindfulness meditation and yoga, and daily assignments are used to build each participant's mindfulness practice. MBSR research has demonstrated measurable neurological changes post-intervention.[16-18] In addition, mindfulness meditation has been shown to differentially impact other non-headache-related outcomes and neurological changes compared to relaxation training, stress management training, and cognitive behavioral therapy.[19-22] Despite the high prevalence of use of such CAM therapies in the general population and in those with headaches and the distinct impact of such therapies compared to previously researched behavioral interventions for headaches, to our knowledge no studies have been done to evaluate the effectiveness of a standardized CAM intervention for headaches.

Although there is evidence supporting mindfulness-based interventions for chronic pain,[23-25] and evidence showing that meditation significantly reduces pain in experimental settings,[26,27] and various forms of meditation may impact migraines,[28] there are no studies evaluating mindfulness meditation specifically for migraines. If MBSR, a standardized mind/body intervention, offers benefits to migraine patients, it could be easily used and recommended in the treatment of migraines. Once patients are trained in the techniques, they can use MBSR anywhere and at any time, potentially to prevent as well as abort headaches.

Conflict of Interest: Timothy T. Houle: Dr. Houle receives research support from GlaxoSmithKline, Merck, and Depomed. All other authors report no conflicts of interest.

*Dr. Wells conducted this pilot trial when she was on faculty at Brigham and Women's Hospital, Harvard Medical School.

This clinical trial was registered 24 February 2012: clinicaltrials.gov identifier NCT01545466.

For these reasons, we conducted a randomized controlled study with the objective of assessing the safety, feasibility, and effect of MBSR in migraineurs vs usual care. Our hypotheses were: (1) MBSR is feasible and safe in migraineurs; (2) MBSR will decrease migraine frequency, severity, and duration; and (3) the MBSR group will demonstrate trends toward improved quality of life and self-efficacy and less depression, anxiety, and migraine-related disability.

METHODS

Study Population.—See the Figure for research design. In this single-site study, we recruited migraine patients via flyers, referrals, and medical records from January-March 2012 from Brigham and Women's Hospital, primarily through the John R. Graham Headache Center, a tertiary care academic headache center in Boston, MA. Potential participants were evaluated via an initial telephone screen and, if deemed potentially eligible, were subsequently evaluated at an in-person visit by a neurology headache specialist (REW or RB) who assessed whether they met criteria for inclusion in the study. Participants then deemed eligible to participate in the study maintained a paper headache log for a 28-day run-in period. Both the Guidelines for Controlled Trials of Drugs in Migraine[29] and the Guidelines for Trials of Behavioral Treatments for Recurrent Headache[30] recommend a 1-month baseline period. This log was then reviewed by the headache experts to confirm eligibility for the study. The study was approved by the Brigham and Women's human subjects' research review board. Each participant signed a written informed consent document. This study was prospectively registered (ClinicalTrials.gov identifier NCT01545466).

Inclusion criteria included: diagnosis of migraine with or without aura (according to the International Classification of Headache Disorders-II);[31] 4-14 migraine days/month; ≥one year history of migraines; ≥18 years old; able and willing to attend weekly sessions and willing to participate in daily mindfulness assignments of up to 30-45 minutes/day; agreeable to participate and to be randomized to either group; fluent in English; and in good general health with no additional diseases expected to interfere with the study. Exclusion criteria included: current regular meditation/yoga practice; major systemic illness or unstable medical/psychiatric condition (eg, suicide risk) requiring immediate treatment or that could compromise protocol adherence; medication overuse headache, (according to the International Classification of Headache Disorders-II);[31] current/planned pregnancy or breastfeeding; new prophylactic migraine medicine started within 4 weeks of the screening visit; unwilling to maintain stable migraine medication dosages; and failure to complete baseline headache logs.

Study Design.—This study was a prospective, randomized (1:1) clinical trial to evaluate if an 8-week MBSR program is superior to usual care. Participants were allowed to continue taking their prophylactic and abortive medications as usual, and were asked to not change dosages for the duration of the trial. As seen in Table 1's baseline characteristics of the study participants, 89% of those in the control group were being treated with daily prophylactic medications, which were allowed to be continued for the duration of the trial. All participants (100% of intervention and 100% of the control group) were already taking abortive headache medications, and they were allowed to continue these for the duration of the trial. Patients randomized to maintain usual care were offered MBSR at the conclusion of the study and were asked not to start a yoga or meditation class on their own in the meantime. Thus, participants in the control group were able to continue in their usual care during the duration of the study but were also offered the intervention as a courtesy at the conclusion of the study. In an attempt to blind the control group, participants were told there were two start times for the MBSR course, with randomization to either date. The group randomized to the later date was the control group, continuing usual care during the interim. Treatment assignments were generated using permuted block randomization with randomly varying block size and sealed in numbered, opaque envelopes. Given the low risk potential for this study, a full data and safety monitoring board was not required.

MBSR Intervention.—The standardized MBSR class met for 8-weekly 2-hour sessions, plus one

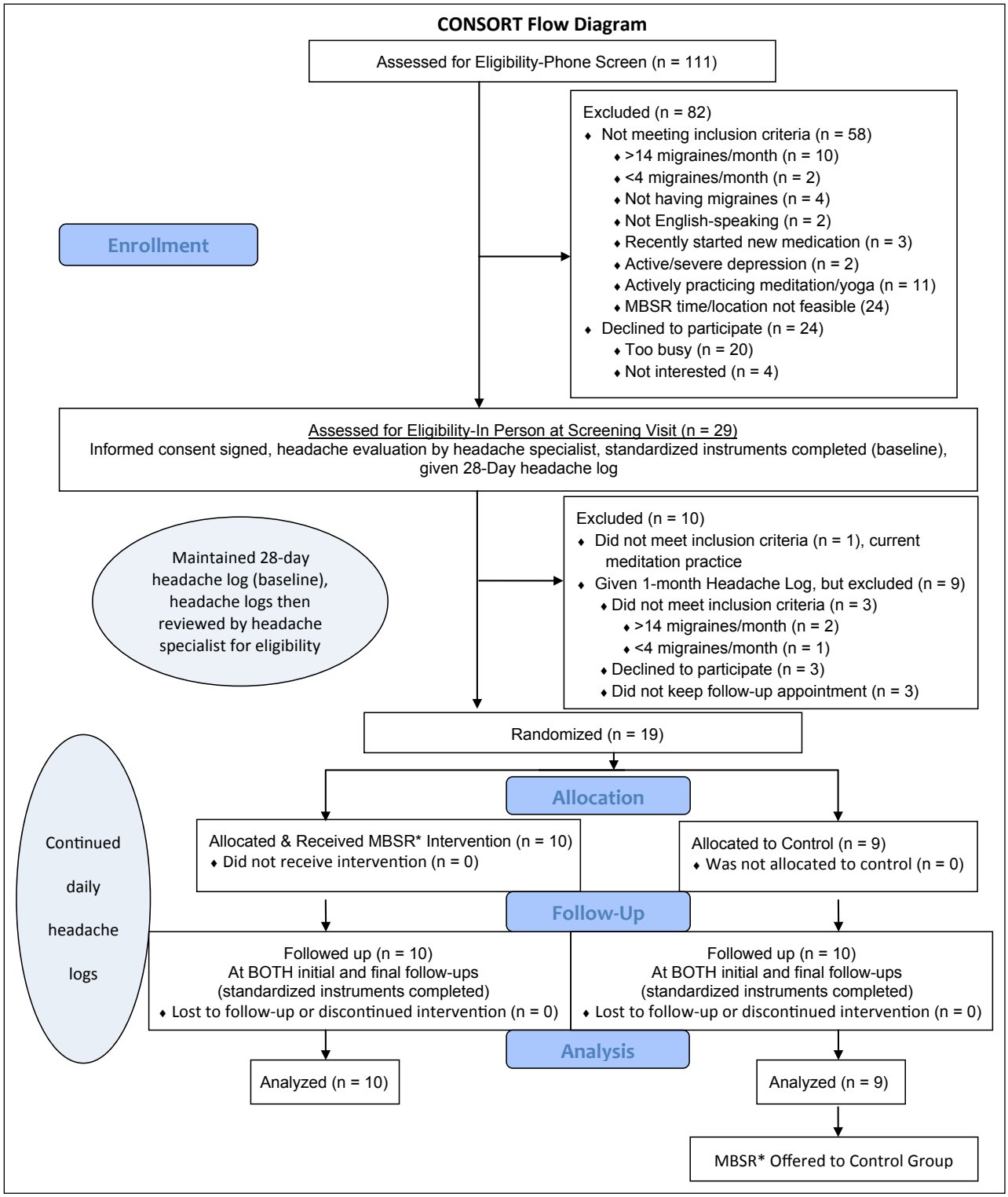

Figure.—CONSORT Flow Diagram: Flow of participants through trial; *Mindfulness Based Stress Reduction (MBSR), 8-weekly group classes plus retreat day taught by trained instructor.

Table 1.—Baseline Characteristics of Study Participants

Baseline Characteristic	Intervention n = 10	Control n = 9
Demographics		
Age (y); mean (SD)	45.9 (17)	45.2 (12)
Gender		
Female, n (%)	9 (90)	8 (89)
Male, n (%)	1 (10)	1 (11)
Race		
White, n (%)	9 (90)	8 (90)
Black, n (%)	1 (10)	1 (10)
Education		
≤High school, n (%)	1 (10)	0
College, n (%)	4 (40)	6 (67)
Graduate degree, n (%)	5 (50)	3 (33)
Headache features		
Years with migraines, mean (SD)	26 (19)	30 (13)
Headache days during 28 day baseline, median, (25^{th}%, 75^{th}%)	10 (8, 12)	12 (10, 14)
Treating with daily prophylactic medication, n (%)	8 (80)	8 (89)
Treating with abortive headache medication, n (%)	10 (100)	9 (100)
HIT-6 at baseline, median, (25^{th}%, 75^{th}%)	63 (55, 71)	63 (61, 70)
MIDAS at baseline, median, (25^{th}%, 75^{th}%)	17 (0, 19)	11 (5, 16)
Menses felt to be migraine trigger (by self-report), n (%)	5 (50)	6 (67)
Stress felt to be migraine trigger (by self-report), n (%)	6 (60)	7 (78)
Referral source		
Graham headache center provider, n (%)	7 (70)	6 (67)
Other headache provider, n (%)	1 (10)	2 (22)
Flyer, n (%)	2 (20)	1 (11)

"mindfulness retreat day" (6 hours) led by a trained instructor (RHP) who followed the structured MBSR protocol created by Dr. Jon Kabat-Zinn.[15] The protocol for this entire course (the 8-weekly classes plus the retreat day) was identical to the Kabat-Zinn protocol, without modifications for migraineurs. The original MBSR protocol was created to be provided in a group setting, as was done with this course. The instructor has been fully trained in MBSR by the Center for Mindfulness in Medicine, Health Care, and Society at the University of Massachusetts Medical School, where Dr. Jon Kabat Zinn created and developed this intervention. In addition, the instructor has had 5 years of supervised MBSR group leadership training under the Center for Mindfulness' staff. The intervention is based on systematic and intensive training in mindfulness meditation and mindful hatha yoga in the context of mind/body medicine. The theoretical underpinnings of mind/body medicine were taught throughout the course with interactive discussions and experiential practice. Mindfulness, defined as non-judgmental moment-to-moment awareness, was cultivated through mindful eating, mindful breathing with sitting and walking meditation, body scan (sequential mindful attention to different body parts) and mindful movement (yoga). Weekly course content is described extensively in Kabat-Zinn's book,[15] but briefly the first class begins with mindfulness of breathing, mindful eating, and the body scan, and subsequent classes build on these practices and slowly add in the other meditative practices. The all-day retreat includes elements of all the mindfulness practices. The instructor also gives information about stress and stress relief during the fourth class. During each class, participants can share their experiences of the practice of mindfulness with other students. A central theme of the course involves teaching participants to use the MBSR skills as a means to reduce the negative effects of stress reactivity and to develop more effective ways of responding positively and proactively in stressful situations and experiences. Specifically, by repeatedly bringing attention back to the natural rhythm of the breath, participants are encouraged to build their capacity to attend to physical and mental percepts. In addition to learning and practicing the formal practices of mindfulness meditation, participants are advised to incorporate mindfulness into their daily lives so that routine activities (brushing teeth, taking a shower, washing dishes, etc) can become a meditative practice. The ultimate goal is for patients to build their mindfulness practice and MBSR skills to develop a more flexible capacity to utilize mindfulness in a variety of everyday situations. During all classes, chairs were provided for seated exercises and mats were provided for the yoga. In addition to practicing during class, each participant

was given the same standard guided audio recordings and encouraged to practice at home to build their daily mindfulness practice for 45 minutes per day, at least 5 additional days per week. Compliance was monitored through class attendance and by daily logs of home practice.

Outcome Measures.—The primary outcome was change in migraine frequency (number of migraines/month [28 days]) from baseline to initial follow-up (immediately after MBSR ended). Secondary outcomes included: change in headache severity, duration, self-efficacy, perceived stress, migraine-related disability/impact, anxiety, depression, mindfulness, and quality of life from baseline to initial follow-up. We also explored results from baseline to final follow-up (a month after MBSR ended).

We tracked recruitment and enrollment rates, class attendance, daily logs of home practice and adverse events. Participants maintained daily paper headache logs from the initial baseline screening period to the final follow-up to record the number of headache days/month, severity of each headache (0-10 scale, 0 being no pain and 10 being severe pain), duration (in minutes), and medicines taken. At all 3 study visits, all participants completed a battery of standardized, validated instruments. Headache-related disability was measured with the Headache Impact Test-6 (HIT-6)[32] and the 1-month (rather than 3 months) Migraine Disability Assessment (MIDAS).[33] Quality of life was measured with the Migraine Specific Quality of Life Questionnaire, version 2.1.[34] Depression was assessed with the PRIME-MD Patient Health Questionnaire-depression module (PHQ-9).[35] Anxiety was measured with the State Trait Anxiety Inventory.[36] Stress was measured with the perceived stress scale-10.[37] Mindfulness was measured with the Five Facet Mindfulness Questionnaire.[38] Self-efficacy was measured with the Headache Management Self-Efficacy Scale.[39]

Study data were collected and managed using the Research Electronic Data Capture system (REDCap) hosted at Brigham and Women's Hospital.[40] REDCap is a secure, web-based application designed to support data capture for research studies, providing: (1) an intuitive interface for validated data entry; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for importing data from external sources.

Sample Size.—We estimated standard deviations for these analyses based on a previous study of yoga for migraines.[41] Allowing for 10% loss due to dropouts, a sample size of 34 would provide 80% power to detect between-group differences of about 3 fewer migraines/month, approximately half the effect size in the yoga study. Time constraints unrelated to the feasibility of the study (eg, REW's relocation) limited recruitment to 3 months and decreased our ability to reach our target sample size.

Statistical Analyses.—Descriptive statistics were used to analyze adherence and baseline characteristics. For the purposes of determining whether potential subjects were eligible for the trial, once subjects were confirmed to have migraine, baseline headaches were considered to be migraines. For all final analyses, migraines were more precisely defined as those headaches that were >4 hours long with a severity of 6-10, based on patient diary information. Mann-Whitney *U*-tests were performed to compare changes from baseline to follow-up in the intervention vs control group and for any change scores that violated parametric assumptions, the 95% CI was produced with the Hodges-Lehman estimate. To estimate effect sizes for variables that satisfied parametric assumptions, we ran independent *t*-tests on the change scores and report the differential change and 95% confidence intervals (CI). Given that headache characteristics were analyzed over 28 days, "baseline" reflects the 28-day period before the intervention, "initial follow-up" reflects the last 28-day period of the intervention, and "final follow-up" reflects the 28-day period after the intervention ended. For the standardized instruments, "baseline," "initial follow-up," and "final follow-up" reflect the time points of each assessment. All analyses were blinded and performed on an intention-to-treat basis using IBM SPSS Statistics 21 (IBM Corporation, Armonk, NY, USA). Although statistical inferences are conducted, this effort is a pilot study, and efforts are made to report and interpret effect sizes throughout. Where appropriate, all testing was 2-tailed with $P < .05$.

RESULTS

Nineteen migraineurs were randomized to either MBSR (n = 10) or usual care (n = 9) (see Figure) and results were analyzed intention-to-treat. Baseline characteristics of participants are shown in Table 1. MBSR was safe (no adverse events), with 0% dropout and excellent adherence (daily meditation average: 34 ± 11 minutes (range 16-50 minutes/day). Median class attendance from 9 classes (including retreat day) was 8 (range [3, 9]); average class attendance was 6.7 ± 2.5. Most participants in the trial were referred by Headache clinicians at the Graham Headache Center (70% in MBSR group, 67% in control group) or by another headache provider (10% in MBSR group, 22% in control group); very few learned of the study via flyer (20% in MBSR group and 11% in control group), see Table 1. Table 2 summarizes changes for headache characteristics. Despite inadequate power due to small sample size, from baseline to initial follow-up, compared to control, MBSR participants had 1.4 fewer migraines/month (3.5 to 1.0 migraines/month in MBSR vs 1.2 to 0 migraines/month in control, 95% confidence interval CI [−4.6, 1.8], P = .38). The severity and duration of all headaches decreased in the MBSR group (−1.3 points/headache on 0-10 scale [−2.3, 0.09], P = .053, which did not reach statistical significance, and 2.9 fewer hours per headache [−4.6, −0.02], P = .043). Table 3 summarizes changes for standardized instruments. Disability decreased in MBSR vs control on HIT-6 (−4.8, [−11.0, −1.0], P = .043) and 1-month MIDAS (−12.6 [−22.0, −1.0], P = .017). Lower HIT-6 and MIDAS scores reflect less headache impact and disability, and a change of 2.3 points on HIT-6 reflects the minimum important difference that reflects meaningful clinical change.[42] Self-efficacy and mindfulness also increased (+13.2 [1.0, 30.0], P = .035 and +13.1 [3.0, 26.0], P = .035, respectively). The effect sizes for migraine-specific quality of life, anxiety, and perceived stress also showed improvement. Effect sizes persisted in all outcomes at final follow-up.

DISCUSSION

This small pilot study suggests that the standardized intervention of MBSR is safe, feasible, and can be done concurrently with pharmacological

Table 2.—Changes in Headaches in MBSR vs Control Group

Headache Characteristic	Group	Baseline‡ Median (25th%, 75th%)	Initial Follow-up§, Median (25th%, 75th%)	Final Follow-up¶, Median (25th%, 75th%)	Difference in Change Score from Baseline‡ to Initial Follow-up§, Median [95% CI]; P Value	Difference in Change Score from Baseline‡ to Final Follow-up¶, Median [95% CI]; P Value
Migraine frequency/	MBSR	3.5 (1.9,6.1)	1.0 (0, 3.8)	1.8 (0,3.7)	Change:−1.4 [−4.6, 1.8];	Change: −1.0 [−5.2, 3.3]
month†	Control	1.2 (0.7,2.2)	0 (0, 1.5)	1.9 (0,4.4)	P = .38	P = .63
Headache frequency/	MBSR	9.9 (8.4,11.8)	9.0 (5.0, 12.8)	9.0 (5.4,14.9)	Change: +1.9 [−1.5, 5.4];	Change: +2.2 [−1.1, 5.4]
month	Control	12.3 (9.5,13.5)	10.0 (5.5, 12.0)	7.7 (5.9,12.1)	P = .14	P = .22
Headache severity	MBSR	4.4 (3.8,5.3)	3.2 (2.6, 3.9)	3.3 (2.9,4.8)	Change: −1.3 [−2.3, 0.09]	Change: −1.4 [−2.7, −0.03]
(0-10 scale)	Control	4.8 (4.0,5.8)	5.2 (3.8, 5.9)	4.8 (4.5,6.5)	P = .053	P = .66
Headache duration (hours)	MBSR	5.1 (3.5,9.9)	2.9 (1.8, 5.8)	3.6 (2.2,6.4)	Change: −2.9 [−4.6, −0.02]	Change: −2.2 [−5.9, 1.4]
	Control	6.4 (5.0,9.2)	6.1 (4.2, 9.3)	6.1 (4.1,9.0)	P = .043	P = .19

†Primary outcome.
‡Baseline reflects results from the baseline 28 day period before the intervention.
§Initial follow-up reflects results from the last 28 day period of the intervention.
¶Final follow-up reflects results from the 28 day period after intervention ended.

Table 3.—Changes in Standardized Instruments in MBSR vs Control Group

Standardized Instrument	Group	Baseline[a] Median (25th%, 75th%)	Initial Follow-up[b], Median (25th%, 75th%)	Final Follow-up[c], Median (25th%, 75th%)	Difference in Change Score From Baseline[a] to Initial Follow-up[b], Median [95% CI]; *P* Value	Difference in Change Score From Baseline[a] to Final Follow-up[c], Median [95% CI]; *P* Value
Headache Impact Test-6 (HIT-6)[d]	MBSR	62.5 (55.3, 70.5)	57.5 (52.3, 62.5)	60.0 (53.8, 62.0)	Change: –4.8[e] [–11.0, –1.0]; *P* = .043	Change: –4.1[e] [–9.0, –1.0]; *P* = .022
	Control	63.0 (61.0, 70.0)	64.0 (61.0, 66.5)	63.0 (61.0, 67.5)		
Migraine Disability Assessment (MIDAS)[f]	MBSR	17.0 (0, 18.5)	4.5 (2.0, 8.8)	6.5 (1.8, 10.0)	Change: –12.6 [–22.0, –1.0]; *P* = .017	Change: –7.7 [–16.1, 0.7]; *P* = .072
	Control	11 (4.5, 16.0)	14.0 (10.0, 20.0)	11.0 (5.5, 14.5)		
Headache Management Self Efficacy[g]	MBSR	111.5 (100.8, 138.0)	124.0 (103.5, 145.3)	123.0 (104.8, 136.0)	Change: 13.2 [1.0, 30.0]; *P* = .035	Change: 13.9[–0.1, 27.8]; *P* = .060
	Control	128 (92.5, 139.5)	117 (95.5, 131.0)	116.0 (97.0, 139.5)		
Five Factor Mindfulness[h]	MBSR	142.0 (133.3, 154.3)	150 (134.8, 163.5)	157.5 (135.3, 170.8)	Change: 13.1 [3.0, 26.0]; *P* = .035	Change: 17.3 [1.3, 33.2]; *P* = .045
	Control	150.0 (125.5, 160.0)	141.0 (123.0, 154.0)	138.0, (120.0, 153.8)		
Migraine-Specific Quality of Life[i]	MBSR	47.0 (30.4, 71.1)	31.5 (25.9, 48.2)	38.1 (27.7, 54.2)	Change: –11.7 [–25.8, 2.4]; *P* = .12	Change: –7.5 [–19.5, 4.6]; *P* = .35
	Control	46.4 (39.9, 58.3)	45.2 (40.5, 53.6)	45.2 (41.1, 54.8)		
Patient Health Questionnaire-depression module[j]	MBSR	3.0 (0.8, 5.5)	2.0 (0.8, 3.0)	2.5 (0.8, 4.3)	Change: 0.6 [–3.8, 5.1]; *P* = .77	Change: 1.7 [–3.6, 7.0]; *P* = .59
	Control	4.0 (2.5, 10.0)	4.0 (3.0, 5.0)	4.0 (2.5, 5.5)		
State Trait Anxiety Inventory[k]	MBSR	71.5 (50.0, 80.5)	59.5 (50.0, 73.8)	57.0 (44.8, 74.5)	Change: –10.3 [–24.5, 3.9]; *P* = .13	Change: –10.3 [–25.1, 4.5]; *P* = .10
	Control	69.0 (53.0, 80.0)	65.0 (58.0, 85.5)	65.0 (61.5, 79.5)		
Perceived Stress Scale-10[l]	MBSR	16.5 (10.5, 21.3)	13.0 (9.8, 17.0)	12.0 (7.8, 17.5)	Change: –0.6 [–5.2, 3.9]; *P* = .87	Change: –3.3 [–9.3, 2.8]; *P* = .27
	Control	11.0 (7.5, 22.0)	11.0 (6.0, 20.0)	11.0 (8.0, 20)		

[a]Baseline reflects results from the baseline assessment.
[b]Initial follow-up reflects results from the follow-up assessment that occurred immediately following the intervention.
[c]Final follow-up reflects results from the follow-up assessment that occurred a month after intervention ended.
[d]Headache Impact Test-6 (HIT-6), Range 36-78; 60+: severe impact; 56-59: substantial impact.
[e]A change of 2.3 points on HIT-6 reflects the minimum important difference that reflects meaningful clinical change.[42]
[f]Migraine Disability Assessment (MIDAS), 1-month, range: 0-5 (minimal), 6-10 (mild), 11-20 (moderate), >21 (severe).
[g]Headache Management Self Efficacy scale, Range 0-175, higher score reflects more self-efficacy.
[h]Five Factor Mindfulness scale, Range 0-195; higher score reflects higher mindfulness.
[i]Migraine-Specific Quality of Life, Scaled 0-100; lower score reflects better QOL.
[j]Patient Health Questionnaire depression module (PHQ-9): 5 (mild), 10 (mod), 15 (mod severe), 20 (severe).
[k]State Trait Anxiety Inventory: Range 20-80; higher score reflects more anxiety.
[l]Perceived Stress Scale-10: Range 0-40; higher score reflects more perceived stress.

treatment. Although the small sample size of this pilot trial did not provide power to detect statistically significant changes in migraine frequency or severity, secondary outcomes demonstrated this intervention had a beneficial effect on headache duration, disability, self-efficacy, and mindfulness. Future studies with larger sample sizes are warranted to further evaluate this intervention for adults with migraines.

In a randomized controlled trial of yoga in patients with migraine without aura, yoga resulted in a significant decrease in headache frequency, pain index, and symptomatic medication usage compared to a self-care group.[41] However, the yoga protocol used was not specified, and participants were instructed to practice yoga only during the prodromal phase of a headache. Our study adds to the literature by reporting the use of a standardized protocol (MBSR) that has been used both clinically and in numerous research studies across many conditions.[43,44] Furthermore, the design of our study tested MBSR as a prophylactic treatment and allowed participants to continue with their customary migraine medications, increasing the external validity and generalizability of the results.

Our study has several limitations. This study has limitations of all pilot studies (eg, small sample size, etc). This small sample size limited the ability of randomization to balance groups at baseline, resulting in groups that had baseline differences in headache frequency. A longer run-in period beyond 28 days may have provided less baseline variability of migraine frequency. The inclusion criterion for migraine frequency was based on a patient's interpretation of their headaches as migraines, while results were analyzed according to diagnostic criteria for migraine. As such, our primary outcome of migraine was determined by assessing the severity and duration of each individual headache from the headache logs, which did not account for associated symptoms or treatment medications. Thus, some headaches might have been misclassified. Given that this was a pilot study, we are primarily interested in effect sizes for outcomes (rather than values of significance from *P* values) in order to evaluate for trends in this non-confirmatory trial. In addition, we clearly defined *a priori* our primary and secondary outcomes, thus we did not correct for multiple comparisons. Many of the numerous comparisons on secondary outcomes would likely be considered nonsignificant had the *P* value been adjusted on the secondary outcomes, although means, variances, and trends would not have changed. Self-reported paper headache logs were used. There was no active/sham control group; our control group continued in usual care. The intervention of MBSR is a multifaceted intervention that, in addition to teaching mindfulness, involves a weekly and daily time commitment, social and intellectual engagement, and instructor attention. Since our usual care control group did not adequately control for these factors, the changes seen in the MBSR group may be reflective of something other or more than just mindfulness meditation, such as common factors inherent to any group treatment (eg, instructor attention, group support, experience of universality, etc). Although participants were aware of receiving MBSR, we attempted to blind participants regarding treatment allocation by offering two dates for MBSR; those randomized to the later date were not told they were the control group. These limitations mean that our results must be interpreted cautiously, and their generalizability to the broader clinical population of patients with headache is uncertain. Nonetheless, our findings in this pilot trial support the potential safety, feasibility, and efficacy of a standardized mind/body intervention for migraineurs.

FUTURE DIRECTIONS

Although this pilot study suggests that the MBSR intervention may have clinically meaningful benefits, our results demonstrate the need for larger studies with an active control group, longer follow-up periods, and the collection of additional information to determine the mechanism of any effects. The biological mechanism for any potential efficacy is unknown, and this study demonstrates the need for further research in this area. MBSR may work by changing how migraineurs interpret pain, or may work through a therapeutic effect on other factors playing a role in headaches, such as improved emotion regulation, less pain catastrophizing, and increased pain acceptance. As an illustration, the MBSR instructor in this trial noted that many of

the participants commented that, "I'm still having migraines, but I don't react to them as much, and am to be able to continue in my normal routine." Headaches are often considered to be a physical disorder influenced by psychosocial and environmental stressors,[45] so mind/body treatments such as MBSR may address these other factors playing a role in headaches. However, these processes are poorly understood and need further study.

Acknowledgments: This study was supported financially by the American Headache Society Fellowship (RW and RB) and the Headache Research Fund of the John Graham Headache Center, Brigham and Women's Faulkner Hospital. We thank Dr. James C. Eisenach at Wake Forest School of Medicine for his help with this project. We thank Drs. Paul Mathew, Luzma Cardona, Paul Rizzoli, Don Levy, Rebecca Burch, Megan Tabor, William Mullally, and Thomas Walshe, III for referring patients to this study. We thank Lynn Simpson of BWH Harvard Catalyst REDCap support, Harvard Catalyst research assistant Peter Douglass, and Harvard Catalyst biostatistician Roger Davis, ScD, for their help with aspects of this study. We thank the Osher Center for Integrative Medicine at Brigham and Women's Hospital for their support of this project, specifically in providing the clinical space for patient evaluations and for the MBSR classes. We appreciate the statistical support from Carol Aschenbrenner and the editing support from Karen Klein, both at Wake Forest School of Medicine.

STATEMENT OF AUTHORSHIP

Category 1

(a) Conception and Design
Rebecca Erwin Wells, Rebecca Burch, Randall H. Paulsen, Peter Wayne, Timothy T. Houle, Elizabeth Loder

(b) Acquisition of Data
Rebecca Erwin Wells, Rebecca Burch, Randall H. Paulsen, Elizabeth Loder

(c) Analysis and Interpretation of Data
Rebecca Erwin Wells, Rebecca Burch, Randall H. Paulsen, Peter M. Wayne, Timothy T. Houle, Elizabeth Loder

Category 2

(a) Drafting the Manuscript
Rebecca Erwin Wells

(b) Revising It for Intellectual Content
Rebecca Erwin Wells, Rebecca Burch, Randall H. Paulsen, Peter Wayne, Timothy T. Houle, Elizabeth Loder

Category 3

(a) Final Approval of the Completed Manuscript
Rebecca Erwin Wells, Rebecca Burch, Randall H. Paulsen, Peter M. Wayne, Timothy T. Houle, Elizabeth Loder

REFERENCES

1. Shamliyan TA, Choi JY, Ramakrishnan R, et al. Preventive pharmacologic treatments for episodic migraine in adults. *J Gen Intern Med*. 2013;28:1225-1237.
2. Bigal M, Rapoport A, Aurora S, Sheftell F, Tepper S, Dahlof C. Satisfaction with current migraine therapy: Experience from 3 centers in US and Sweden. *Headache*. 2007;47:475-479.
3. Astin JA. Why patients use alternative medicine: Results of a national study. *JAMA*. 1998;279:1548-1553.
4. Jacobs GD. Clinical applications of the relaxation response and mind-body interventions. *J Altern Complement Med*. 2001;7(Suppl. 1):S93-S101.
5. Houle TT, Butschek RA, Turner DP, Smitherman TA, Rains JC, Penzien DB. Stress and sleep duration predict headache severity in chronic headache sufferers. *Pain*. 2012;153:2432-2440.
6. Hashizume M, Yamada U, Sato A, et al. Stress and psychological factors before a migraine attack: A time-based analysis. *Biopsychosoc Med*. 2008;2:14-20.
7. Kelman L. The triggers or precipitants of the acute migraine attack. *Cephalalgia*. 2007;27:394-402.
8. Lin KC, Huang CC, Wu CC. Association between stress at work and primary headache among nursing staff in Taiwan. *Headache*. 2007;47:576-584.
9. Wober C, Brannath W, Schmidt K, et al. Prospective analysis of factors related to migraine attacks: The PAMINA study. *Cephalalgia*. 2007;27:304-314.
10. Lipton RB, Buse DC, Hall CB, et al. Reduction in perceived stress as a migraine trigger: Testing the "let-down headache" hypothesis. *Neurology*. 2014;82:1395-1401.

11. Campbell JK, Penzien DB, Wall EM. Evidence-based guidelines for migraine headache: Behavioral and physical treatments. US Headache Consortium 2000.
12. Wells RE, Smitherman TA, Seng EK, Houle TT, Loder EW. Behavioral and mind/body interventions in headache: Unanswered questions and future research directions. *Headache*. 2014;54:1107-1113.
13. Wells RE, Bertisch SM, Buettner C, Phillips RS, McCarthy EP. Complementary and alternative medicine use among adults with migraines/severe headaches. *Headache*. 2011;51:1087-1097.
14. Eisenberg DM, Kessler RC, Van Rompay MI, et al. Perceptions about complementary therapies relative to conventional therapies among adults who use both: Results from a national survey. *Ann Intern Med*. 2001;135:344-351.
15. Kabat-Zinn J. *Full Catastrophe Living (Revised Edition): Using the Wisdom of your Body and Mind to Face Stress, Pain, and Illness*. New York, NY: Random House; 2013.
16. Holzel BK, Carmody J, Vangel M, et al. Mindfulness practice leads to increases in regional brain gray matter density. *Psychiatry Res*. 2011;191:36-43.
17. Lazar SW, Kerr CE, Wasserman RH, et al. Meditation experience is associated with increased cortical thickness. *Neuroreport*. 2005;16:1893-1897.
18. Davidson RJ, Kabat-Zinn J, Schumacher J, et al. Alterations in brain and immune function produced by mindfulness meditation. *Psychosom Med*. 2003; 65:564-570.
19. Arch JJ, Ayers CR. Which treatment worked better for whom? Moderators of group cognitive behavioral therapy vs adapted mindfulness based stress reduction for anxiety disorders. *Behav Res Ther*. 2013;51:434-442.
20. Holzel BK, Hoge EA, Greve DN, et al. Neural mechanisms of symptom improvements in generalized anxiety disorder following mindfulness training. *Neuroimage Clin*. 2013;2:448-458.
21. Jain S, Shapiro SL, Swanick S, et al. A randomized controlled trial of mindfulness meditation vs relaxation training: Effects on distress, positive states of mind, rumination, and distraction. *Ann Behav Med*. 2007;33:11-21.
22. Zeidan F, Gordon NS, Merchant J, Goolkasian P. The effects of brief mindfulness meditation training on experimentally induced pain. *J Pain*. 2010;11:199-209.
23. Kabat-Zinn J. An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: Theoretical considerations and preliminary results. *Gen Hosp Psychiatry*. 1982;4:33-47.
24. Reiner K, Tibi L, Lipsitz JD. Do mindfulness-based interventions reduce pain intensity? A critical review of the literature. *Pain Med*. 2013;14:230-242.
25. Rosenzweig S, Greeson JM, Reibel DK, Green JS, Jasser SA, Beasley D. Mindfulness-based stress reduction for chronic pain conditions: Variation in treatment outcomes and role of home meditation practice. *J Psychosom Res*. 2010;68:29-36.
26. Grant JA, Courtemanche J, Duerden EG, Duncan GH, Rainville P. Cortical thickness and pain sensitivity in zen meditators. *Emotion (Washington, DC)*. 2010;10:43-53.
27. Zeidan F, Martucci KT, Kraft RA, Gordon NS, McHaffie JG, Coghill RC. Brain mechanisms supporting the modulation of pain by mindfulness meditation. *J Neurosci*. 2011;31:5540-5548.
28. Wachholtz AB, Pargament KI. Migraines and meditation: Does spirituality matter? *J Behav Med*. 2008;31:351-366.
29. Tfelt-Hansen P, Pascual J, Ramadan N, et al. Guidelines for controlled trials of drugs in migraine: Third edition. A guide for investigators. *Cephalalgia*. 2012;32:6-38.
30. Penzien DB, Andrasik F, Freidenberg BM, et al. Guidelines for trials of behavioral treatments for recurrent headache, first edition: American Headache Society Behavioral Clinical Trials Workgroup. *Headache*. 2005;45(Suppl. 2):S110-S132.
31. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia*. 2004;24(Suppl. 1):9-160.
32. Kosinski M, Bayliss MS, Bjorner JB, et al. A six-item short-form survey for measuring headache impact: The HIT-6. *Qual Life Res*. 2003;12:963-974.
33. Stewart WF, Lipton RB, Dowson AJ, Sawyer J. Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability. *Neurology*. 2001;56:S20-S28.
34. Martin BC, Pathak DS, Sharfman MI, et al. Validity and reliability of the migraine-specific quality of life questionnaire (MSQ Version 2.1). *Headache*. 2000; 40:204-215.

35. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16:606-613.
36. Spielberger C, Gorsuch R, Lushene R. *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychology Press; 1970.
37. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav*. 1983;24:385-396.
38. Baer RA, Smith GT, Lykins E, et al. Construct validity of the five facet mindfulness questionnaire in meditating and nonmeditating samples. *Assessment*. 2008;15:329-342.
39. French DJ, Holroyd KA, Pinell C, Malinoski PT, O'Donnell F, Hill KR. Perceived self-efficacy and headache-related disability. *Headache*. 2000;40:647-656.
40. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research Electronic Data Capture (REDCap) – A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42:377-381.
41. John PJ, Sharma N, Sharma CM, Kankane A. Effectiveness of yoga therapy in the treatment of migraine without aura: A randomized controlled trial. *Headache*. 2007;47:654-661.
42. Coeytaux RR, Kaufman JS, Chao R, Mann JD, Devellis RF. Four methods of estimating the minimal important difference score were compared to establish a clinically significant change in Headache Impact Test. *J Clin Epidemiol*. 2006;59:374-380.
43. Barrows KA, Jacobs BP. Mind-body medicine. An introduction and review of the literature. *Med Clin North Am*. 2002;86:11-31.
44. Praissman S. Mindfulness-based stress reduction: A literature review and clinician's guide. *J Am Acad Nurse Pract*. 2008;20:212-216.
45. Nash JM, Thebarge RW. Understanding psychological stress, its biological processes, and impact on primary headache. *Headache*. 2006;46:1377-1386.