Randomized Controlled Trial of Mindfulness-Based Stress Reduction for Prehypertension

Joel W. Hughes, PhD, David M. Fresco, PhD, Rodney Myerscough, PhD, Manfred H. M. van Dulmen, PhD, Linda E. Carlson, PhD, and Richard Josephson, MS, MD

Objective: Mindfulness-based stress reduction (MBSR) is an increasingly popular practice demonstrated to alleviate stress and treat certain health conditions. MBSR may reduce elevated blood pressure (BP). Treatment guidelines recommend life-style modifications for BP in the prehypertensive range (systolic BP [SBP] 120–139 mm Hg or diastolic BP [DBP] 80–89 mm Hg), followed by antihypertensives if BP reaches hypertensive levels. MBSR has not been thoroughly evaluated as a treatment of prehypertension. A randomized clinical trial of MBSR for high BP was conducted to determine whether BP reductions associated with MBSR exceed those observed for an active control condition consisting of progressive muscle relaxation (PMR) training. **Methods:** Fifty-six men (43%) and women (57%) averaging (standard deviation) 50.3 (6.5) years of age (91% white) with unmedicated BP in the prehypertensive range were randomized to 8 weeks of MBSR or PMR delivered in a group format. Treatment sessions were administered by one treatment provider and lasted approximately 2.5 hours each week. Clinic BP was the primary outcome measure. Ambulatory BP was a secondary outcome measure. **Results:** Analyses were based on intent to treat. Patients randomized to MBSR exhibited a 4.8-mm Hg reduction in clinic SBP, which was larger than the 0.7-mm Hg reduction observed for PMR ($p = .016$). Those randomized to MBSR exhibited a 1.9-mm Hg reduction in DBP compared with a 1.2-mm Hg increase for PMR ($p = .008$). MBSR did not result in larger decreases in ambulatory BP than in PMR. **Conclusions:** MBSR resulted in a reduction in clinic SBP and DBP compared with PMR. **Trial Registration:** ClinicalTrials.gov identifier: NCT00440596. **Key words:** mindfulness, meditation, prehypertension, blood pressure, clinical trial, MBSR.

AHA = American Heart Association; **AHRQ** = Agency for Healthcare and Research Quality; **BP** = blood pressure; **DBP** = diastolic blood pressure; **MBSR** = mindfulness-based stress reduction; **PMR** = progressive muscle relaxation training; **SBP** = systolic blood pressure; **TM** = transcendental meditation.

INTRODUCTION

Nearly 60 million adults in the United States have high blood pressure (BP) in the prehypertensive range (systolic BP [SBP] of 120–139 mm Hg or diastolic BP [DBP] of 80–89 mm Hg) (1,2). Current treatment guidelines recommend health-promoting life-style modifications, including exercise, weight loss, and dietary changes (e.g., adopting the Dietary Approaches to Stop Hypertension diet) for individuals with BP in the prehypertensive range. Antihypertensive medication is not indicated but should be initiated if life-style changes fail to prevent BP from reaching hypertensive levels (2).

Mindfulness-based stress reduction (MBSR) is an increasingly popular practice that has been purported to alleviate stress, treat depression and anxiety, and treat certain health conditions. MBSR incorporates meditation and stress management into a structured stress management program. Meditation treatments such as MBSR are not substitutes for health behavior changes but have been evaluated for their potential to lower BP. MBSR has been alleged to reduce BP, although there has been only one published controlled trial of a similar treatment, mindfulness meditation, on BP (3). In this study, 73 normotensive middle-school students were randomly assigned to 10 minutes of daily meditation for 3 months or to a health education control condition. A larger reduction in resting SBP was associated with the meditation intervention, as well as larger reductions in ambulatory BP during certain periods (e.g., SBP and DBP after school). Although these findings are encouraging, applying the data from normotensive children to the adult population with elevated BP is speculative. A recent American Heart Association (AHA) Scientific Statement (4) reviewed this literature and acknowledged that there are few trials of meditation techniques (other than transcendental meditation [TM]; see below) for BP reduction.

Other stress management therapies and meditation practices have shown some promise in reducing elevated BP (5–10). For example, two meta-analyses of stress management treatments for hypertension concluded that multicomponent stress management therapies can be effective in reducing BP and that single-component stress management therapies (e.g., relaxation alone) are less effective (11,12). However, a later meta-analysis reported that stress management training was not very effective in lowering BP (13).

Relaxation therapies such as progressive muscle relaxation (PMR) have not consistently lowered high BP. The Hypertension Intervention Pooling Project integrated data from 12 randomized controlled trials and concluded that relaxation provided a small treatment effect for DBP and no treatment effect for SBP among unmedicated patients with hypertension (14). Despite good patient acceptance of PMR, it is consequently not currently considered an effective treatment of high BP. It was thus chosen as an active control condition because PMR can seem to be a credible treatment and can be matched with the MBSR condition for therapist contact and homework.

TM has been the most extensively studied meditation therapy for high BP. A report commissioned by the Agency for Healthcare and Research Quality (AHRQ) concluded that TM, Qi Gong, and Zen Buddhist meditation reduced BP (15). Although not without

From the Kent State University (J.W.H., D.M.F., M.H.M.v.D), Kent, Ohio; Summa Health System (J.W.H., R.M.), Akron, Ohio; University of Calgary (L.E.C.), Calgary, Alberta, Canada; Harrington Heart & Vascular Institute (R.J.), University Hospitals Case Medical Center, Cleveland, Ohio; and Department of Medicine (R.J.), Case Western Reserve University School of Medicine, Cleveland, Ohio.

Address correspondence and reprint requests to Joel W. Hughes, PhD, Department of Psychology, PO Box 5190, Kent, OH 44242. E-mail: jhughes1@kent.edu

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controversy, the AHRQ report also concluded that the studies often had poor methodological quality and that the effect of TM on BP was small when compared with a health education control condition (e.g., 1.1 mm Hg SBP). A subsequent meta-analysis, which included additional studies, concluded that TM reduced SBP by 5.0 mm Hg and DBP by 2.8 mm Hg compared with control conditions (13). The recent AHA statement concluded that TM produces modest reductions in BP (4).

Although both MBSR and TM can be regarded as meditation therapies, there are obvious differences in how they are taught and practiced. For example, TM consists solely of meditation, whereas MBSR includes three skills: meditation, body scan, and nonstrenuous yoga. TM is taught via personal instruction and practice, whereas MBSR is a structured 8-week group stress management program. Thus, they are not necessarily equivalent treatments merely by virtue of involving meditation. There are few trials comparing TM with other meditation interventions (4). The relative effectiveness of existing meditation methods for reducing BP is not known, although there is less evidence that meditation techniques besides TM are effective for lowering BP. It remains an empirical question and one beyond the scope of this study to address whether MBSR and TM have differing effects on BP.

Collectively, the widespread use of MBSR, the trial showing some BP reduction in adolescents (3), the AHRQ report (15), and the AHA statement (4) suggest the need for randomized trials of MBSR for BP reduction. When combined with life-style modification advice, MBSR may be an appropriate complementary treatment of prehypertension or adjunct to pharmacotherapy for hypertension. There are several potential mechanisms for how MBSR might lower BP. Meditation may affect the sympathetic nervous system, effectively reducing cardiac output, increased heart rate, and increased norepinephrine levels observed in the early stages of elevated BP (16,17). MBSR may improve subjective feelings of stress, reduce negative affect, or improve coping with negative affect. It is also possible that mindfulness training can improve adherence to life-style modification advice. Prehypertension was targeted not only because pharmacological treatments are necessary for BP above the prehypertensive range but also because the magnitude of BP lowering obtained with MBSR may be adequate for patients who desire to avoid or delay antihypertensive medication.

This study examined the effects of MBSR on high BP using a small-scale randomized controlled design. A total of 56 patients with unmedicated elevated BP in the prehypertensive range (SBP 120–139 mm Hg or DBP 80–89 mm Hg) were randomized to MBSR or an active control condition, PMR. All patients received life-style modification advice in keeping with current guidelines for the treatment of prehypertension. It was hypothesized that MBSR would result in greater BP reductions than PMR.

METHODS

Study Participants

Healthy individuals aged 30 to 60 years with unmedicated BP in the prehypertensive range (SBP 120–39 mm Hg or DBP 80–89 mm Hg) were sought for this trial. Participants could not be taking antihypertensive medication, could not be experienced with meditation practices, could not be current smokers, and could not report any disease (e.g., myocardial infarction, heart failure, chronic kidney disease, and diabetes) that would mandate treatment with drugs that could substantially affect BP.

Enrollment began in January 2006. Participants were enrolled in seven cohorts ranging in size from 3 to 11. MBSR and PMR treatment groups included some nonprotocol patients to increase the group size so that a high-quality group treatment experience could be provided to every patient enrolled in the trial. That is, some individuals who were not enrolled in the trial participated in the treatment groups. The circumstances of their involvement were that they had responded to the advertisements but were not eligible for enrollment. Reasons for ineligibility included falling outside the age range, taking antihypertensive medication, previous experience with meditation, being a smoker, or not being prehypertensive. When patients were ineligible but remained interested in participating in treatment, they were allowed to opt to participate in one of the treatments. There were 13 nonprotocol participants in each group. No baseline BP data were collected from nonprotocol patients, and their presence was designed to maintain an adequate group size. The CONSORT chart in Figure 1 presents the flow of patients through the trial. Patient accrual from recruiting efforts and eligibility screening is presented in Figure 2.

Procedure

The institutional review boards of Kent State University and SUMMA Health System reviewed and approved the study procedures. Prospective participants completed a telephone screening that included questions about their medical history. If there were any concerns about whether a patient was "healthy" for purposes of eligibility, the case was reviewed by the study physician (R.A.J.). Those who seemed eligible then scheduled an initial BP screening, which consisted of three separate BP readings separated by 5 minutes after 10 minutes of quiet rest (additional details in the measures below). This initial screening was followed by a second screening approximately 1 week later that followed the same procedures, and participants were scheduled for a pretreatment assessment approximately 1 week later. When they returned, a third screening that used the same procedures was conducted. If BP remained in the prehypertensive range, the patient was enrolled and the pretreatment assessment was completed at the same visit. Thus, BP had to remain in the prehypertension range on three separate determinations over a 3-week period for patients to be eligible. If BP was not in the prehypertensive range at any of the three screenings, the patient was no longer eligible and was not enrolled. Participants who were eligible and who consented to participate in the study were enrolled in the study and completed a pretest assessment including clinic and ambulatory BP. After the pretest assessment, patients were randomized to eight weekly sessions of MBSR or PMR using an order of assignment generated by random number, stratified for sex and ethnicity. After the eight sessions, patients returned for reassessment of both clinic and ambulatory BP, as described below in the measurement procedures.

Blinding

Concealment of treatment allocation was maintained by having different study personnel perform recruitment and treatment assignment functions, so the investigators responsible for recruiting and assessments were not aware of random assignment. The adequacy of this blinding procedure was assessed using a questionnaire asking the primary research assistants to predict group membership. No patient volunteered their treatment assignment to the research assistants, and research assistants were unable to predict group membership (Cohen $\kappa = 0.135$, $p = .37$), confirming adequacy of blinding. Furthermore, investigators responsible for random assignment and the delivery of the treatments were not aware of assessment results (e.g., BP values) until after the study was complete. The blind was not broken until after the final assessment.

Mindfulness-Based Stress Reduction

The MBSR program consisted of eight group sessions, each 2.5 hours long, and delivered on consecutive weeks. MBSR included instruction and

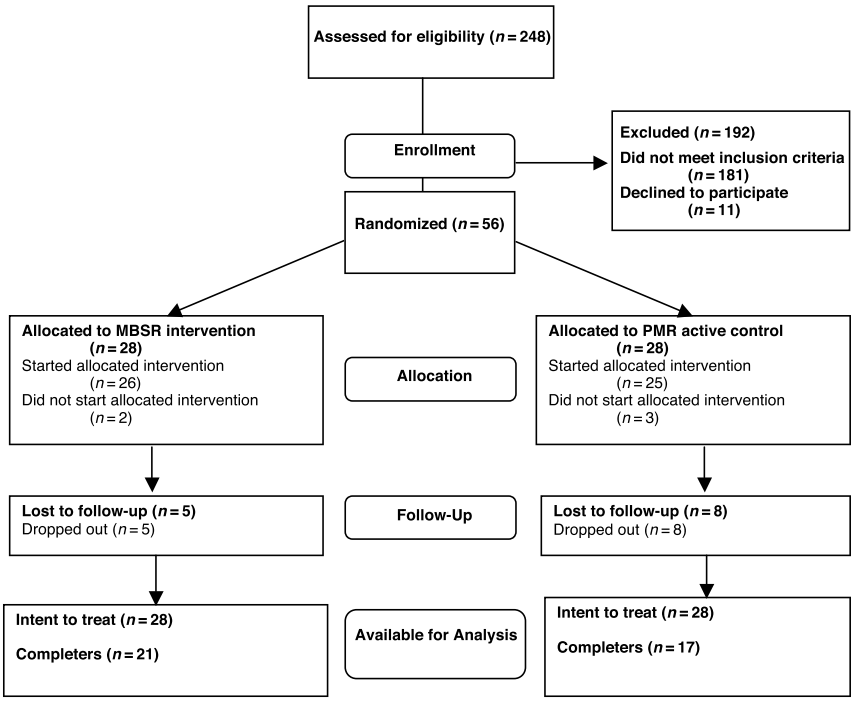

Figure 1. CONSORT chart. PMR = progressive muscle relaxation. MBSR = mindfulness-based stress reduction.

practice in mindfulness meditation skills along with discussion of stress, coping, and homework assignments. The MBSR therapist participated in the mindfulness exercises with group members during the weekly sessions, and group members were instructed to practice these mindfulness exercises outside group meetings for at least 45 minutes per day, 6 days per week. Homework was collected by the study therapist and consisted of weekly logs in the participant folder with spaces for each day of the week for participants to record the duration of homework completed.

Group members were taught three main varieties of mindfulness skills: the body scan exercise, sitting meditation, and yoga exercises. The body scan exercise entails lying down with one's eyes closed and deliberately focusing one's attention on various parts of the body, with the goal of noticing nuances of sensations going on within the body. In sitting meditation, participants sit in a relaxed and wakeful posture with eyes closed and deliberately bring their attention to the sensations of breathing. Finally, group members learned a series of physically nonstrenuous yoga exercises designed to bring mindful attention to bodily sensations during gentle movements and stretching. The daily homework exercises consisted of repeating body scan work, sitting meditation, and yoga exercises at home to provide practice and generalization of the skills. Group members were provided audiotapes or CDs with guided MBSR exercises to assist their homework. In addition, group members were encouraged to bring mindful attention to daily activities such as walking, standing, and eating.

PMR Training

The PMR treatment was based on a manual created for this study, adapted from other sources (18). PMR consisted of eight group sessions lasting 2.5 hours each delivered on consecutive weeks. PMR patients received instruction and practice in PMR skills, which involved learning to achieve a state of relaxation by alternately tensing and relaxing various muscle groups, along with homework assignments. The PMR therapist participated in the exercises with group members during the weekly sessions. Sessions progressed from 16-muscle group relaxation to 7 muscle groups, 4 muscle groups, and finally relaxation by recall. Relaxation by recall was intended to allow participants learning PMR to apply relaxation skills during their daily lives, and there was an explicit instruction on generalizing the relaxation response to stressful situations. Group members were instructed to practice these exercises outside group meetings for at least 45 minutes per day, 6 days per week. Homework was collected by the study therapist and consisted of weekly logs in the participant folder with spaces for each day of the week for participants to record the duration of homework completed. They were provided with audio recordings of to assist their home PMR exercises.

Measures

Clinic BP

All clinic BP assessments were completed in a quiet, climate-controlled room. All measures were completed in the same room and in accordance with AHA guidelines for taking BP (19). Participants were asked to refrain from consuming caffeine for at least 60 minutes before their appointment time. Patients had their BP assessed on their nondominant arm while sitting in a chair with their feet flat on the floor and their arm supported at heart level. Patients rested quietly for 10 minutes, and then had 3 seated BP readings taken, each 5 minutes apart using an automated oscillometric BP device (Accutor Plus Oscillometric BP Monitor; Datascope Corp, Mahwah, NH). An

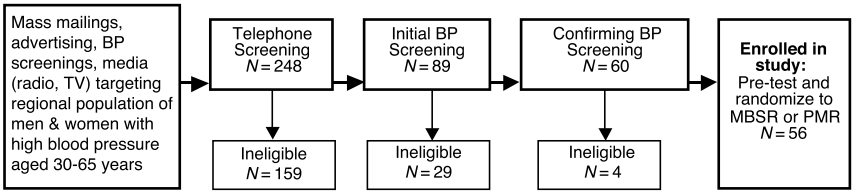

Figure 2. Patient accrual from recruiting efforts and eligibility screening. PMR = progressive muscle relaxation. MBSR = mindfulness-based stress reduction; BP = blood pressure.

automated oscillometric BP device was chosen in favor of manual sphygmomanometer for several reasons. First, mercury has been phased out (20). Second, the Accutor Plus performed well in a validation study (21). Specifically, the Datascope Accutor Plus received a grade of A (British Society of Hypertension) for both SBP and DBP and met the Association for the Advancement of Medical Instrumentation guidelines (the mean difference between the BP device and the mercury standard was ≤5 mm Hg). Finally, an automated device eliminated any potential experimenter bias. Clinic BP assessment procedures were the same at the BP screening, pretest, and posttest assessment visits. Pretest and posttest clinic BPs are based on one visit and are not aggregated across several visits.

Ambulatory BP

After the laboratory assessments, participants completed 24-hour ambulatory BP monitoring. Participants were instrumented with an Oscar (Suntech, Raleigh, NC) oscillometric BP monitor at the time of their assessment, and the monitor was programmed to take three BP measurements each hour between the hours of 6 AM to 11 PM and two BP measurements were taken each hour between the hours of 11 PM to 6 AM. Participants were instructed to lower their arms to their sides as soon as they sensed the cuff inflating and to keep it relaxed and still until a few seconds after the deflation had finished because of possible movement artifact. Artifactual values were deleted after inspection by an experienced examiner blind to patient condition using the modified Casadei criteria (22). Participants wore the ambulatory BP device for a continuous 24-hour period. Daytime and nighttime BP values were defined by patient diary entries indicating sleep and waking times.

Data Analysis

The primary outcome measures were clinic SBP and DBP, and secondary outcome variables were ambulatory SBP and DBP. Clinic BP for analyses was derived by taking the average of the three BP readings from the final pretest visit and the three readings from the posttest assessment visit. Ambulatory SBP and DBP were derived by computing the mean of all valid readings obtained during waking hours and nighttime sleep. Hierarchical linear regression analyses using preintervention clinic BP levels as control variables were conducted separately for change in clinic SBP and DBP. A variable representing treatment condition was regressed on change in clinic BP score from pretest to posttest while controlling for pretest clinic BP levels in separate analyses. The same analytic strategy was used for ambulatory BP. Analyses were based on intent to treat, with baseline values carried forward when posttreatment values were missing, although analyses were repeated with completers to check for consistency. That is, discrepant results for completers could reveal a bias in the intent-to-treat analyses given the higher dropout among patients randomized to PMR. Furthermore, although evaluating group effects on change scores is equivalent to the interaction term from a 2 (group; MBSR versus PMR) × 2 (time; pretreatment versus posttreatment) factorial design, for completeness these interaction terms were reported for clinic BP and mean values of posttreatment BP. All analyses were conducted at the .05 level of significance and were not corrected for multiple comparisons. Data were analyzed using IBM SPSS Version 20 (Chicago, IL) using linear regression procedures with forced entry of control variables. Means reported in the table are unadjusted means from simple descriptive statistics.

RESULTS

Description of the Sample

Participants included 56 men (24) and women (32) with a mean (standard deviation [SD]) age of 50.3 (6.5) years (91% white) with unmedicated BP in the prehypertensive range. Demographic and medical characteristics (Table 1) were similar between groups. Patients were generally overweight, with a mean (SD) body mass index of 30.0 (5.9) kg/m^2. Clinic BPs were similar in both the MBSR and PMR groups at baseline. However, ambulatory BPs were slightly lower among those assigned to the MBSR group, as shown in Table 1.

Treatment Adherence and Fidelity

Equal numbers of patients were randomized to the MBSR and PMR conditions (Fig. 1). Two patients did not begin the MBSR intervention, and three did not start the PMR intervention because of unanticipated conflicts with the scheduled group treatment times. Five participants did not complete the MBSR

TABLE 1. Clinical and Demographic Characteristics of Study Sample

	All Patients	MBSR	PMR	p^a
n^b	56	28	28	
Age, y	50.3 (6.5)	51.2 (5.8)	49.5 (7.2)	.338
Sex (% female)	57%	61%	54%	.589
Race (% white)	91%	89%	93%	.639
Body mass index, kg/m^2	30 (5.9)	30 (6.5)	30 (5.2)	.964
Employed	66%	57%	75%	.317
Education	15.7 (2.6)	16.0 (2.7)	15.4 (2.5)	.407
Blood pressure, mm Hg				
Systolic				
Clinic	129.5 (6.3)	130.2 (6.3)	128.8 (6.3)	.428
Daytime	137.1 (10.8)	134.4 (9.3)	139.9 (11.6)	.055
Nighttime	117.3 (10.8)	113.8 (8.9)	120.6 (11.6)	.019
Diastolic				
Clinic	77.8 (5.5)	77.3 (4.8)	78.3 (6.1)	.484
Daytime	82.9 (7.5)	79.9 (5.6)	85.7 (8.1)	.033
Nighttime	67.3 (7.8)	65.3 (6.3)	69.3 (8.7)	.061

MBSR = mindfulness-based stress reduction; PMR = progressive muscle relaxation training.
Data are shown as mean (standard deviation), unless otherwise indicated.
[a] Group difference at baseline using a *t* test for independent groups for continuous variables and the χ^2 test for dichotomous variables (e.g., employment and race).
[b] For ambulatory BP, $n = 27$ in the MBSR group.

intervention, and eight did not complete the PMR condition. One additional individual in the MBSR group did not have ambulatory BP data available because of equipment failure. In the MBSR group, attendance at treatment sessions was 89%, and in the PMR condition, attendance was 90%. Home practice logs were submitted 74% of the time by participants in the PMR groups and 74% of the time by participants in the MBSR groups.

Participants were treated by a licensed clinical psychologist (R.M.) with a longtime personal meditation practice who also received formal training in MBSR by Jon Kabat-Zinn and Saki Santorelli. Treatment sessions were video recorded, and a clinical trial researcher with extensive familiarity with MBSR (L.C.) evaluated approximately half (45/112) for treatment fidelity and adherence to the treatment manuals. Using a scale of 1 to 5, with higher ratings indicating greater adherence, MBSR sessions received an average rating of 4.4 (range, 4.2–4.7); PMR sessions received an average rating of 4.3 (range, 4.1 to 4.7).

Clinic BP

MBSR resulted in substantial and statistically significant reductions in the primary outcomes of clinic SBP and DBP (see Fig. 3). Hierarchical multiple linear regression analyses were performed to evaluate the effect of the two treatments on changes in clinic SBP and DBP. The first step regressed change in BP on pretest BP. For clinic SBP, the equation containing these variables accounted for less than 2% of the variability in SBP change ($F(1,54) = 0.96$, $p = .331$). Adding treatment condition to the model explained an additional 10.3% of the variance in change in SBP ($F(1,53) = 6.23$, $p = .016$). Thus, the 4.9-mm Hg reduction in clinic SBP observed in the MBSR treatment condition exceeded the 0.7-mm Hg reduction observed in the PMR group. The interaction term from the group × time ANOVA was similar ($F(1,54) = 6.77$, $p = .012$), although simple main effects revealed that posttreatment SBP for the MBSR group (mean [M; SD] = 128.1 [9.1]) was not lower than SBP for the PMR group (M [SD] = 125.3 [7.4], $p = .208$). When regression analyses were repeated with completers, treatment condition accounted for 12.4% of the variability in SBP change after controlling for pretreatment clinic SBP ($F(1,35) = 5.2$, $p = .029$). The 6.5-mm Hg reduction in clinic SBP observed in the MBSR treatment condition exceeded the 1.1-mm Hg reduction observed in the PMR group.

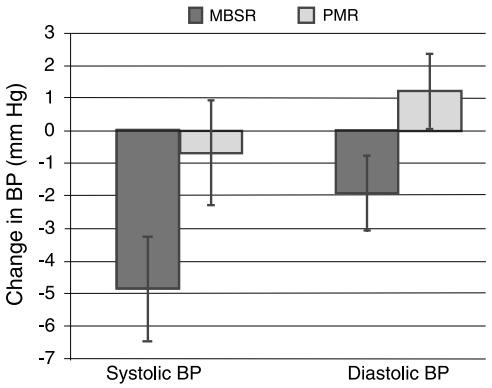

Figure 3. Change in clinic blood pressure by treatment (intent-to-treat). Mean change in clinic SBP and DBP from pretreatment to posttreatment. Error bars represent the standard error of the mean. PMR = progressive muscle relaxation. MBSR = mindfulness-based stress reduction; BP = blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure.

For clinic DBP, pretest values and sex accounted for less than 1% of the variance in change in DBP ($F(1,54) = 0.15$, $p = .702$). Adding treatment condition to the model explained an additional 12.5% of the variance in change in DBP ($F(1,53) = 7.58$, $p = .008$). Thus, the 1.9-mm Hg reduction in clinic DBP observed in the MBSR treatment condition was a larger reduction in DBP than the 1.2-mm Hg increase observed in the PMR group. The interaction term from the group × time ANOVA was similar ($F(1,54) = 7.38$, $p = .009$), and simple main-effects revealed that posttreatment DBP for the MBSR group (M [SD] = 75.4 [5.1]) was lower than SBP for the PMR group (M [SD] = 79.4 [8.0], $p = .023$). When regression analyses were repeated with completers, treatment condition accounted for 18.5% of the variability in DBP change after controlling for pretreatment clinic DBP ($F(1,35) = 8.0$, $p = .008$). The 2.6-mm Hg reduction in clinic DBP observed in the MBSR treatment condition exceeded the 2.0-mm Hg increase observed in the PMR group.

The consistency of the effects was examined for exploratory purposes. In the MBSR group, 18 (86%) of 21 completers experienced at least a 1-mm Hg reduction in SBP compared with 7 (41%) of 17 in the PMR group. For DBP, 13 (61%) of 21 completers exhibited at least a 1-mm Hg reduction in BP compared with 7 (41%) of 17 in the PMR group.

Ambulatory BP

Hierarchical multiple linear regression analyses were performed to evaluate the effect of the two treatments on changes in daytime and sleeping ambulatory SBP and DBP, which were secondary outcomes. The first step regressed change in BP on pretest BP. The second step added treatment condition. For change in daytime ambulatory SBP, pretest SBP accounted for 12.2% of the variability in SBP change ($F(1,53) = 7.33$, $p = .009$). Adding treatment condition to the model did not explain additional variance in change in daytime ambulatory SBP ($\Delta R^2 = 0.03$, $F(1,52) = 2.06$, $p = .157$). The 3.1-mm Hg drop in daytime ambulatory SBP in the MBSR treatment condition was not appreciably larger than the 1.5-mm Hg decrease observed for the PMR group. For sleeping ambulatory SBP, pretest ambulatory BP explained 7.5% of the variance in change in SBP ($F(1,53) = 4.31$, $p = .043$). Adding the treatment group to the model did not explain additional variance in sleeping ambulatory SBP ($\Delta R^2 = 0.04$, $F(1,51) = 2.38$, $p = .129$). The 2.3-mm Hg decrease in sleeping ambulatory SBP observed in the MBSR treatment group did not exceed the 0.8-mm Hg decrease in the PMR group. For ambulatory SBP, completer analyses were not appreciably different from intent-to-treat analyses.

For change in daytime ambulatory DBP, pretest BP accounted for 1% of the variability in DBP change ($F(1,53) = 0.52$, $p = .476$). No additional variance was explained by adding treatment condition to the model ($\Delta R^2 < 0.001$, $F(1,52) = 0.07$,

$p = .795$). The 1.4-mm Hg drop in daytime ambulatory DBP in the MBSR treatment condition was not smaller than the 2.2-mm Hg decrease observed for participants randomized to PMR. For sleeping ambulatory DBP, pretest BP explained 2% of the variance in change in DBP ($F(1,53) = 1.16$, $p = .286$). Adding the treatment group explain no additional variance in sleeping ambulatory DSBP ($\Delta R^2 = 0.03$, $F(1,52) = 1.55$, $p = .218$). The 1.7-mm Hg decrease in sleeping ambulatory DBP among patients treated with MBSR was not larger than the 0.6-mm Hg decrease observed in the PMR group. For ambulatory DBP, completer analyses were not appreciably different from intent-to-treat analyses.

DISCUSSION

MBSR is a popular practice used by the public and is claimed to treat stress-related high BP. The primary finding from this randomized trial is that MBSR is effective in lowering elevated BP compared with an active control, and results show decreases in clinic SBP and DBP in prehypertensive individuals. The magnitude of reduction in BP was similar to those reported in a recent meta-analysis of TM (13) and similar to the difference in BP reductions between the active and the control treatment groups in the PREMIER trial of comprehensive life-style modification for high BP (23). BP changes of this magnitude have been shown to be of public health importance and, if sustained, may lead to reductions in myocardial infarction, stroke, and cardiovascular death (24). Exploratory examinations of the consistency of BP changes suggested that a few outliers did not account for clinic BP differences between groups. However, effects were limited to clinic BP and were not found for ambulatory BP. Interestingly, the Hypertension Analysis of stress Reduction using Mindfulness meditatiON and Yoga trial also reported null results for ambulatory BP (25), so our results are consistent with their findings. Whether null results for ambulatory BP were caused by white-coat hypertension (26), the contribution of behavioral factors to ambulatory BP (e.g., activity patterns) or other influences cannot be derived from this study. One intriguing possibility is that patients were more able to apply the principles learned in the intervention during seated resting BP assessments in a controlled room than they were when going about their daily lives. Although patients were not coached to meditate or relax during the assessments, they were instructed to apply the principles of relaxation and mindfulness meditation broadly to their lives. It would also have been possible for patients to use relaxation by recall and mindfulness meditation during the waking ambulatory BP measurements, so this may not fully explain why the results for clinic and ambulatory BP were discrepant.

Our results provide evidence that MBSR, when added to life-style modification advice, may be an appropriate complementary treatment of BP in the prehypertensive range. Given that patients who desire to avoid or delay antihypertensive medication use may prefer controlling elevated BP with nonpharmacological interventions such as life-style changes and stress-management approaches, MBSR was shown to hold promise in this regard. When used with otherwise healthy patients with BP in the prehypertensive range, using MBSR does not contradict treatment recommendations and could prove useful for this highly prevalent condition that is often poorly controlled. Patients with hypertension often require multiple pharmacological agents and even then frequently do not achieve goal BP levels (2). MBSR could potentially be an important nonpharmacological adjunctive treatment for these individuals as well, decreasing polypharmacy and/or improving BP control; these hypotheses require additional study.

Strengths and Limitations

Despite much talk in the lay press, prospective and randomized controlled trials of complementary medicine techniques are scarce. To our knowledge, this and the Hypertension Analysis of stress Reduction using Mindfulness meditatiON and Yoga trial (25) were the first randomized controlled trials of MBSR in individuals with elevated BP. This trial used an active (versus wait list) control, which provided a stringent test of the MBSR intervention. A recent systematic review of clinical trials of mindfulness-based treatments (27) argued that the lack of an active control group is a limitation of much MBSR research suggesting that evaluations of MBSR use an active treatment as a comparison condition. Since the completion of this study, an active control intervention has been created and validated for comparison with MBSR (28). For this trial, the PMR control intervention was chosen because, although it is not considered an effective treatment of high BP, it was a very credible placebo. That is, to the patients, PMR seemed to be a bona fide treatment of high BP. Furthermore, PMR could be matched with the MBSR treatment for therapist contact hours and homework. Both MBSR and PMR were well tolerated by patients. Treatment fidelity and self-reported compliance were high. Thus, PMR and MBSR were procedurally similar on a superficial level, although there are differences in the treatments. PMR is designed to achieve a relaxation response, which is a state that may not persist beyond the relaxation exercises. PMR does not specifically address adopting a way of life that may improve adherence to health behavior changes, whereas MBSR does (e.g., mindful eating). These speculations cannot be confirmed in the current study, but future research may be able to identify the mechanistic differences that affect BP.

Limitations of this intervention include the modest sample size, high dropout rates, questionable validity of the homework measures, the inclusion of nonprotocol participants, and the current lack of long-term follow-up. With respect to the dropout rates, 75% of the patients in the MBSR condition finished the posttreatment assessment, which is at the low end of reported completion rates (although a couple of studies with 40%+ dropout have been reported) (27). Future studies may be more feasible if conducted at centers with more clinical capacity, as scheduling treatment groups at mutually convenient times was a challenge. With respect to the homework measures, not all participants consistently remembered to turn in their homework, and self-report logs are not necessarily valid. Future studies may benefit from including experience sampling methodologies that

measure homework completion on an ongoing basis. With respect to nonprotocol participants, a desire to have larger and ecologically valid treatment groups was balanced against the possibility that including participants who were not enrolled or randomized and who did not complete the study BP assessments may have changed the character of the groups in some way. Finally, the lack of a follow-up precludes any conclusions about sustained effects of MBSR on BP. Future trials should investigate more long-term effects of MBSR on BP.

No conclusions about the ability of meditation to prevent hypertension can be drawn from this design, as firm conclusion would require prevention trials with incident hypertension as the primary outcome. In addition, the mechanism whereby MBSR reduced BP was not determined. MBSR may reduce BP by reducing stress, altering sympathetic nervous system activity, altering hemodynamic regulation of BP, or improving compliance with life-style modification advice. For example, to the extent that patients cultivated a mindful approach to daily living, they may have been more able to monitor and control their food and alcohol intake and their exercise habits. This is an important possibility, and evidence that meditation reduces BP should not be taken as a recommendation to neglect needed health behavior changes (e.g., exercise, diet). However, these limitations were consistent with the pilot-and-feasibility nature of the study, which should be followed by larger trials addressing these concerns.

The MBSR program was initially developed and applied in behavioral medicine settings as an adjunctive therapy for patients with a wide range of chronic pain and stress-related disorders (29). Our patients were broadly representative of individuals in the community and recruited via a variety of methods. Thus, they were not recruited from a hospital setting and were enrolled based on being otherwise "healthy" (i.e., by self-report) adults with unmedicated prehypertension. An attempt was made to implement MBSR as it was designed, with the exception of the all-day (8-hour) intensive mindfulness retreat that typically occurs in the sixth week of treatment. The 2.5-hour weekly group sessions included instruction and practice in mindfulness meditation skills along with discussion of stress, coping, and homework assignments. Whether this duration of treatment is necessary for BP reduction is not known, and for comparison, the trial of meditation conducted with adolescents required only 10 minutes of daily meditation in school and at home to achieve BP reductions. Thus, it is possible that a shortened protocol could prove effective, while improving feasibility of larger trials by reducing patient burden.

It was only possible to able to evaluate what happens to BP after patients were taught MBSR. Although patients in both the MBSR and PMR conditions were taught to use their stress management skills to cope with daily life, the extent to which these skills and practices were adopted by patients as lasting life-style changes was not evaluated. The possible effects on BP of longer-term personal meditation practices could not be evaluated. That is, MBSR may be more likely to reduce BP for those patients who effectively integrate it into their lives over a long period.

CONCLUSIONS

The primary finding from this small randomized trial is that MBSR is more effective in lowering elevated BP than an active control and resulted in significant decreases in SBP and DBP in prehypertensive individuals, but for clinic BP only. If sustained, reductions in BP could prove important for health outcomes, but future research is necessary to evaluate these questions. The magnitude of change in BP is similar to that reported in meta-analyses of TM. This was one of the first prospective randomized trials of MBSR as a nonpharmacologic treatment of elevated BP. MBSR could prove to be an adjunct to individuals with poorly controlled BP and could potentially decrease polypharmacy and/or improve BP control, a possibility that merits additional study. Future research should also focus on whether MBSR-related BP reductions can be sustained.

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Author contributions: Drs. Hughes and Fresco served as coprincipal investigators of this trial, had full access to all of the data, and take responsibility for the integrity of the data and the accuracy of the data analyses. They were responsible for study concept and design, acquisition of data, analysis of data, and drafting of the manuscript. Rodney Myerscough served as the trial therapist, delivering both group treatments and also aided in study concept and design and critical revision of the manuscript. Manfred H. M. van Dulmen served as the statistical consultant for this trial and was involved in study design including power analyses and the data analytic strategy. Linda E. Carlson served as a consultant on this study and contributed to study concept and design, as well as treatment fidelity ratings and critical revision of the manuscript. Richard Josephson was the medical director of this clinical trial and was involved in study concept and design, study supervision, and critical revision of the manuscript.

REFERENCES

1. American Heart Association. Heart Disease and Stroke Statistics—2004 Update. Dallas, TX: American Heart Association; 2003.
2. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JLJ, Jones DW, Materson BJ, Oparil S, Wright JTJ, Roccella EJ. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003;289:2560–72.
3. Barnes VA, Davis HC, Murzynowski JB, Treiber FA. Impact of meditation on resting and ambulatory blood pressure and heart rate in youth. Psychosom Med 2004;66:909–14.
4. Brook RD, Appel LJ, Rubenfire M, Ogedegbe G, Bisognano JD, Elliott WJ, Fuchs FD, Hughes JW, Lackland DT, Staffileno BA, Townsend RR, Rajagopalan S. Beyond Medications and Diet: Alternative Approaches to Lowering Blood Pressure: A Scientific Statement From the American Heart Association. Hypertension 2013;61:1368–83.
5. Linden W, Lenz JW, Con AH. Individualized stress management for primary hypertension: a randomized trial. Arch Intern Med 2001;161:1071–80.
6. Patel C, Marmot MG, Terry DJ, Carruthers M, Hunt B, Patel M. Trial of relaxation in reducing coronary risk: four year follow up. BMJ 1985;290:1103–6.

7. Patel C, Marmot MG, Terry DJ. Controlled trial of biofeedback-aided behavioural methods in reducing mild hypertension. BMJ 1981;282:2005–8.
8. Schneider R, Alexander CN, Staggers F, Orme-Johnson D, Rainforth M, Salerno J, Castillo-Richmond A, Barnes V, Nidich S. A randomized controlled trial of stress reduction in African Americans treated for hypertension for over one year. Am J Hypertens 2005;18:88–98.
9. Spence JD, Barnett PA, Linden W, Ramsden V, Taenzer P. Lifestyle modifications to prevent and control hypertension. 7. Recommendations on stress management. Canadian Hypertension Society, Canadian Coalition for High Blood Pressure Prevention and Control, Laboratory Centre for Disease Control at Health Canada, Heart and Stroke Foundation of Canada. CMAJ 1999;160(suppl 9):S46–50.
10. Schneider RH, Staggers F, Alxander CN, Sheppard W, Rainforth M, Kondwani K, Smith S, King CG. A randomised controlled trial of stress reduction for hypertension in older African Americans. Hypertension 1995;26:820–7.
11. Eisenberg DM, Delbanco TL, Berkey CS, Kaptchuk TJ, Kupelnick B, Kuhl J, Chalmers TC. Cognitive behavioral techniques for hypertension: are they effective? Ann Intern Med 1993;118:964–72.
12. Linden W, Chambers L. Clinical effectiveness of non-drug treatment for hypertension: a meta-analysis. Ann Behav Med 1994;16:35–45.
13. Rainforth MV, Schneider RH, Nidich SI, Gaylord-King C, Salerno JW, Anderson JW. Stress reduction programs in patients with elevated blood pressure: a systematic review and meta-analysis. Curr Hypertens Rep 2007;9:520–8.
14. Kaufmann PG, Jacob RG, Ewart CK, Chesney MA, Muenz LR, Doub N, Mercer W. Hypertension intervention pooling project. Health Psychol 1988;(suppl 7):209–24.
15. Ospina MB, Bond TK, Karkahah M, Tjosvold L, Vandermeer B, Liang Y, Bialy L, Hooton N, Buscemi N, Dryden DM, Klassen TP. Meditation Practices for Health: State of the Research. AHRQ Publication No. 07-E010. 2007. Rockville, MD, Agency for Healthcare Research and Quality. Evidence Report/Technology Assessment No. 155.
16. Julius S. Treatment of borderline (nonsustained) hypertension. In: Izzo JLJ, Black HR, editors. Hypertension Primer. 3rd ed. Dallas: American Heart Association; 2003:449–52.
17. Julius S. The blood pressure seeking properties of the central nervous system. J Hypertens 1988;6(3):177–85.
18. Bernstein DA, Borkovec TD, Hazlett-Stevens H. New Directions in Progressive Relaxation Training: A Guidebook for Helping Professionals. Westport, CT: Praeger Publishers; 2000.
19. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves JW, Hill MN, Jones DH, Kurtz T, Sheps SG, Roccella EJ. Recommendations for blood pressure measurement in humans: an AHA scientific statement from the Council on High Blood Pressure Research Professional and Public Education Subcommittee. J Clin Hypertens (Greenwich) 2005;7:102–9.
20. O'Brien E. Demise of the mercury sphygmomanometer and the dawning of a new era in blood pressure measurement. Blood Press Monit 2003;8: 19–21.
21. O'Brien E, Waeber B, Parati G, Staessen J, Myers MG. Blood pressure measuring devices: recommendations of the European Society of Hypertension. BMJ 2001;322:531–6.
22. Winnicki M, Canali C, Mormino P, Palatini P. Ambulatory blood pressure monitoring editing criteria: is standardization needed? Hypertension and Ambulatory Recording Venetia Study (HARVEST) Group, Italy. Am J Hypertens 1997;10(4 pt 1):419–27.
23. Appel LJ, Champagne CM, Harsha DW, Cooper LS, Obarzanek E, Elmer PJ, Stevens VJ, Vollmer WM, Lin PH, Svetkey LP, Stedman SW, Young DR. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. JAMA 2003;289:2083–93.
24. Whelton PK, He J, Appel LJ, Cutler JA, Havas S, Kotchen TA, Roccella EJ, Stout R, Vallbona C, Winston MC, Karimbakas J. Primary prevention of hypertension: clinical and public health advisory from The National High Blood Pressure Education Program. JAMA 2002;288:1882–8.
25. Blom K, How M, Dai M, Baker B, Irvine J, Abbey S, Abramson BL, Myers M, Perkins N, Tobe SW. Hypertension Analysis of stress Reduction using Mindfulness meditatiON and Yoga (The HARMONY Study): study protocol of a randomised control trial. BMJ Open 2012;2:e000848.
26. Pickering TG. White coat hypertension. Curr Opin Nephrol Hypertens 1996;5:192–8.
27. Fjorback LO, Arendt M, Ornbol E, Fink P, Walach H. Mindfulness-based stress reduction and mindfulness-based cognitive therapy: a systematic review of randomized controlled trials. Acta Psychiatr Scand 2011;124:102–19.
28. MacCoon DG, Imel ZE, Rosenkranz MA, Sheftel JG, Weng HY, Sullivan JC, Bonus KA, Stoney CM, Salomons TV, Davidson RJ, Lutz A. The validation of an active control intervention for mindfulness based stress reduction (MBSR). Behav Res Ther 2012;50:3–12.
29. 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.