Advances in Integrative Medicine 6 (2019) 66–72

Contents lists available at ScienceDirect

Advances in Integrative Medicine

journal homepage: www.elsevier.com/locate/aimed

Original Research Papers

Take a deep breath: A randomized control trial of Pranayama breathing on uncontrolled hypertension

Shamita Misra[a], Jamie Smith[a], Nuha Wareg[a], Kelvin Hodges[a], Mukti Gandhi[a], Jane A. McElroy[a,b,*]

[a] Family and Community Medicine Department, University of Missouri, Columbia, Missouri, United States
[b] Missouri University Research Reactor, University of Missouri, Columbia, Missouri, United States

ARTICLE INFO

Article history:
Received 13 June 2018
Received in revised form 21 August 2018
Accepted 23 August 2018
Available online 23 August 2018

Keywords:
Hypertension
Pranayama breathing
Video intervention

ABSTRACT

Objective: Our objective was to determine whether 15 min yogic breathing exercises practiced 5 times a week can lower blood pressure in uncontrolled hypertensive patients.
Design: Take a deep Breath study was a 3-arm randomized controlled blood pressure trial, 2016–2017 with in-class instruction, home DVD/YouTube instruction, and a control arm. Blood pressure measurements with a 1-month follow-up.
Methods: A list of uncontrolled hypertensive patients (n = 5507) generated from Family Medicine Department's Electronic Medical Record registry was given to their respective providers to recommend. After chart review of the 1682 recommended patients, the number reduced to 984 of which 610 were contacted and 22% of 610 (n = 133) were enrolled. Eligible participants were randomly assigned to in-class instruction (n = 44), DVD/YouTube group (n = 57), or control (n = 32). The outcome measured was at least 5 mm Hg systolic blood pressure reduction.
Results: Participants were predominately white (89%), approximately half male (52%) with a mean age of 61 years (sd = 12 years). Of the 133 participants who were allocated to a study arm, 30 never participated in any aspect of the study, 20 partially completed and 83 completed the study. Compared to those who completed the study, no differences were noted in demographics or initial blood pressure for those who partially completed. From chart review 6% of participants made a change to their blood pressure medications during the study. Intervention participants were significantly more likely to have ≥5 mm Hg decrease in systolic blood pressure (OR = 4.49, 95% CI: 1.18–17.0) compared to controls in the multivariable logistics model. DVD/YouTube instruction did just as well as in-class instruction group.
Conclusions: In this RCT, statistically significant systolic blood pressure reduction was noted in the intervention groups. Yogic breathing exercises may provide an additional non- pharmacologic tool to treat uncontrolled blood pressure.

1. Introduction

Hypertension is a common condition for primary care visits and can cause significant morbidity if uncontrolled. About 74 to 76 percent of hypertensive adults in the United States take some medication to control blood pressure [1]. Approximately 46% of patients with hypertension are uncontrolled on multiple medications and could benefit from alternative therapies. Based on a 2015 National Health Statistics Report, approximately one-third of American adults use other non-conventional treatments, known as complementary and alternative medicine (CAM), to supplement their standard therapies [2]. In a study using National Health Interview Survey, any CAM use was higher in those diagnosed with hypertension compared to those without hypertension. However, less than 10% of CAM users reported using CAM therapy for treating hypertension [3].

Literature review of the effect of yoga on decreasing blood pressure has shown it to be promising [4–8]. However, it is difficult to know which aspect of yoga, singly (i.e. postures, meditation or breathing) or in combination contributes most to a decrease in blood pressure. For example, in Park and colleagues' meta-analysis

* Corresponding author at: University of Missouri, Family and Community Medicine Department, 7 Hospital Drive, MA306 Medical Science Building, DC032.00, Columbia, MO, 65211, United States.
E-mail addresses: misras@health.missouri.edu (S. Misra), smithjami@health.missouri.edu (J. Smith), waregn@health.missouri.edu (N. Wareg), hodgeskl@health.missouri.edu (K. Hodges), gandhim@health.missouri.edu (M. Gandhi), mcelroyja@health.missouri.edu, mcelroyja@missouri.edu (J.A. McElroy).

https://doi.org/10.1016/j.aimed.2018.08.002
2212-9588/

of meditation/mindfulness and yoga for blood pressure reduction, meditation/mindfulness practices influenced reduction of blood pressure in patients over 60 years old whereas yoga decreased blood pressure in those younger than 60 years of age [6,9–11].

Yogic breathing exercises (aka Pranayama) is the practice of voluntary breath control in which the rhythm of inhalation, retention, and exhalation are consciously controlled. Mourya and colleagues used an RCT design to evaluate the effect of fast and slow breathing exercises (a type of yogic breathing) in hypertensive patients and found reduction in blood pressure [12]. They along with other researchers suggest that both sympathetic and parasympathetic reactivity associated with the slow-breathing aspect of the exercise may be the mechanism for blood pressure reduction [12,13]. However, recent studies using device guided slow breathing exercises have not shown consistent results in lowering blood pressure [14]. This suggests that blood pressure reduction may be more complex than just altering breathing rates [10,14,15].

In 2011, a single-arm feasibility pilot study reported significant reduction in blood pressure using within subject measurements from baseline to one month follow-up [16]. This study enrolled pre-hypertensive patients (n = 8) and evaluated one aspect of yoga, breathing exercises and found an 11 mm Hg decrease in systolic blood pressures. As the next step, this study with a control population was conducted to evaluate this promising CAM approach. Specifically, to further test the influence of yogic breathing exercises on blood pressure, a 3-arm randomized controlled trial with a 1- and 3-month follow-up was initiated in October 2016, enrolling uncontrolled hypertensive patients from Family and Community Medicine practices in Columbia, Missouri. Analyses were completed on the 1-month follow-up due to the poor compliance of participants at the 3-month follow-up.

2. Materials and methods

2.1. Design

The study design consisted of a 3-arm randomized controlled trial for a 6-week intervention with a 1-month follow-up and 3-month follow-up, enrolling participants with uncontrolled hypertension, regardless of pharmacological therapy use. Following Eighth Joint National Committee (JNC 8) recommendations, participants were considered eligible for the study if they were: less than 60 years of age with blood pressure measurements of ≥140/ ≥90 mm Hg; 60 years of age or older with blood pressure measurements of ≥150/ ≥90 mm Hg; diagnosed with diabetes with blood pressure measurements of ≥140/ ≥90 mm Hg; and had blood pressure measurements of <180/ <110 mm Hg without hypertensive urgency symptoms [17]. Additionally, participants were excluded from the study if they were: less than 18 years of age, had chronic obstructive pulmonary disease, chronic renal disease stage II or above, a history of alcoholism, cognitive problems, mental health diagnosis such as schizophrenia, were non-English speakers, had advanced stage congestive heart failure, or did not have access to internet or a DVD player.

A list of uncontrolled hypertensive participants (n = 5507) was generated from Family Medicine Department's Electronic Medical Record (EMR) registry. Contact information for each patient was collected and 96% had a primary care physician (PCP) listed. Each physician including resident physicians (n = 54) was given a list of their eligible hypertension participants, and asked to identify patients suitable for this study. A total of 1682 participants were marked as either highly recommended or recommended by 31of 54 PCPs who returned their lists. A chart review of these participants reduced the number of highly recommended to 310 and recommended to 674 participants. All 310 'highly recommended' participants and a random selection of 300 of 674 'recommended' participants were sent invitation letters followed by screening telephone calls. Of the 610 participants who were contacted, 22% (n = 133) enrolled in the study, see flowchart in Fig. 1. For allocation concealment the 133 participants who agreed to participate were listed on an Excel spreadsheet and then assigned to an arm of the study (A, B, or C) by a staff member using Excel random generator. A separate random assignment to the A, B, and C group for mode of instruction (class, DVD/YouTube, control) was also achieved using Excel random generator. After assignment to an arm of the study, participants were sent an email informing them of their assigned groups, next steps in the study, and important dates. Another email generated from REDCap, a secure web application for managing online surveys, was also sent inviting accepted participants to take the baseline survey. This study was approved by the University of Missouri Health Sciences Institutional Review Board and all participants signed written consents. The Clinical Trial Registration information is Pranayama Breathing and Uncontrolled Hypertension and number NCT03320577.

The in-class instruction group participants performed yogic breathing exercises once in a classroom setting located at the clinic, led by an instructor, and then four times at home, totaling at least five times weekly. Participants recorded date and time of yogic breathing exercises and turned in their logs each week at the clinic. The DVD/YouTube group viewed their video at home and performed yogic breathing exercises at least five times a week. The DVD/ YouTube contained breathing instructions and a 15-minute guided practice. Participants recorded date and time of yogic breathing exercises and turned in their logs each week at the clinic. Controls were asked to record their dinner time at least 5 times a week and turned in their logs each week at the clinic. No other type of intervention was given to the control group; they received treatment as usual. After the 6-week intervention period, participants were told they could continue the breathing, if they so desired. All participants had their blood pressure measured each week for 6 weeks, 1-month (week 10) follow-up and 3-month (week 18) follow-up using standard clinic protocol for blood pressure measurement. Clinical personnel measuring the blood pressure measurements were not aware of the participants' assigned group. Height and weight were measured at baseline, weight was again measured at week 6, 1-month (week 10) follow-up and 3-month (week 18) follow-up. The DVD/ YouTube group was evaluated in week three by two independent examiners for accuracy on their learning of these yogic breathing exercises.

2.2. Breathing exercise instructions

1) Bellow Breathing (2-minute duration or 30 repetitions): Take a deep breath and fill the lungs all the way up to the collar bones with air and then exhale. 2) Rapid Exhalations (5 min or 20 cycles): exhalation by breathing in air normally and pushing air out with force so that the stomach goes in. Breathe in then with a short contraction of your abdomen expel air out through your nostrils in rapid successions or repetitions. Aim for 10–15 exhalations per inhalation. One inhalation with repetitive exhalations is one cycle. 3) Alternate Nostril Breathing (5 min or 20 cycles): Close the right nostril with the right thumb and breathe in from left nostril. Using the same hand, close the left nostril with the little finger (fifth), lift right thumb and breathe out from right nostril. Now breathe in through right and breathe out through left. This makes one cycle. 4) Bumblebee Breathing (repeat 3 times): Close ears with thumb, index finger on forehead, remaining three on side of nose, eyes lightly closed. Breathe in and breathe out through nose while humming like a bee. 5) Om Singing (repeat 3 times): Breathe in

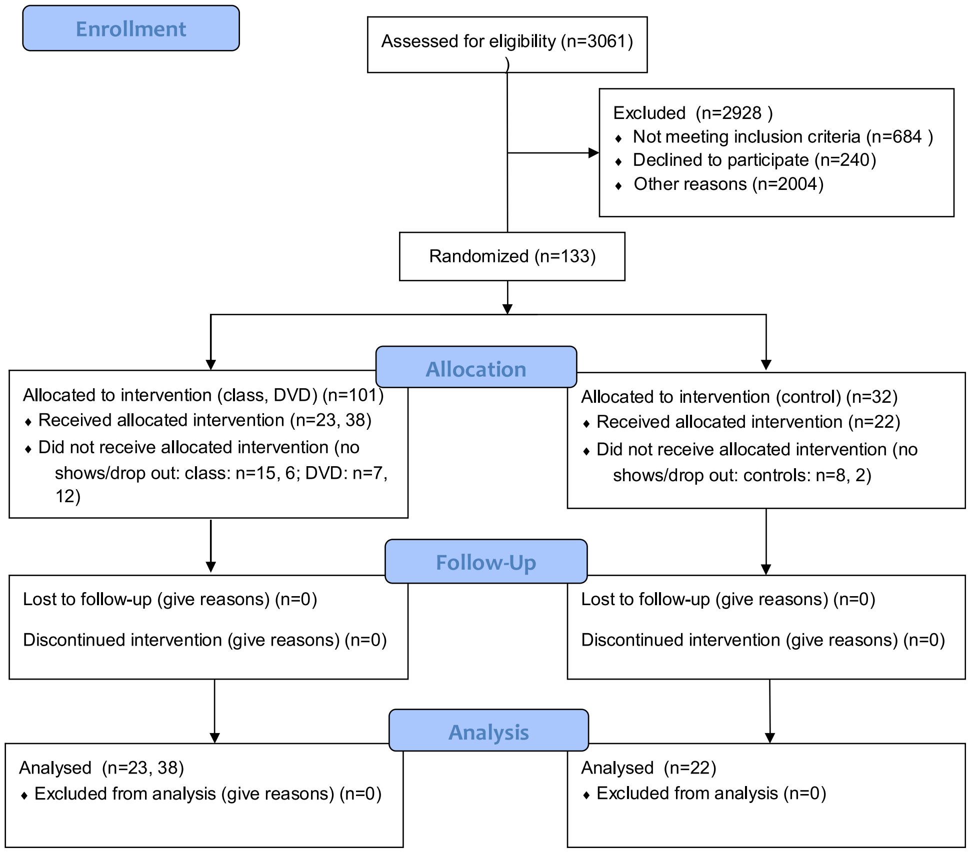

Fig. 1. CONSORT Flow Diagram.

normally and say 'Om' as you exhale. Time to say 'O' is three times longer than time on 'mmm'.

2.3. Measurement

Sociodemographic data (i.e., age, gender, race, education, employment, marital status, income, family history, and smoking status) was collected at baseline, along with current medications (compiled from their electronic medical record and verified by participants). Participants were also asked to complete baseline, post intervention at 6 weeks, one-month, and 3-month follow-up surveys on relevant lifestyle habits and attitudes, standardized measures of mental and physical health, as well as any changes in medication and/or other conditions, such as changes in diet. Furthermore, due to the timing of the study (i.e., occurred pre- & post-presidential 2016 election), participants were asked retrospectively in February 2017 to answer two questions about political stress they experienced immediately before and immediately after the election. Political stress ranged from 1 (not at all significant) to 5 (extremely significant). Participants were then categorized into low (1, 2) and moderate/high (3, 4, 5) political stress experienced.

2.4. Sample size

In McElroy and colleagues' 9-week feasibility pilot study [16], they reported a reduction in systolic blood pressure of approximately 11 mm Hg (sd 6) among pre-hypertensive patients. Besides these pilot findings a review of three other studies [18–20], found comparable results in yogic breathing effectiveness on reducing blood pressure. Using these findings [16,18–20], power calculations resulted in an estimated sample size of at least 25 participants per group, or a total of 75 participants (25 for each intervention arm, and 25 controls), to provide approximately 80% power when testing one-sided alternatives for group differences at the 0.05 level of significance for a change (of at least 5 mm Hg) for systolic blood pressure.

2.5. Analysis

Descriptive statistics were examined for all participant characteristics for the entire study population, as well as by study arm. In order to examine differences between the study arms, chi-square analyses (or t-tests for continuous variables) were utilized. Multivariable logistic regressions were used to model the associations between select participant characteristics (age, gender, BMI, smoking and family histories, depression and stress levels) and study arm (class, DVD/YouTube, control) with decreases ($\geq$ 5 mm Hg) in systolic blood pressure. Odds ratios (OR) and 95% confidence intervals (CI) were calculated, model discrimination was assessed with the c-statistic, and the Hosmer-Lemeshow goodness-of-fit X^2 test was used to determine model fit. Participants analyzed in the study only included those in which the main outcome, blood pressure measurement, was obtained at baseline, week 6 and 1-month follow-up (week 10) [21]. Of the original 133 participants enrolled, 30 never showed up for the baseline blood pressure measurement or completed the baseline survey. Among those who never showed up, the control group had the fewest (26%) whereas the intervention groups had more (class: 50% and DVD/YouTube: 23%). Of the 20 participants who dropped out (control: 15%; class: 30% and DVD/YouTube: 55%), 80% provided only baseline (n = 11) or 2 weeks of blood pressure data (n = 5); none stayed in the study past week 4. All analyses were performed in SAS version 9.4 (SAS Institute, Cary, NC).

3. Results

3.1. Participant characteristics

The study's sample size included 83 participants: 26% controls, 28% in-class instruction, and 46% participants DVD/YouTube group, see Table 1. Participants had a mean age of 61 years, nearly half of the participants in the study were women (48%), a majority were white (89%) and college educated (63%). The majority (85%) reported a family history of either high blood pressure (77%), stroke (35%), or heart disease (54%) and one fourth of the sample was using beta blockers at the start of the study. Only 6% of participants reported having made any change to their blood pressure medications during the study. No participant started a blood pressure medication within three months of the study start date whereas most (80%) had been on their current medication(s) for ≥ one year. At baseline, the percent of participants on blood pressure medication were similar across groups at 96% for class, 90% for DVD/YouTube and 91% for control groups. Only 2 participants in the control group and 2 participants in the intervention group changed blood pressure medication from baseline to 1-month intervention. Slightly more than half (52%) of the participants reported moderate to high levels of election-related stress before the election, while 60% reported moderate to high levels of election-related stress after the election. No significant differences, however, were noted between intervention and control participants in regards to any of these characteristics; see Table 1. A similar percentage of participants self-reported a history of practicing breathing exercises at baseline ('Are you currently practicing any breathing exercises") between the intervention group (12%) and the control group (14%). For the breathing exercises used in this intervention, at one month follow-up, 20% of the participants practiced never or sporadically (less than once a week) since the end of the intervention whereas 46% practiced sporadically or never at 3-month follow-up.

3.2. Outcome

Systolic and diastolic blood pressure measurements at baseline, post-intervention (week 6) and 1-month follow-up (week 10) were examined. Overall, systolic blood pressure decreased over time for the study population, with an average decrease of 2.17 mm Hg from

Table 1
Sample characteristics.

	Overall (n = 83) n (%)	Controls (n = 22) n (%)	Class (n = 23) n (%)	DVD (n = 38) n (%)	Class/DVD (n = 61) n (%)	p[a]	p[b]	p[c]
Demographics								
Age, mean (sd)	60.8 (11.5)	58.6 (12.0)	59.6 (13.1)	62.8 (10.1)	61.6 (11.3)	0.78	0.15	0.30
Gender - female	40 (48)	12 (54)	10 (43)	18 (47)	28 (46)	0.45	0.59	0.48
Race - white	74 (89)	21 (95)	20 (87)	33 (87)	53 (87)	0.31	0.40	0.33
Education - college/grad	52 (63)	13 (59)	13 (56)	26 (68)	39 (64)	0.11	0.72	0.55
Employment - part/full	51 (61)	13 (59)	19 (83)	19 (50)	38 (62)	0.08	0.49	0.79
Marital status - married	68 (82)	19 (86)	16 (70)	33 (87)	49 (80)	0.17	0.95	0.52
Smoking - former/current	32 (39)	9 (41)	8 (35)	15 (39)	23 (38)	0.67	0.91	0.79
Family History								
High blood pressure	64 (77)	16 (73)	19 (83)	29 (76)	48 (79)	0.42	0.75	0.56
Stroke	29 (35)	8 (36)	9 (39)	12 (31)	21 (34)	0.84	0.70	0.87
Heart disease	45 (54)	14 (64)	13 (56)	18 (47)	31 (51)	0.62	0.22	0.30
Any of the above	71 (85)	20 (91)	20 (87)	31 (81)	51 (84)	0.67	0.32	0.40
Medication								
Beta blockers	21 (25)	8 (36)	6 (26)	7 (18)	13 (21)	0.45	0.12	0.16
ACE/ARB	53 (64)	12 (54)	15 (65)	26 (68)	41 (67)	0.46	0.28	0.28
CCB	18 (22)	5 (23)	6 (26)	7 (18)	13 (21)	0.79	0.68	0.89
Diuretic	47 (57)	12 (54)	14 (61)	21 (55)	35 (57)	0.66	0.95	0.81
Any change during study	5 (6)	2 (9)	1 (4)	2 (9)	3 (5)	0.52	0.56	0.48
Health, baseline, mean (sd)								
Global health	3.30 (0.85)	3.23 (0.61)	3.17 (0.90)	3.42 (0.95)	3.33 (0.93)	0.81	0.39	0.63
BMI	32.3 (7.6)	32.2 (8.5)	33.4 (7.4)	31.8 (7.2)	32.4 (7.3)	0.53	0.80	0.95
Stress	12.2 (6.3)	13.9 (5.6)	12.7 (6.9)	11.0 (6.1)	11.7 (6.4)	0.34	0.07	0.14
moderate/high, n (%)	31 (38)	10 (48)	9 (39)	12 (32)	21 (34)	0.53	0.22	0.28
Depression	3.3 (3.5)	3.9 (3.9)	3.9 (3.3)	3.9 (3.9)	3.1 (3.4)	0.99	0.17	0.35
moderate/high, n (%)	6 (7)	3 (14)	1 (4)	2 (5)	3 (5)	0.25	0.23	0.15
Election Stress, mean (sd)								
Before election	2.6 (1.2)	2.9 (1.4)	2.5 (1.2)	2.5 (1.1)	2.5 (1.1)	0.27	0.18	0.14
moderate/high, n (%)	43 (52)	14 (64)	11 (48)	18 (47)	29 (47)	0.28	0.22	0.19
After election	2.9 (1.3)	3.1 (1.2)	2.8 (1.4)	3.0 (1.3)	2.9 (1.3)	0.49	0.79	0.63
moderate/high, n (%)	50 (60)	14 (64)	13 (56)	23 (60)	36 (59)	0.62	0.81	0.70
Systolic blood pressure, mean (sd)								
Baseline	152.4 (18.1)	149.2 (23.7)	155.4 (15.9)	152.5 (15.5)	153.6 (15.6)	0.30	0.56	0.42
Post (week 6)	150.3 (16.5)	151.6 (18.9)	152.1 (19.1)	148.4 (13.4)	149.8 (15.8)	0.92	0.44	0.66
Follow up (week 10)	148.0 (14.7)	150.1 (17.2)	150.5 (16.3)	145.3 (11.7)	147.2 (13.7)	0.93	0.25	0.43
Blood pressure Δ (baseline to post intervention)								
mean difference (sd)	2.17 (14.9)	2.34 (15.6)	3.28 (12.7)	4.12 (15.6)	3.80 (14.5)	0.19	0.12	0.10
Blood pressure Δ (baseline to 1-month follow up)								
mean difference (sd)	4.41 (17.4)	0.86 (17.8)	5.59 (15.9)	6.85 (17.9)	6.38 (17.1)	0.21	0.11	0.09

Column percentages presented.
*p < .05.
[a] chi-square (or two-sided t-statistic for continuous variable) p-value between control and class.
[b] chi-square (or two-sided t-statistic for continuous variable) p-value between control and DVD.
[c] chi-square (or two-sided t-statistic for continuous variable) p-value between control and any intervention.

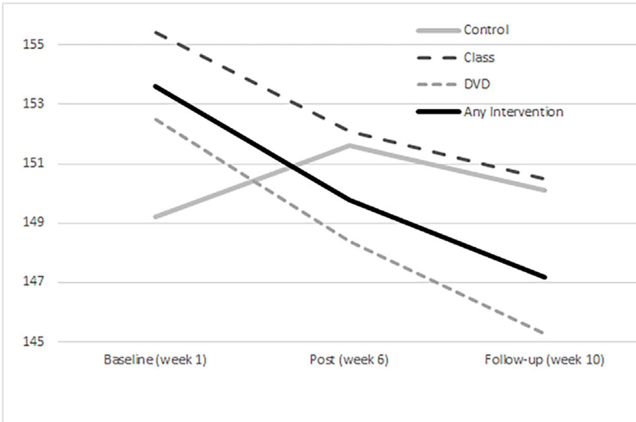

Fig. 2. Systolic blood pressure over time by intervention group.

baseline to post-intervention and 4.41 mm Hg from baseline to 1-month follow-up. Systolic blood pressure for control participants however increased between baseline and post intervention (increase of 2.34 mm Hg) and baseline and 1-month follow-up (increase of 0.86 mm Hg), as compared to intervention participants (baseline to post-intervention = decrease of 3.80 mm Hg; baseline to 1-month follow-up = decrease of 6.38 mm Hg), see Fig. 2. Overall diastolic blood pressure decreased less than 1 mm Hg from baseline to post-intervention and 1.5 mm Hg from baseline to 1-month follow-up. All diastolic blood pressure measurements decreased from baseline to 1-month follow-up in all three groups: 1.0 mm Hg (controls), 2.3 mm Hg (class) and 1.3 mm Hg (DVD). Comparison of diastolic blood pressure measurements in the class intervention group and DVD intervention group to control group was not statistically significantly different. Therefore, the remaining analysis will focus on systolic blood pressure results.

Among the intervention groups, about half (54%) of the study participants decreased ≥5 mm Hg systolic blood pressure from their baseline and 1-month follow-up measurements; see Fig. 3. Systolic blood pressure decreased in fewer control subjects (27%) by ≥5 mm Hg from baseline to 1-month follow-up, than intervention subjects (54%; $X^2 = 4.67$, $p = .03$).

3.3. Models

In order to examine the association of select participant characteristics (i.e., age, gender, BMI, beta blocker use, change in blood pressure medication during the study and through one-month follow-up, family history, smoking status, global health and stress, depression, election-related stress, and continued practice at least 1 or more times a week vs. not weekly practice) and study arm (class, DVD/YouTube, control) with a decrease (≥ 5 mm Hg) in systolic blood pressure, two sets of multivariable logistic regression models were conducted. We also included self-reported data of current practice of breathing exercises in the model as an independent variable but results were unchanged so this variable was not included in the final model. A multivariable logistic model examining systolic blood pressure change between baseline and post-intervention was conducted but no significant main effects were found and therefore not tabled. When looking at change between baseline and 1-month follow-up however, significant main effects were noted. As seen in Table 2, participants were more likely have a ≥ 5 mm Hg decrease in systolic blood pressure between baseline and 1-month follow-up if they had a family history of high blood pressure, stroke, or heart disease (OR = 1.95, 95% CI = 1.07–3.56). Additionally, intervention participants (Class and DVD/YouTube groups) were more than 4 times as likely to have a ≥5 mm Hg decrease in systolic blood pressure, than control participants. Model discrimination for both models was good with a c-statistic of 0.80 and model fit was adequate ($X^2 = 6.2$, $p = 0.61$).

4. Discussion

We found practicing yogic breathing exercises was significantly associated with ≥5 mm Hg reduction in systolic blood pressure among uncontrolled hypertensive patients. One strength of this study was that potential confounders, such as psychosocial factors, weight, stress, medications, gender and family history that may influence blood pressure, were adjusted for in the models. Further, we obtained the patient list from a large family and community medicine practice. Demographics among the three groups were similar. Similarly, baseline demographics and baseline mean blood pressure measurements were similar between those who were part of the analysis (n = 83) and those who dropped out of the study (n = 20).

Small reductions in systolic blood pressure (i.e., 5 mm Hg) through diet and mind body therapies significantly reduce CVD morbidity [22,23]. Further multiple interventions addressing diet and exercise reported a reduction of blood pressure, on average, by about 5 mm Hg [23,24]. In one study, the main outcome was reduction in systolic blood pressure with device assisted slow

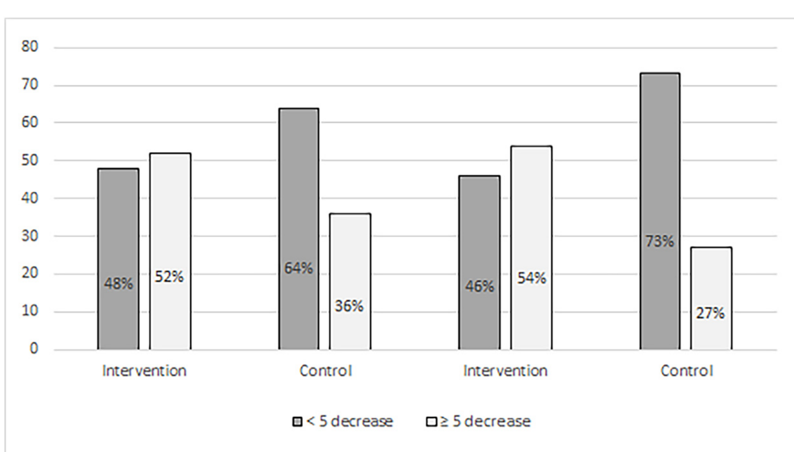

Fig. 3. Percent of participants with ≥ 5 mm Hg decrease in systolic blood pressure over time.

Table 2
Multivariable logistic regression decrease (≥ 5 pts) in systolic blood pressure from baseline to follow-up.

	Model 1			Model 2		
	OR	95% CI (low-high)	p-value	OR	95% CI (low-high)	p-value
Age[a]	1.81	(0.89-3.66)	.09	1.80	(0.91-3.56)	.09
BMI[a]	0.53	(0.27-2.82)	.07	0.53	(0.27-1.05)	.07
General health[a]	0.54	(0.27-1.05)	.07	0.54	(0.27-1.06)	.07
Any family history[b]	1.95	(1.07-3.56)	.02	1.95	(1.07-3.56)	.02
Stress before election	0.33	(0.10-1.07)	.06	0.33	(0.10-1.07)	.06
Study Arm						
Class vs. control	4.64	(0.97-21.9)	.05			
DVD vs. control	4.41	(1.06-18.2)	.04			
Class/DVD vs. control				4.49	(1.18-17.0)	.02

Model 1 includes a three level study variable, whereas model 2 includes a two level study variable.
The following covariates were also controlled for but non-significant ($p > 0.10$): gender.
beta blocker use, smoking history, depression and global stress.
OR = odds ratio; CI = confidence interval.
[a] collected at baseline and standardized prior to inclusion.
[b] collected at baseline, family history of high blood pressure, stroke, or heart disease.

breathing [25]. In this RCT, systolic blood pressure decreased by 15 mm Hg in participants who spent more than 180 min over an 8 week period practicing slow breathing. This RCT showed a similar reduction in systolic blood pressure (14 mm Hg) in the DVD/YouTube group in the third wave participants who enrolled in February 2017 after elections were over. A large systematic review and meta-analysis of 42 trials comprising 144,220 patients compared groups of patients with a 5 mm Hg difference in systolic blood pressure and reported consistent reduction of cardiovascular risk and all-cause mortality for the group with the lower systolic blood pressure [37].

Regular deep breathing exercises slow down sympathetic activity using a Breathe with Interactive Music device [26]. However it is not possible to ascertain if the music component or deep slow breathing influenced blood pressure reduction. Another CAM approach using breathing that has been studied involves device-guided breathing exercises [10,27–30]. The device, worn by the participant, ascertains the participant's breathing pattern and then uses synchronized music to guide the participant towards slow and regular breathing of less than 10 breaths per minute. These studies on device-guided breathing exercises have suffered from methodological weaknesses, including lack of an appropriate active control group [31] or with one exception using only healthy participants (without any comorbidity) leading to inconclusive findings [10,14]. Information on patient's adherence to breathing exercises, the minimum necessary number of sessions per week, and the long-term effects has yet to be reported [32,33].

Current evidence favors the role of the autonomic system in the etiology of essential hypertension [34]. There is some evidence that supports the hypothesis of sympathetic hyperactivity and parasympathetic underactivity in the etiology of essential hypertension [34]. The autonomic nervous system, through arterial baroreceptors and pulmonary stretch receptors, influences blood pressure [35]. Yogic breathing involves deep diaphragmatic breathing possibly stimulating stretch receptors. This hypothesis is likely to increase vagal tone and decrease sympathetic activity thereby decreasing blood pressure. This needs further testing by measuring biomarkers to validate.

There are some limitations to this small RCT. In this study, 15% of the participants dropped out of the study after attending one or two meetings. It is likely that the timing of study being launched amidst the 2016 presidential election time may have affected the degree of blood pressure reduction. Similarly, although the sample size was adequate to identify significant reduction in systolic blood pressure between the intervention group, between each intervention arm of the study and control group, the confidence intervals were large due to relatively small sample size for each group. Finally, only one participant reported continuing the breathing exercises per protocol at the 3-month follow-up, whereas almost half stopped practicing. Additional incentives or encouragements might be needed to support continued practice.

Since completing this study and data analysis, 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/ APhA/ASH/ASPC/NMA/PCNA Guidelines for defining hypertension have emerged [36]. Stage 1 hypertension is defined per these guidelines as systolic blood pressure 130–139 mm Hg and /or diastolic blood pressure 80–89 mm Hg. In this class of patients who have a <10% cardiovascular disease risk, non-pharmacologic therapy with behavior modification is the first-line management recommendation. In McElroy and colleagues' pilot study in 2011, enrolled participants belonged to this group, then called prehypertension, and had a significant reduction in systolic blood pressure by 11 mm Hg. This non-pharmacologic intervention seems to be effective with both stage 1 and uncontrolled hypertension patient.

5. Conclusions

Yogic breathing exercises may provide an additional non-pharmacologic tool to treat uncontrolled hypertension. The substantial blood pressure reduction in the intervention groups and particularly in third wave for the DVD/YouTube group, was a promising finding. Delivery of this therapy is scalable to widespread implementation since DVD/YouTube link does not require qualified instructors, weekly in-person meetings, electronic gadgets or physical space. Additional research is needed to better understand the underlying mechanism which can then inform the optimal protocol in duration, number and type of yogic breathing exercises, and frequency of practicing.

Funding

This study was partially supported from the Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality. Clinician's time for this study was supported by internal funds, Family and Community Medicine Department's Leader Explore and Achieve Proficiency (LEAP) programinternal funds. LEAP provides busy clinicians protected time to engage in research activities.

Declarations of interest

None.

Contributions

Shamita Misra: the conception and design of the study, acquisition of data, and interpretation of data, drafting the article, and final approval of the version that is submitted.

Jamie Smith: data management; statistical analysis; drafting of sections of the article, final approval of submission

Nuha Wareg: data collection, interpretation of data, drafting of sections of the article, final approval of submission

Kelvin Hodges: data collection, interpretation of data, drafting of sections of the article, final approval of submission

Mukti Gandhi: data collection, interpretation of data, drafting of sections of the article, final approval of submission

Jane A. McElroy: the conception and design of the study, acquisition of data, and interpretation of data, drafting the article, and final approval of the version that is submitted

References

[1] I. Hajjar, T.A. Kotchen, Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988-2000, JAMA 290 (2) (2003) 199–206.

[2] T.C. Clarke, L.I. Black, B.J. Stussman, P.M. Barnes, R.L. Nahin, Trends in the use of complementary health approaches among adults: United States, 2002-2012, Natl. Health Stat. Report (79) (2015) 1–16.

[3] R.A. Bell, C.K. Suerken, J.G. Grzywacz, W. Lang, S.A. Quandt, T.A. Arcury, CAM use among older adults age 65 or older with hypertension in the United States: general use and disease treatment, J. Altern. Complement. Med. 12 (9) (2006) 903–909.

[4] A. Tyagi, M. Cohen, Yoga and hypertension: a systematic review, Altern. Ther. Health Med. 20 (2) (2014) 32–59.

[5] N.R. Okonta, Does yoga therapy reduce blood pressure in patients with hypertension?: an integrative review, Holist. Nurs. Pract. 26 (3) (2012) 137–141.

[6] S.H. Park, K.S. Han, Blood pressure response to meditation and yoga: a systematic review and meta-analysis, J. Altern. Complement. Med. 23 (9) (2017) 685–695.

[7] J. Wang, X. Xiong, W. Liu, Yoga for essential hypertension: a systematic review, PLoS One 8 (10) (2013) e76357.

[8] J.Z. Brandani, J. Mizuno, E.G. Ciolac, H.L. Monteiro, The hypotensive effect of Yoga's breathing exercises: a systematic review, Complement. Ther. Clin. Pract. 28 (2017) 38–46.

[9] T. Rosenthal, A. Alter, E. Peleg, B. Gavish, Device-guided breathing exercises reduce blood pressure: ambulatory and home measurements, Am. J. Hypertens. 14 (1) (2001) 74–76.

[10] S.J. Logtenberg, N. Kleefstra, S.T. Houweling, K.H. Groenier, H.J. Bilo, Effect of device-guided breathing exercises on blood pressure in hypertensive patients with type 2 diabetes mellitus: a randomized controlled trial, J. Hypertens. 25 (1) (2007) 241–246.

[11] S. Nagarajan, Effect of slow breathing training for a month on blood pressure and heart rate variability in healthy subjects, Natl. J. Physiol. Pharm. Pharmacol. 4 (3) (2014) 245–248.

[12] M. Mourya, A.S. Mahajan, N.P. Singh, A.K. Jain, Effect of slow- and fast-breathing exercises on autonomic functions in patients with essential hypertension, J. Altern. Complement. Med. 15 (7) (2009) 711–717.

[13] Y. Zou, X. Zhao, Y.Y. Hou, T. Liu, Q. Wu, Y.H. Huang, et al., Meta-analysis of effects of voluntary slow breathing exercises for control of heart rate and blood pressure in patients with cardiovascular diseases, Am. J. Cardiol. 120 (1) (2017) 148–153.

[14] K.R. Mahtani, D. Nunan, C.J. Heneghan, Device-guided breathing exercises in the control of human blood pressure: systematic review and meta-analysis, J. Hypertens. 30 (5) (2012) 852–860.

[15] G.W. Landman, K.J. van Hateren, P.R. van Dijk, S.J. Logtenberg, S.T. Houweling, K.H. Groenier, et al., Efficacy of device-guided breathing for hypertension in blinded, randomized, active-controlled trials: a meta-analysis of individual patient data, JAMA Intern. Med. 174 (11) (2014) 1815–1821.

[16] J.A. McElroy, S. Misra, M. Vasile, M.C. Hosokawa, Take a deep breath: a pilot study demonstrating a significant reduction in blood pressure with 15 minute daily Pranayama breathing, Ann. Behav. Sci. Med. Educ. 18 (2) (2012) 15–18.

[17] P.A. James, S. Oparil, B.L. Carter, W.C. Cushman, C. Dennison-Himmelfarb, J. Handler, et al., 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8), JAMA 311 (5) (2014) 507–520.

[18] S. Biswas, V. Malhotra, U. Dhar, R. Garg, Beneficial effects of forty days of pranayama training on cardiorespiratory parameters, Physiother. Occup. Ther. J. 7 (4) (2014) 173–180.

[19] K. Harinath, A.S. Malhotra, K. Pal, R. Prasad, R. Kumar, T.C. Kain, et al., Effects of Hatha yoga and Omkar meditation on cardiorespiratory performance, psychologic profile, and melatonin secretion, J. Altern. Complement. Med. 10 (2) (2004) 261–268.

[20] P.D. Dandekar, Impact of short term training of anulom vilom pranayam on blood pressure and pulse rate in healthy volunteers, Intern. J. Res. Ayurveda Pharm. 4 (2) (2013) 253–256.

[21] T.R. Ten Have, S.L. Normand, S.M. Marcus, C.H. Brown, P. Lavori, N. Duan, Intent-to-treat vs. Non-intent-to-treat analyses under treatment non-adherence in mental health randomized trials, Psychiatry Ann. 38 (12) (2008) 772–783.

[22] D.L. Cohen, Yoga and hypertension, J. Yoga Phys. Ther. 3 (4) (2013).

[23] National Clinical Guideline Centre (UK), Hypertension: the Clinical Management of Primary Hypertension in Adults: Update of Clinical Guidelines 18 and 34 [Internet] (NICE Clinical Guidelines, No. 127), Royal College of Physicians (UK), London, 2011. (Accessed 15 December, 2017) https://www.ncbi.nlm.nih.gov/books/NBK83274/.

[24] Hypertension in Adults: Diagnosis and Management. Clinical Guideline [CG127], National Institute for Health and Care Excellence, London, 2016. (Accessed 15 December, 2017) https://www.nice.org.uk/guidance/cg127#.

[25] W.J. Elliott, J. Izzo, W.B. White, D.R. Rosing, C.S. Snyder, A. Alter, et al., Graded blood pressure reduction in hypertensive outpatients associated with use of a device to assist with slow breathing, J. Clin. Hypertens. (Greenwich) 6 (10) (2004) 553–561.

[26] B. Oneda, K.C. Ortega, J.L. Gusmao, T.G. Araujo, D. Mion Jr, Sympathetic nerve activity is decreased during device-guided slow breathing, Hypertens. Res. 33 (7) (2010) 708–712.

[27] M.H. Schein, B. Gavish, M. Herz, D. Rosner-Kahana, P. Naveh, B. Knishkowy, et al., Treating hypertension with a device that slows and regularises breathing: a randomised, double-blind controlled study, J. Hum. Hypertens. 15 (4) (2001) 271–278.

[28] S. Pandic, I. Ekman, L. Nord, K.I. Kjellgren, Device-guided breathing exercises in the treatment of hypertension - perceptions and effects, CVD Prev. Control 3 (3) (2008) 163–169.

[29] M.R. Altena, N. Kleefstra, S.J. Logtenberg, K.H. Groenier, S.T. Houweling, H.J. Bilo, Effect of device-guided breathing exercises on blood pressure in patients with hypertension: a randomized controlled trial, Blood Press 18 (5) (2009) 273–279.

[30] S.Z. Wang, S. Li, X.Y. Xu, G.P. Lin, L. Shao, Y. Zhao, et al., Effect of slow abdominal breathing combined with biofeedback on blood pressure and heart rate variability in prehypertension, J. Altern. Complement. Med. 16 (10) (2010) 1039–1045.

[31] H.Y. Tang, V. Harms, S.M. Speck, T. Vezeau, J.T. Jesurum, Effects of audio relaxation programs for blood pressure reduction in older adults, Eur. J. Cardiovasc. Nurs. 8 (5) (2009) 329–336.

[32] G. Parati, R. Carretta, Device-guided slow breathing as a non-pharmacological approach to antihypertensive treatment: efficacy, problems and perspectives, J. Hypertens. 25 (1) (2007) 57–61.

[33] R. Jerath, J.W. Edry, V.A. Barnes, V. Jerath, Physiology of long pranayamic breathing: neural respiratory elements may provide a mechanism that explains how slow deep breathing shifts the autonomic nervous system, Med. Hypotheses 67 (3) (2006) 566–571.

[34] S. Julius, A.V. Pascual, R. London, Role of parasympathetic inhibition in the hyperkinetic type of borderline hypertension, Circulation 44 (3) (1971) 413–418.

[35] C.N. Joseph, C. Porta, G. Casucci, N. Casiraghi, M. Maffeis, M. Rossi, et al., Slow breathing improves arterial baroreflex sensitivity and decreases blood pressure in essential hypertension, Hypertension 46 (4) (2005) 714–718.

[36] A.S. Cifu, A.M. Davis, Prevention, detection, evaluation, and management of high blood pressure in adults, JAMA 318 (21) (2017) 2132–2134.

[37] J.D. Bundy, C. Li, P. Stuchlik, X. Bu, T.N. Kelly, K.T. Mills, H. He, J. Chen, P.K. Whelton, J. He, Systolic Blood Pressure Reduction and Risk of Cardiovascular Disease and Mortality: A Systematic Review and Network Meta-analysis, JAMA Cardiol. 2 (7) (2017) 775–781.