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Lifestyle Modification in Blood Pressure Study II (LIMBS): Study protocol of a randomized controlled trial assessing the efficacy of a 24 week structured yoga program versus lifestyle modification on blood pressure reduction ☆,☆☆,★

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ABSTRACT

Hypertension is a major public health issue affecting 68 million adults in the United States. Lifestyle modifications including complementary therapies such as the movement based mind body practice of yoga have become increasingly popular in the United States and have been considered as a potential alternative to medication in blood pressure reduction. We completed a pilot study in 2009 which showed meaningful decreases in 24-hour ambulatory blood pressure readings after a 12 week period of yoga participation. Based on data from our pilot study we are now completing The Lifestyle Modification and Blood Pressure Study (LIMBS II) which is a phase 2 randomized controlled trial designed to determine the effects of yoga therapy and enhanced lifestyle modification on lowering blood pressure in pre-hypertensive and stage 1 hypertensive subjects. Using 24-hour ambulatory blood pressure monitoring, LIMBS II aims to compare the effects on blood pressure reduction in subjects randomized for 24 weeks to one of the three following groups: yoga therapy versus blood pressure education program (sodium restriction and walking program) versus a combination program that involves components of both groups. LIMBS II will also examine the impact that changes in blood pressure have on cerebral blood flow. If successful, the LIMBS study will determine if yoga therapy combined with enhanced lifestyle modification will result in clinically meaningful decreases in blood pressure and thus can be implemented as an alternative to drug therapy for patients with prehypertension and stage 1 hypertension.

1. Introduction

Hypertension is a major public health issue affecting more than 70 million US adults and is a major risk factor in the development of stroke, cardiovascular (CV) and chronic kidney disease [1]. Patients with high normal blood pressure (BP)

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(Systolic BP of 130–139 mm Hg or Diastolic BP of 85–89 mm Hg) fall into the category of pre-hypertension [2] and are also at an increased risk for adverse CV events compared to normotensive controls [3]. Lifestyle modifications (LSM) have been recommended as first line approach for both prehypertensive and stage 1 hypertension patients [2]. LSM such as weight loss, dietary sodium reduction, limiting alcohol intake, aerobic exercise and adopting the DASH diet (a diet rich in fruits, vegetables, and low fat dairy products with a reduced content of saturated and total fat) have been shown to lower systolic BP in the range of 4–9 mm Hg [4,5]. Complementary and Alternative Medicine (CAM) modalities including mind-body therapies (MBT) have been used in managing modest elevations in BP [6]. Yoga has been shown to be one of the most popular CAM therapies with growing use particularly in older hypertensive patients [7–10].

Although yoga has been beneficial in treating a variety of medical conditions [11,12] limited data suggest a benefit of yoga on hypertension. There are now a number of published studies investigating the effects of various forms of yoga on hypertension [13–21] however there are only 6 randomized controlled trials (RCT) of any form of yoga for hypertension [13,17–21]. This includes our own previous study which demonstrated clinically meaningful reductions in 24-hour ambulatory BP readings with yoga [19].

It is not clear how the effects of MBTs on the brain result in changes in BP although there is evidence suggesting that there might be a specific relationship between frontal lobe activity and BP [22]. Previous work from our group and others has shown that the medial prefrontal cortex and anterior cingulate gyrus areas are activated during attention focusing tasks [23–25]. We have also observed increased regional cerebral blood flow (CBF) in the prefrontal cortex and anterior cingulate gyrus during several different types of meditation practices and yoga relaxation techniques [26]. Since yoga also involves physical activity, it is possible [40] that there will be an even greater enhanced effect on frontal lobe function via a combination of attention focusing and movement. One class of MRI perfusion techniques utilizes magnetically labeled arterial blood water as a noninvasive diffusible tracer for blood flow measurement. This approach has been termed arterial spin labeling (ASL), and can provide quantitative perfusion images in brain and other tissues.

The purpose of this study is to conduct a randomized clinical trial of yoga utilizing gold standard methodologies in the measurement of BP and neuroimaging techniques to rigorously evaluate the efficacy of a popularized form of yoga in subjects with prehypertension and stage 1 hypertension.

2. Methods

2.1. Study design

The Lifestyle Modification in Blood Pressure Lowering Study II (LIMBS) is a randomized, non-blinded prospective controlled trial to assess the safety and efficacy of a 24 week structured yoga program (YP) vs. blood pressure education program (BPEP) vs. combined intervention (YP and BPEP). The study population consists of adults with prehypertension to stage 1 hypertension who are not taking any antihypertensive medications. This study is being performed at a single center using a parallel design. The main outcome is mean awake and 24 hour systolic and diastolic ambulatory BP. Based on the power analysis, the established recruitment goal is 120 subjects aiming for 102 completers (34 subjects per intervention). Eligibility is determined by 2 screening visits with a mean

Table 1
Inclusion/exclusion criteria.

Inclusion criteria
1). Subjects must be willing able to give written informed consent.
2). Age $\geq$ 18 years, but <75 years.
3). BP criteria: SBP of $\geq$130, but <160 mm Hg.
4). Willing to comply with all study-related procedures

Exclusion criteria
1) Subjects who are pregnant or post partum <3 months.
2) Subjects currently taking BP lowering medications or dietary supplements (magnesium, potassium, calcium >1200 mg/day, fish oils, ephedra, hawthorn, forskolin, etc).
3) Stage II hypertension (SBP > 160 mm Hg OR DBP ≥ 100 mm Hg)
4) Non-dominant arm circumference >50 cm.
5) BMI ≥ 40.0 kg/m^2. Subjects with BMI above 40 may be enrolled if PI deems subject physically able to perform all study exercises.
6) Practicing yoga >1×/month in the previous 6 months
7) Received/used experimental drug or device within 30 days prior to screening, or donated blood $\geq$1 pint within 8 weeks of screening
8) Diabetes mellitus
9) Established cardiovascular disease
10) Known arrhythmias or cardiac pacemakers
11) Current users (within 30 days) of any tobacco products
12) History of renal insufficiency (glomerular filtration rate < 60 ml/min)
13) Women consuming >7 alcoholic drinks/week; men consuming >14 drinks/week.
14) Known autonomic neuropathy
15) Known secondary cause of hypertension (renal artery stenosis, pheochromocytoma, coarctation of aorta, hyperaldosteronism).
16) Benzodiazepine, anti-psychotic drugs (3 month stable use of SSRIs are allowed), or steroid use.
17) Known severe musculoskeletal problems such as spinal stenosis that may limit participation in yoga.
18) Use of other MBT such as Qi Gong, Tai Chi, meditation.
19) Lack of internet access
20) Presence of non-removable metallic foreign object, surgically implanted electrical device, surgically placed metallic clip (aneurysm clip), ear implants, any history of metal implants in the eye