Research

Effects of Yoga Versus Sham Yoga on Oxidative Stress, Glycemic Status, and Anthropometry in Type 2 Diabetes Mellitus: A Single-Blinded Randomized Pilot Study

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Abstract

Studies have shown a beneficial role of yoga in treating type 2 diabetes mellitus. The present study proceeds in the field by providing an active control. We aimed to evaluate the effect of 3 months of yoga on oxidative stress, glycemic status, and anthropometry in type 2 diabetes mellitus. Forty participants were randomized to receive either yoga (n = 20) or sham yoga (n = 20) as a control. Yoga included postures and breathing exercises, and nonaerobic stretching exercise comprised the control. Significant within-group differences in malondialdehyde, vitamin C, superoxide dismutase, fasting blood glucose, glycosylated hemoglobin, body mass index, waist circumference, and blood pressure were evident in both groups. Yoga participants had significantly greater improvement in reduced glutathione compared to controls. No significant differences between groups were observed in any other outcome variables. Yoga and sham yoga had identical effects on oxidative stress, glycemic status, and anthropometry in type 2 diabetes mellitus. Levels of reduced glutathione improved only in the yoga group. This research needs to be confirmed by larger and sufficiently powered studies. *Hegde et al. Int J Yoga Therapy 2020(30). doi: 10.17761/D-18-2020-00018.*

Keywords: yoga, sham yoga, oxidative stress, antioxidants, type 2 diabetes mellitus, randomized controlled pilot

Introduction

The global prevalence of diabetes mellitus is rapidly increasing as a result of population aging, urbanization, and associated lifestyle changes.[1] Type 2 diabetes mellitus is estimated to affect 552 million people worldwide.[2] India follows this global trend, with diabetes currently affecting more than 62 million Indians, a figure estimated to reach 98 million by the end of 2030.[2]

Oxidative stress is defined as excess formation and/or insufficient removal of reactive molecules such as reactive oxygen and reactive nitrogen species. Increased oxidative stress is widely accepted as a component in the development and progression of diabetes and its complications.[3,4] Glucose oxidation is believed to be the main source of free radicals in diabetes mellitus. Hyperglycemia stimulates oxidation of low-density lipoprotein (LDL) by a superoxide-dependent pathway. The ox-LDL is not recognized by LDL receptors and is taken up by scavenger receptors in macrophages, leading to foam cell formation and atherosclerotic plaques.[5] Glucose can interact with proteins, leading to the formation of advanced glycation endproducts.[6] Activation of sorbitol pathways by glucose is a component of diabetes complications like cataracts or peripheral neuropathy.[7,8]

Hyperglycemia not only promotes free radical propagation but also impairs the endogenous antioxidant defense system in diabetes.[9] Common antioxidants are both enzymatic (superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase) and nonenzymatic (glutathione and vitamins A, C, and E). The antioxidants work in

synergy with each other and against different types of free radicals. Reduced glutathione (GSH) acts as a direct scavenger as well as a cosubstrate for GSH peroxidase.[9] It is a major intracellular antioxidant required for the generation of a reduced antioxidant form of vitamin C. Vitamin C is a chain-breaking antioxidant that can generate vitamin E in its reduced form. Vitamin C deficiency results in decreased plasma GSH levels as a result of decreased conversion of glutathione (GSSG-oxidized) back to its reduced form.[10]

Superoxide dismutase (SOD) converts superoxide anion radicals produced in the body to hydrogen peroxide, reducing the interaction of anion radicals with nitric oxide to form reactive peroxynitrite. Activity of SOD is increasingly thought to be important for the regulation of oxidative status in diabetes. However, levels of this enzyme vary in diabetes patients. Some studies have reported decreased SOD activity,[11–14] whereas others have shown increases in its activity.[15,16] Several studies have revealed a higher magnitude of malondialdehyde (MDA; a marker of oxidative stress) and decreased antioxidant status with diabetes and its complications.[13,14,16–18]

Yoga is a well-accepted intervention in India to manage type 2 diabetes mellitus.[19] Yoga is a mind-body practice incorporating three major components: *asana* (physical postures), *pranayama* (breathing exercises), and meditation.[20] Previous controlled trials have reported that yoga can be beneficial for the control of oxidative stress and blood glucose in type 2 diabetes mellitus.[21–24]

A common methodological limitation of many yoga intervention studies is selection of appropriate control groups. For behavioral interventions, selection of a control condition can be a complex undertaking.[25] In addition to passive controls like waitlists[26,27] or usual treatment,[21,23,28–30] some investigators have employed relaxation,[31,32] exercise,[22,33] and walking[34,35] as active control arms. Several nonspecific factors, including interaction with the instructor, time spent in the intervention, attention, and expectancy effects, may affect the final outcome.[36,37]

Previous studies have shown that exercise and relaxation may lower oxidative stress in type 2 diabetes mellitus.[33,38] These control conditions may constitute a stronger comparison group for yoga. Hence, in the present study we used a stretching exercise group (referred to as "sham yoga") as a control. A *sham procedure* can be defined as one performed on a control group participant to ensure that he or she experiences the same incidental effects of the intervention as do those participants on whom the true intervention is performed.[39] Using sham yoga may help us to determine whether effects of yoga are "merely" exercise or whether yoga provides something more than does a physical activity. The present study was conducted to examine the hypothesis that 3 months of yoga benefits type 2 diabetes patients in control of oxidative stress, antioxidant variables, glycemic control, and anthropometry compared to sham yoga.

Methods

This randomized controlled pilot study was conducted in Mangalore, India. Participants were recruited from a screening camp for diabetes organized by Kasturba Medical College Hospital. Recruitment was open to all members of the community. The study was reviewed and approved by the Institutional Ethical Board, and written informed consent was obtained from all participants randomized to the study.

The camp included a lecture on diabetes management in the beginning. Visit 1 (day 1 of the camp) comprised a complete medical history, blood glucose measurements, electrocardiogram (ECG), serum creatinine, fasting lipid profile, microalbumin, and detailed dilated fundus examination to suggest any complication from diabetes. The study was described as a stress reduction program for type 2 diabetes mellitus. Inclusion criteria were type 2 diabetes patient with age not exceeding 75 years, nonalcoholic, nonsmoker, stable medication for the previous 30 days, willingness to engage in the "stress reduction" intervention, and a working telephone. Exclusion criteria were acute macrovascular complications, any form of severe infection, practicing any form of exercise, and previous enrollment in a yoga program. Walking for exercise and home yoga practice were also considered exclusion criteria.

Of the total 97 type 2 diabetes patients, 40 patients met the inclusion criteria and agreed to participate in the "stress reduction" program (Fig. 1). Patient randomization to either of the two arms—yoga or sham yoga—was performed on visit 2.

Randomization

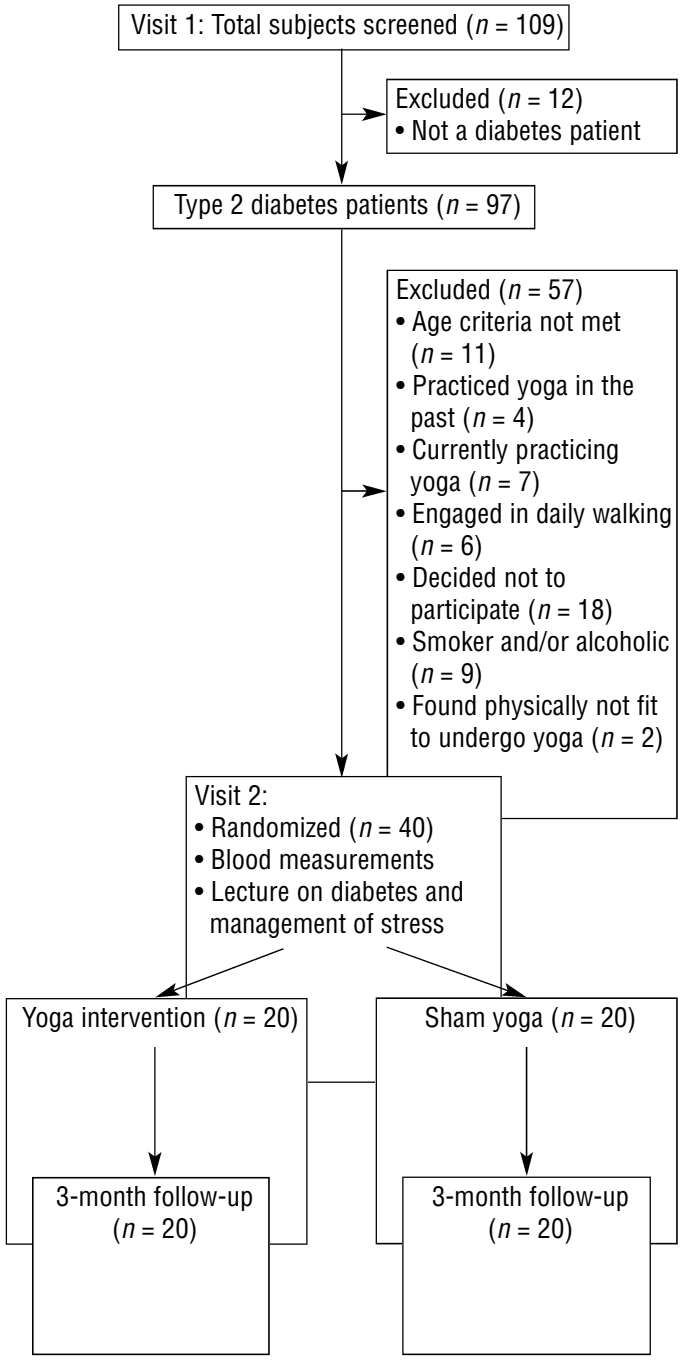
Participant allocation was randomized. Twenty papers with the word *yoga* and 20 with the words *sham yoga* were put in an opaque envelope, and the paper each subject drew out determined their group. After allocation, participants were aware of their group assignments.

Outcome Measures

Primary outcome measures were MDA, GSH, vitamin C, and SOD. Secondary outcomes comprised fasting plasma glucose, glycosylated hemoglobin (HbA1c), waist circumference, body mass index (BMI), and blood pressure. These were assessed at baseline and 3-month follow-up. The principal investigator performing the analysis was blinded to the intervention allocation.

Twelve-hour fasting blood samples were collected and centrifuged at 3,000 rpm to separate the plasma. Plasma

Figure 1. Flow Diagram of Subject Enrollment



glucose was measured by the glucose oxidase method and HbA1c by the particle-enhanced immunoturbidimetric method using DiaSys diagnostic kits. MDA and GSH in red blood cells were measured according to the methods of Stocks and Dormandy[40] and Beutler et al.[41] Plasma vitamin C and E levels were estimated by 2, 4-dinitro phenyl hydrazine[42] and Bieri et al.'s method.[43] SOD in red blood cells was measured by Beauchamp and Fridovich's method.[44] Weight was measured to the nearest 0.1 kg using digital scales while the subjects were minimally clothed without shoes. Height was measured in a standing position without shoes using a stadiometer. BMI was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured using a nonelastic measuring tape midway between the iliac crest and lower rib cage with the measurement taken at the end of expiration while the patient was breathing quietly. Blood pressure was recorded as the mean of the second and third readings taken 5 min apart in a seated position after the patient had completely relaxed.

Interventions

During the interventions, participants did not individually receive any type of counseling on diet/exercise/stress management. The classes were held in a community hall in two separate batches, one for yoga and one for sham yoga. Both classes were monitored by the same yoga instructor. Classes were held in a group format at different times in the evening. Both classes lasted for 75–90 minutes at a maximum, 6 days a week. Practices of yoga or exercise were never done continuously; there was always a gap between two yoga poses or exercises in the respective intervention groups to avoid exertion and fatigue. All participants were provided with printed material describing the intervention and a video of the respective interventions on a DVD. Classes had similar social interaction opportunities for participants.

The Hatha Yoga intervention comprised asana, pranayama, and savasana (Table 1).[24] Floor exercises *(vajrasana, pavana muktasana, bhujangasana, salabhasana, dhanurasana,* and *viparita karani)* were waived for patients with heart disease. Only these patients had a comparatively shorter duration of yoga. They were comfortably seated while others practiced.

Participants in the sham yoga group were taught nonaerobic exercises consisting of chair exercises, standing exercises, and 20 minutes of slow walking (Table 2). The active control arm was designed by the lead author (SVH) and coauthor (PA). Participants were asked to perform slow walking inside the community hall at the end of each class. Including the rest breaks, the total 75-minute time was approximately equivalent to that of the yoga class. None of the control exercises used breathing techniques taught in the Hatha Yoga sessions.

Compliance with the intervention was defined as attendance for a minimum of 3 days/week for a 3-month period as noted by the instructor. Home yoga was never discouraged, but it was not recorded during the study.

Attendance was measured as the total number of classes attended. Drug dosages for diabetes and blood pressure management in patients of both the groups were kept constant during the study period. Participants in the sham yoga group had access to 1 month of yoga classes after completion of this study, but they were not followed up to measure the outcome variables.

Statistical Analysis

Data were analyzed by intention to treat. Means and standard deviations were reported for continuous variables. Comparison of demographic data was done by student's unpaired *t* test and chi-square test (gender and attendance). As the variables were not normally distributed, the within-group pre and post comparisons were done by Wilcoxon signed rank sum test. The Mann-Whitney *U* test was used to study differences between the study and active control arms. All variables were analyzed using the statistical package SPSS, version 17.0. A p value < 0.05 was considered statistically significant.

Table 1. Asana and Pranayama Included in the Yoga Intervention

Asana	Duration (min)
Tadasana (mountain)	2
Padahastasana (standing forward bend)	3
Vriksasana (tree)	3
Trikonasana (triangle)	3
Parsvottanasana (lateral forward stretch)	3
Vajrasana (thunderbolt)	3
Vakrasana (seated twist)	4
Gomukhasana (cow-face pose)	4
Paschimottasana (seated forward bend)	4
Uttanapadasana (raised-leg pose)	4
Pavana muktasana (wind-releasing pose)	5
Bhujangasana (cobra)	3
Salabhasana (locust)	3
Dhanurasana (bow)	3
Viparita karani (inverted-action, or supported shoulder stand, pose)	4
Sitkari pranayama (teeth hissing)	8
Brahmari pranayama (bee breath)	6
Nadi shodhana (alternate-nostril breath)	10
Savasana (corpse)	10

Table 2. Nonaerobic Exercises and Walking Comprising the Sham Yoga Intervention (Control Group)

Activity	Duration (min)
Chair exercises	
Neck stretches	5
Shoulder shrugs	3
Shoulder circles	3
Seated leg raise	3
Knee lifts	3
Standing exercises	
Hip rotations	4
Knee rotations	4
Chest expansions	3
Backward bend	3
Forward bend	5
Side stretch	3
Heel walk	3
Toe walk	3
Slow walking	20

Results

Average attendance for both interventions was 90%–95% (Table 3). Class attendance did not significantly differ between the two groups. There were no dropouts by the end of the study period in either group. No adverse events were observed during the intervention. Mean age of participants in the yoga group was 57.10, which did not differ significantly from the 57.55 in the sham yoga group. There were no significant differences in gender, duration of diabetes, or hypertension between the groups at baseline.

There were significant reductions in MDA and SOD with both interventions (Table 4). Oxidative stress as analyzed by MDA values decreased by 12% in the yoga group and by 8.5% in the sham yoga group. GSH and vitamin C showed improvement in both groups. In between-group comparisons, yoga participants had significantly greater improvement in GSH (14%) than did the sham yoga group (5%). There were no significant between-group differences in fasting blood sugar, HbA1c, waist circumference, BMI, or blood pressure. There were, however, significant reductions in these secondary outcomes within both groups over the course of the 3-month study. Diastolic blood pressure did not show a significant reduction in the yoga intervention, unlike in sham yoga.

Discussion

Both yoga and sham yoga demonstrated favorable effects on oxidative stress parameters in type 2 diabetes mellitus. Yoga practitioners achieved a 12% reduction in oxidative stress compared to sham yoga (8.5%). Within-group differences in vitamin C and SOD were similar in both arms. GSH improved significantly in yoga participants compared to the sham yoga group. Although both groups had statistically significant within-group improvement in secondary outcome measures, there were no significant differences between groups. The sham yoga group experienced significant reduction in diastolic blood pressure.

Table 3. Baseline Characteristics and Class Attendance of Subjects in the Yoga and Sham Yoga Groups

Characteristic	Yoga (n = 20)	Sham Yoga (n = 20)
Male	11	10
Female	9	10
Age (y)	57.10 ± 5.99	57.55 ± 5.59
Duration of diabetes (y)	8.05 ± 8.15	8.95 ± 7.42
Duration of hypertension (y)	2.93 ± 4.68	3.46 ± 5.79
Class attendance (%)	93.4	92.7

Table 4. Mean (± Standard Deviation) Changes in Clinical and Oxidative Stress

	Yoga Group (n = 20)			Sham Yoga Group (n = 20)			
Variable	**Baseline**	**After 3 mo**	**Change at 3 mo**	**Baseline**	**After 3 mo**	**Change at 3 mo**	***p* Value**
Fasting plasma glucose (mmol/L)	8.0 ± 0.8	7.3 ± 0.7	0.7 ± 0.3*	8.1 ± 0.8	7.4 ± 0.6	0.7 ± 0.4*	0.764
HbA1c (%)	8.1 ± 0.6	7.6 ± 0.5	0.7 ± 0.3*	8.2 ± 0.5	7.7 ± 0.5	0.5 ± 0.3*	0.594
BMI (kg/m^2)	26.4 ± 0.7	25.2 ± 0.9	1.2 ± 0.7*	26.4 ± 0.7	25.4 ± 0.9	0.9 ± 0.5*	0.322
Waist circumference (cm)	92.0 ± 4.0	90.8 ± 2.9	1.2 ± 1.4*	91.7 ± 3.3	90.4 ± 2.5	1.3 ± 1.2*	0.585
Systolic blood pressure (mmHg)	144.4 ± 13.2	133.2 ± 11.8	11.2 ± 7.3*	145.3 ± 12.2	133.8 ± 11.7	11.5 ± 6.7*	0.714
Diastolic blood pressure (mmHg)	80.6 ± 7.9	79.6 ± 6.9	1.0 ± 2.9	82.0 ± 6.6	80.0 ± 6.7	1.9 ± 3.3*	0.251
Malondialdehyde (µmol/L)	52.6 ± 5.1	45.9 ± 4.1	6.6 ± 4.3*	52.8 ± 4.8	48.3 ± 3.7	4.4 ± 2.9*	0.110
Glutathione (µmol/gHb)	7.2 ± 1.3	8.2 ± 0.8	–1.0 ± 0.7*	7.6 ± 0.9	7.9 ± 0.6	–0.3 ± 0.7*	0.017
Vitamin C (µmol/L)	28.1 ± 4.0	29.5 ± 2.4	–1.3 ± 2.4*	28.3 ± 3.8	29.4 ± 2.4	–1.1 ± 2.3*	0.645
Superoxide dismutase (unit/gHb)	5,519.9 ± 402.3	4,974.6 ± 302.5	545.3 ± 258.5*	5,555.1 ± 354.5	5,017.6 ± 256.4	537.5 ± 238.6*	0.787

*Statistically significant (Wilcoxon signed-rank sum test). Between the groups there was no significant difference except glutathione (p = 0.017; Mann-Whitney U test).
HbA1c = glycosylated hemoglobin; BMI = body mass index.

Studies on Yoga Using Passive Controls

Several previous studies have discussed the effectiveness of a yoga intervention in control of type 2 diabetes mellitus.[21–24,28–30,33–35,45] Mahapure et al.[21] (6-week intervention), Jyotsna et al.[28] (6-week intervention), and Habibi et al.[30] (3-month intervention) found that yoga can significantly reduce glycemic index and SOD[21] compared to usual treatment. In our previous study,[23] we observed that 3 months of yoga can effectively reduce oxidative stress with improvements in BMI and glycemic parameters. In our earlier study, we noticed an increase in oxidative stress in the standard care group.

Vaishali et al.[45] (3-month yoga intervention) observed a significant decrease in fasting blood sugar and HbA1c levels compared with an educational group as the control. Skoro-Kondza et al.[26] did not find any significant improvement in weight, waist circumference, blood pressure, or HbA1c after 3 months of yoga compared to a waitlist control. This was the only study with very low attendance (50%) at yoga classes.

Studies on Yoga Using Active Controls

Subramaniyan et al.[34] showed that both yoga and brisk walking can decrease fasting blood sugar in 15 days without any significant difference between the two groups. McDermott et al.[35] found that 8 weeks of yoga improves waist circumference and BMI in type 2 diabetes mellitus compared to walking as a control. There was no between-group difference in fasting blood sugar, postprandial blood sugar, or insulin resistance. Gordon et al.[22] compared 24 weeks of yoga with traditional physical training as an active control. Both groups showed significant improvement in fasting blood sugar, MDA, and SOD with no difference between the groups. Usual care—here a passive control—did not show any change in the variables at the end of follow-up.

Compared to earlier studies on yoga, the present study's results are in accordance with studies using an active comparator.[22,34,35] Usual care as a control for mind-body interventions like yoga is limited for different nonspecific factors (e.g., expectancy effect, attention, time spent) that may confound study results. Group interaction in an intervention may constitute an important element that could be matched only by using an active control. In the present study, the control conditions were carefully matched for staff attention, class time, setting, and social interaction. In the current study, the yoga and nonaerobic exercise (sham yoga) groups both showed positive changes in oxidative stress markers, glycemic indices, and anthropometry without any differences between groups. Our study revealed, however, that practicing yoga can significantly improve GSH levels (endogenous antioxidant) compared to sham yoga. Our results are in accordance with few earlier reports on yoga.[23,24,46,47] A literature survey also showed that acute bouts of exercise can change the glutathione redox status of a cell toward an oxidized state.[48,49]

The sham yoga method employed here, being a form of physical exercise, could have had a similar effect. A larger, sufficiently powered trial with a longer follow-up is needed to confirm the results of this pilot study.

Conclusions

The results of our study indicate that yoga may help to improve GSH in type 2 diabetes mellitus. Over time, improvement in antioxidants could yield additional moderation of oxidative stress. Both yoga and sham yoga had a favorable effect on oxidative stress, vitamin C, superoxide dismutase, glycemic status, and anthropometric measures in type 2 diabetes mellitus. To further test any noticeable benefit of yoga versus sham yoga, future studies of longer duration and larger sample size are needed.

Conflict-of-Interest Statement

The authors have no conflicts of interest to disclose.

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