Yoga Training In Heart Failure (NYHA I-II) Reduces Oxidative Stress and Inflammation

Bandi Hari Krishna¹, Pravati Pal¹, G. K. Pal¹, M. G. Sridhar², J. Balachander³, E. Jayasettiaseelon⁴, Y. Sreekanth³, G. S. Gaur¹

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ABSTRACT

Krishna BH, Pal P, Pal GK, Sridhar MG, Balachander J, Jayasettiaseelon E, Sreekanth Y, Gaur GS. Yoga Training In Heart Failure Reduces Oxidative Stress And Inflammation. JEPonline 2014;17(1):10-18. The purpose of this study was to evaluate whether yoga training in addition to standard medical therapy can reduce oxidative stress and inflammatory markers in heart failure (HF) patients. The patients were randomly allocated either to the control group (CG) or to 12 wks of yoga training in the yoga group (YG). Blood samples were collected in the CG (n = 48) and the YG (n = 44) at the beginning and after 12 wks to assess the oxidative stress and inflammatory markers. Oxidative stress was assessed with total antioxidant status (TAOS), malondialdehyde (MDA), and redox ratio (RER). Inflammatory markers were estimated with high sensitive C reactive protein (hsCRP), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF alpha). TAOS improved 99.66% in the YG and 19.90% in the CG; MDA was reduced 59.49% in the YG and 19.90% in the CG; RER was reduced 77.19% in the YG and 20.59% in the CG; hsCRP was decreased 68.07% in the YG and 5.12% in the CG; IL-6 was reduced 33.96% in the YG and 20.59% in the CG; and TNF alpha was reduced 31.02% in the YG and 14.79% in the CG. These results indicate that the addition of yoga therapy to standard medical therapy for HF patients has a markedly better effect on reducing the oxidative stress and inflammation.

Key Words: Yoga Therapy, Total Antioxidant Status, Inflammatory Markers, Malondialdehyde
INTRODUCTION

Heart failure (HF) is defined as a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood (1,2). Clinical and experimental studies indicate that oxidative stress, described as an excess production of reactive oxygen species (ROS) about antioxidant defense, is enhanced in HF (3-6). Elevated levels of markers of oxidative stress such as plasma malondialdehyde (MDA) (7,8) and elevated levels of inflammatory markers such as interleukin-6 (IL-6) and high sensitive C reactive protein (hsCRP) (9,10) have been associated with HF, and increased levels of tumor necrosis factor alpha (TNF alpha) is associated with subjective New York Heart Association functional class (11).

Current therapy is based on afterload reduction by agents such as angiotensin converting enzyme (ACE) inhibitors, reduction of fluid retention by diuretics, drugs to enhance myocardial contractility and use of beta-blockers. With the existing therapy, the mortality rate remains high and the quality of life and morbidity are significantly impaired (12). Though these agents have improved the symptoms of congestive HF, prognosis is still poor. There is a need for alternative or further treatment strategies. This point is supported by Shapiro and colleagues (13) who indicate that exercise training is not enough to maintain the redox status of the body.

One immensely popular additional treatment strategy is Yoga (14). It is a mind and body relaxation technique that involves a set of physical exercises performed in sync with regulated breathing and meditation. La Rovere et al. (15) indicate that yoga benefits cardiac rehabilitation patients. It has also been suggested that yoga may decrease oxidative stress (16,17) and reduce MDA (18). In fact, in normal healthy subjects, Sinha et al. (19) indicate that yoga improves total anti oxidant status (TAOS). However, to our knowledge, the role of yoga therapy on oxidative stress in HF patients has not been investigated. We hypothesized that yoga therapy in addition to standard medical therapy may reduce oxidative stress, increase TAOS and reduce the inflammatory markers. Therefore, the purpose of this study was to evaluate the effect of yoga therapy on oxidative stress and inflammatory markers in HF patients.

METHODS

Subjects and Setting
The HF patients were recruited from the cardiology outpatient department of the Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India. The inclusion criteria consisted of patients: (a) with systolic and/or diastolic dysfunction; (b) with an ejection fraction of 30 to 50%; (c) who satisfied the New York Heart Association (NYHA) Class I-II; (d) who were able to walk without assistance; and (e) who were on stable medical therapy.

Patients were excluded from the study if they: (a) had chronic obstructive pulmonary disease; (b) were unable to attend Yoga sessions; (c) had orthopedic impediments to Yoga; (d) had undergone hospitalization within the last 3 months; and (e) suffered from myocardial infarction or recurrent angina within the last 6 months. The study was approved by the Institute Ethics Committee.

Nine hundred and 42 patients were initially interviewed regarding their participation in this study. Seven hundred and 48 patients did not meet the inclusion criteria, 64 patients declined to participate. One hundred and thirty patients were recruited and randomized into two groups. The Control Group (CG) (n = 65) received standard medical therapy while the Yoga Group (YG) received yoga therapy in
addition to the standard medical therapy. Forty-four patients in the YG and 48 patients in the CG completed the study.

Yoga Protocol
Yoga sessions were conducted at the Advanced Center for Yoga Therapy Education and Research (ACYTER), JIPMER, in the vicinity of the Department of Cardiology. Yoga therapy was designed in consultation with a cardiologist who was experienced in this form of therapy and research in conjunction with a yoga therapist with expertise in cardiac rehabilitation. Each session lasted ~60 min. After 2 wks of participation in monitored sessions, the patients practiced the same procedure for 3 days under our direct supervision and, then, 3 days at their homes for a total duration of 12 wks.

Modifications were made on an individual basis, according to each subject’s specific medical or orthopedic limitations. Chairs were used for those who were unable to stand up directly from the floor and the wall was used as a support during the standing-balance postures. Pranayama breathing exercises (i.e., breath awareness training) consisted of deep inhalation and exhalation in a 1:1 ratio, without breath retention. Inhalation was taught to commence with sequential involvement of the abdomen, lower chest and the upper chest, and, then the same sequence was performed in reverse, during exhalation. Meditation and relaxation practice were performed in a supine or seated position according to the subject’s comfort level and preference.

Baseline and Clinical Characteristics
Age, gender, height, and weight were recorded for all the subjects. The medical chart was reviewed for the following clinical characteristics: hypertension, diabetes, coronary artery disease, pulmonary disease, NYHA classification, and ejection fraction.

Blood Sampling
Blood was collected through venipuncture, which was allowed to clot and centrifuged at 3,000 RPM at 4°C for 10 min (Remi-refrigerated centrifuge) from which the serum was separated and stored in a frozen state at –80°C for analysis.

Measurement of TAOS, MDA, RER
TAOS and MDA, measured in the form of thiobarbituric acid reactive substances were analyzed by using a commercially available kit (Cayman chemical company). RER was calculated as the ratio of MDA and TAOS.

Measurement of Inflammatory Markers
The measurements of TNF alpha and IL-6 were performed using ELISA kits (Ani Biotech Oy, Orgenium Laboratories) while hs CRP was assessed using the ELISA kit (Diagnostic Biochem Canada Inc.).

Statistical Analysis
Statistical analysis was performed using the Statistical Package for Social Sciences 19 (IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp.). The data are expressed as mean ±SD. The Student’s Paired t-Test was applied for parametric data and the Mann - Whitney U Test was applied for non-parametric data to compare various parameters before and after intervention in the yoga group and the control group separately. To compare the change from baseline between the yoga group and the control group, the Student’s Unpaired t-Test was used. The null hypothesis was rejected at P≤0.05.
RESULTS

The baseline physiological characteristics of the 44 patients in the YG and the 48 patients in the CG are depicted in Table 1.

<table>
<thead>
<tr>
<th>Sl.no</th>
<th>Total Patients (n = 92)</th>
<th>Yoga Group (YG) (n = 44)</th>
<th>Control Group (CG) (n = 48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age (yrs)</td>
<td>49.34 ± 5.70</td>
<td>50.14 ± 4.54</td>
</tr>
<tr>
<td>2</td>
<td>Men / Women, n (%)</td>
<td>32 / 12, (72.72%) / (27.27%)</td>
<td>32 / 16, (66.66%) / (33.33%)</td>
</tr>
<tr>
<td>3</td>
<td>Height (cm)</td>
<td>162.74 ± 8.03</td>
<td>163.24 ± 6.88</td>
</tr>
<tr>
<td>4</td>
<td>Weight (kg)</td>
<td>70.16 ± 8.24</td>
<td>70.46 ± 6.71</td>
</tr>
</tbody>
</table>

The mean difference between the CG and YG groups and within the group differences for oxidative stress and inflammatory markers are presented in Table 2. As shown in Figure1, MDA reduced 59.49% in the YG and 15.81% in the CG, TAOS increased 99.66% in the YG and 19.9% in the CG, and RER reduced 77.19% in the YG and 20.59% in the CG. Figure 2 shows a decrease in the inflammatory markers assessed by hsCRP, IL-6, and TNF alpha while hs CRP decreased 68.07% in the YG and 68.07% in the CG, IL-6 decreased 33.96% in the YG and 10.41% in the CG, and TNF alpha decreased 31.02% in the YG and 14.79% in the CG.

<table>
<thead>
<tr>
<th>Sl.no</th>
<th>Parameter</th>
<th>Time (0 months)</th>
<th>Time (3 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TAOS (mM)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>0.40 ± 0.14</td>
<td>0.45 ± 0.16*</td>
</tr>
<tr>
<td></td>
<td>Yoga</td>
<td>0.50 ± 0.14</td>
<td>0.99 ± 0.33**$$</td>
</tr>
<tr>
<td>2</td>
<td>MDA (uM)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>11.41 ± 9.72</td>
<td>9.08 ± 9.08*</td>
</tr>
<tr>
<td></td>
<td>Yoga</td>
<td>11.98 ± 5.26</td>
<td>4.30 ± 1.87**$$</td>
</tr>
<tr>
<td>3</td>
<td>RER</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>31.60 ± 32.70</td>
<td>21.49 ± 21.53*</td>
</tr>
<tr>
<td></td>
<td>Yoga</td>
<td>26.22 ± 16.12</td>
<td>5.00 ± 2.9**$$</td>
</tr>
<tr>
<td>4</td>
<td>hsCRP (ng·ml⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>9062.71 ± 2103.66</td>
<td>8260.47 ± 2369.90*</td>
</tr>
<tr>
<td></td>
<td>Yoga</td>
<td>9192.26 ± 2568.93</td>
<td>2655.21 ± 1286.35**$$</td>
</tr>
<tr>
<td>5</td>
<td>TNF alpha (pg·ml⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>237.50 ± 89.15</td>
<td>185.75 ± 58.17*</td>
</tr>
<tr>
<td></td>
<td>Yoga</td>
<td>200.64 ± 81.45</td>
<td>128.74 ± 43.59**</td>
</tr>
<tr>
<td>6</td>
<td>IL-6 (pg·ml⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>312.38 ± 95.61</td>
<td>272.11 ± 91.89*</td>
</tr>
<tr>
<td></td>
<td>Yoga</td>
<td>311.54 ± 94.51</td>
<td>204.23 ± 73.21**$$</td>
</tr>
</tbody>
</table>

TAOS: Total Anti Oxidant Status, MDA: Malondialdehyde, RER: Redox ratio, hsCRP: high sensitive C-reactive protein, TNF alpha: Tumor Necrosis Factor alpha, IL-6: Interleukin 6. *Indicates within group, **Indicates between groups. *P<0.05, **P<0.01
DISCUSSION

Although significant advances have been made in pharmacological management of HF patients, one-third of the patients are admitted for exacerbation of HF symptoms (20). The findings indicate...
that the addition of a 12-wk yoga therapy program to standard medical therapy in patients with stable HF resulted in a safe and effective decrease in oxidative stress and inflammatory markers.

The findings over the past several decades in human and animal models of HF indicate that oxidative stress is increased in HF, which contributes to disease progression (21). Increased oxidative stress may cause cellular dysfunction, lipid peroxidation, and DNA damage. It may lead to irreversible cell damage and cell death, which has been implicated in a wide range of pathological cardiovascular conditions. The clinical importance of oxidative stress is increasingly emerging with respect to a pathophysiological mechanism of cardiac remodeling responsible for the development of progression of HF (22). It is disappointing that essentially no antioxidant strategy has translated to therapeutic in the treatment of HF. Potential explanations appear to comprise inadequate appreciation of the critical disease-modifying sources of reactive oxygen species, the use of a wrong antioxidant approach, or an incomplete understanding of individual variability in human antioxidant defenses (23). In fact, to our knowledge this is the first study that has explored the effect of yoga therapy in addition to standard medical therapy on oxidative stress. Kostaropoulos et al. (24) indicated that while catalase activity is mainly increased by aerobic exercise training (24), it is not sufficient to maintain the redox status of the body (19).

During the last 3 decades, extensive research has been done on yoga practices that combine structured physical exercises with breathing techniques and meditation. Previous findings (16,17) suggest that yoga can reduce oxidative stress by improving TAOS, reducing MDA, and by increasing superoxide dismutase and catalase activity (18) in healthy individuals. These findings support our study, where TAOS was significantly increased, and MDA and RER were significantly reduced in the YG compared to the CG. The reduction in RER was positively correlated with the inflammatory marker IL-6 (r = 0.338, P <0.05). This beneficial result could be due to the effect of the asana practice, as it has been proposed that the suspension of asana causes decrease in oxidant production, up-regulation of antioxidants, and mobilization of antioxidants from tissues to the blood (25).

Also, the meditation component of the yoga schedule might have contributed to this effect. It has been shown that meditation acutely increases circulating level of melatonin (26), which leads to the activation of pineal gland (27). Melatonin, being small and amphophilic, distributes throughout all tissue components and fluids. It can be found in greatest subcellular concentrations in mitochondria (28). Melatonin has been shown to protect healthy tissues from a wide range of offending agents like toxins, radiation, caloric, and metabolic insult through antioxidant and anti-apoptopic mechanisms in healthy tissues (29,30). Pranayama practice in the yoga schedule might have a role in reducing the oxidative stress. As an example, diaphragmatic breathing has been reported to reduce oxidative stress by decreasing cortisol that which inhibits enzymes responsible for the antioxidant activity of cells and by increasing melatonin, which is a strong antioxidant (31).

Inflammatory markers such as hsCRP and IL-6 are increased in cardiac patients (9,10), and the TNF alpha is associated with subjective NYHA functional class (11). In the present study, the levels of hsCRP, IL-6, and TNF alpha were reduced significantly following the additional therapy of 12 wks of yoga compared to the CG. These findings point to another potential mechanism by which adjunct yoga therapy might improve endothelial function. That is, by improving inflammation and oxidative stress at the level of vasculature. The findings are also consistent with prior research by Pullen et al. (32) who reported that the effects of an 8-wk yoga program on inflammatory markers in HF patients reduction the IL-6 and hsCRP levels (32).
To assess the safety of the subjects during the yoga training, vital signs and blood pressure were checked before and after each session. In addition, the subjects were asked about muscle soreness before and after the yoga practice as well as any hospitalization or emergency department visits since the last yoga session. We found that there were no orthopedic injuries, cardiac symptoms (shortness of breath, light-headedness) or cardiac problems during or in relation to the yoga sessions.

CONCLUSIONS

The findings indicate that yoga training in addition to the standard medical therapy for HF patients was not only safe, but resulted in significant improvement in oxidative stress and inflammatory markers. Continued efforts should be made by researchers and clinicians to educate the stable HF patients regarding the benefit of yoga therapy in order to improve TAOS, reduce MDA, RER, and inflammatory markers.

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