Preventive Effects of a Three-month Yoga Intervention on Endothelial Function in Patients with Migraine

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Original Article

ABSTRACT

Background: Migraine is a neurovascular disorder and any interventions improving endothelial function may contribute to its treatment and prevention of vascular complications like ischemic stroke. Yoga has been shown to have several beneficial effects on cardiovascular systems. However, no randomized controlled studies to date have investigated its effects on endothelial function of migraineurs.

Methods: A total of 42 women patients with migraine were enrolled and randomized into either a Yoga exercise group or a control group. The control group received only medication for 12 weeks and the Yoga group was placed in yoga training program in addition to the same medical treatment. Blood test was given from all patients in order to measure plasma levels intercellular adhesion molecule (ICAM) and vascular cell adhesion molecule (VCAM) after yoga training program.

Results: Totally 32 patients were participated in the final analyses (yoga: $n = 18$, control: $n = 14$). By analyzing data between yoga and control groups after the treatment period, there was a significant decreased in plasma level of VCAM in yoga group compare with the control group (15.29 ± 2.1 ng/ml vs. 21.70 ± 3.0 ng/ml, $P < 0.05$), whereas there was no significant difference in ICAM level between groups (19.1 ± 1.8 ng/ml vs. 20.97 ± 1.9 ng/ml $P > 0.05$).

Conclusions: It seems that yoga exercises, as a complementary treatment beside pharmacological treatments, can be potentially an effective way of improving vascular functions in migraineurs.

Keywords: Asana, endothelial function, pranayama, yoga

INTRODUCTION

Yoga originates from Ayurveda-ancient knowledge that aims to realize the true sense of human life and tries to find remedies for diseases. It is a form of mind-body medicine and also a part of Complementary and Alternative Medicine.[1] It has been shown that yoga has the potential to improve chronic and

acute pain; however, the underlying mechanisms remained unknown. Based on evidences, these kinds of exercises may increase tissues oxygenation and release of enkefalins or endorphins.[2] Other potential mechanisms of action may include decreases in sympathetic nervous system activity or reductions in inflammatory markers.[3] Yoga creates not only inner, physical and emotional balance through the use of postures, called asanas, combined with breathing techniques or pranayama, but also has diverse clinical and non-clinical applications as a result of the degree of complexity and multidimensionality of these exercises. Yoga also may be helpful through reducing anxiety and depression of individuals deal with the emotional aspects of chronic pain.[4,5] A few studies investigating the effects of yoga on migraine have reported positive benefits. Migraine is the most common primary headache disorder.[6] Although its pathophysiology is still unknown, three different mechanisms including: Vascular, neurological and neuroinflammatory theories have been suggested for it.[7]

Migraine is associated with an increased risk for several vascular disorders, including ischemic stroke and coronary artery disease.[8] Altered vascular structure and function may be the underlying pathophysiology of migraine. Surveys have been shown endothelial dysfunction in patients with migraine without aura.[9-14]

Established techniques to detect Endothelial Dysfunction are divided at least into three large groups of functional, cellular and biochemical markers.[15]

Functional diagnosis of endothelial dysfunction includes tests of endothelium dependent vasorelaxation, arterial stiffness and pulse wave propagation. Flow-mediated vasodilatation which uses high resolution ultrasound equipment to measure the post-occlusive increase in diameter and flow of brachial or radial arteries is reflective of the shear stress-stimulated production of nitric oxide (NO).[16]

A broader appreciation of the endothelial functions can be obtained by study of the levels of molecules of endothelial origin in circulating blood. When the endothelium is activated, the direct products of endothelial cells (ECs) such as NO metabolites and adhesion molecules are released and let us know something about the status of the endothelium. In this category, it has been shown that intercellular adhesion molecule (ICAM) and vascular cell adhesion molecule (VCAM) can provide important information regarding the severity of Endothelial Dysfunction.[17]

Risk factors and other hazardous states for the vascular system induce up regulation of endothelial adhesion molecules such as VCAM-1, ICAM-1, selections (L, E and P) and integrins. These molecules are thought to regulate the attachment and transendothelial migration of inflammatory cells into the intima and trigger the inflammatory response to injury.[15] Among them circulating levels of soluble ICAM and VCAM are frequently used for monitoring endothelial function.[18]

The present study was designed to test the hypothesis that, whether 3 months of yoga training would have a greater preventive action on migraine headache and endothelial dysfunction in migraineours.

METHODS

Study design and setting

This study was a randomized, controlled trial conducted at physiology research center, Isfahan, Iran, from April to June 2012. The Ethical Committee of Isfahan University of Medical Sciences approved the project and the protocol. All participants gave written informed consent before baseline assessment and randomization.

Patients

Patients were recruited from Neurological Institute under the supervision of neurologist. All potential subjects were informed that we were conducting a study of a migraine treatment intended to reduce the negative effect on their personal, family and social lives. Evaluations (with diagnosis) were performed by neurologists and detailed case histories were taken by trained interviewers. The criteria for selection of the subjects among the other migrainous were according to the definition of the International Headache Society.[19] All the patients were in menstrual age and have not had any experience of yoga training before. They also did not have any other exercise during the treatment period and were taken similar drugs.

Eighty-five patients agreed to participate in the program. Forty-three patients were excluded.

Seventeen of them were omitted due to different medical treatments. Seven migrainous were crossed out for additional diseases and nineteen of them did not meet the inclusion criteria. The rest of migraine patients were accidently divided into two groups (yoga exercise group and control group). In the control group, four patients left the intervention because of worsening their symptoms, two refused to participate in blood test and one left the program because of her working problem. In experiment group, one patient refused to continue because of drugs' side-effects and two patients left the treatment due to unknown reason. Thirty-two patients were finally analyzed.

Procedure

Patients were informed of the details of the treatment plan. The initial examination and medication were performed by a neurologist who confirmed the diagnosis of migraine. Personal information, family headache history, frequency and duration of headache and medication were recorded. Patients were randomly divided into two groups (yoga and control groups). The control group received only medication for 12 weeks and the yoga group was placed in yoga training program 3 sessions/week (each session 75 min) in addition to the same medical treatment. Yoga program were chosen from Hatha yoga Pradipika. It included asanas (yoga movements), pranayama (breathing exercises) and shavasanas (relaxation). Asanas largely deal with the positions which were related to the head and neck part although lower extremity exercises, arms and shoulders were also involved. Eye-related exercises, Pawanmuktasana, pre-pranayama and pranayama, Standing-sitting- and lying out screw position, Palming, Neti exercises and Shavasana were kinds of exercises which were done under the supervision of the trainer. Surya namaskar was another part of a program which includes 12 positions itself and it is mainly used for warm up, Stretch, strength and flexibility increase.

Blood test was given from all patients in physiology research center at Isfahan Faculty of Medicine in the morning between 8 am and 10 am in a fasting status. In the first session of exercises, patients were told to mark their headache frequency whenever their attack begins during these 3 months in the diary which was given to them. The Flow diagram of patient participation through the study is illustrated in the Figure 1.

Blood sample analysis

In order to measure ICAM and VCAM levels, 2 cc of a blood sample was obtained from the antecubital vein and plasma was extracted by centrifuging the blood sample. The plasma was aliquot and then stored at −70°C until assayed.

Statistical analysis

Statistical analyses were performed with SPSS 16 (SPSS Inc, Chicago, Illinois, USA) software by a blind analyzer. We calculated that a sample size of 30 patients was required to identify a difference of 1.25 in the number of migraine headache days/month with 80% power, with $P = 0.05$ as level of significance and assuming a common standard deviation of 2.5 for yoga and control groups. The results are expressed as mean ± standard error. Between groups differences were examined by independent-sample *t*-test $P = 0.05$ was considered significant.

RESULTS

The mean age was 35.4 ± 7.9 years old in the exercise group and 34.9 ± 8.37 years old in the control group. As it has been illustrated in Figure 2, when comparing yoga and control group after 12 weeks, a significant decreased levels of VCAM level was seen in yoga group (yoga group = 15.29 ± 2 ng/ml, control group = 21.70 ± 3.0 ng/ml, $P < 0.05$). Although blood ICAM level also decreased after 3 months treatment period, the difference was not significant (yoga group = 19.1 ± 1.8 ng/ml, control group = 20.97 ± 1.2 ng/ml, $P > 0.05$).

DISCUSSION

To the best of our knowledge, this is the first randomized controlled trial showed the effectiveness of yoga-based intervention on migraine headache and endothelial dysfunction. As a result, yoga was found to have a beneficial effect on various migraine parameters (frequency, intensity, duration of attack and medication score) and biomarkers of endothelial dysfunction.[20]

The benefits of yoga and meditation on cardiovascular disease (CAD) risk factors are

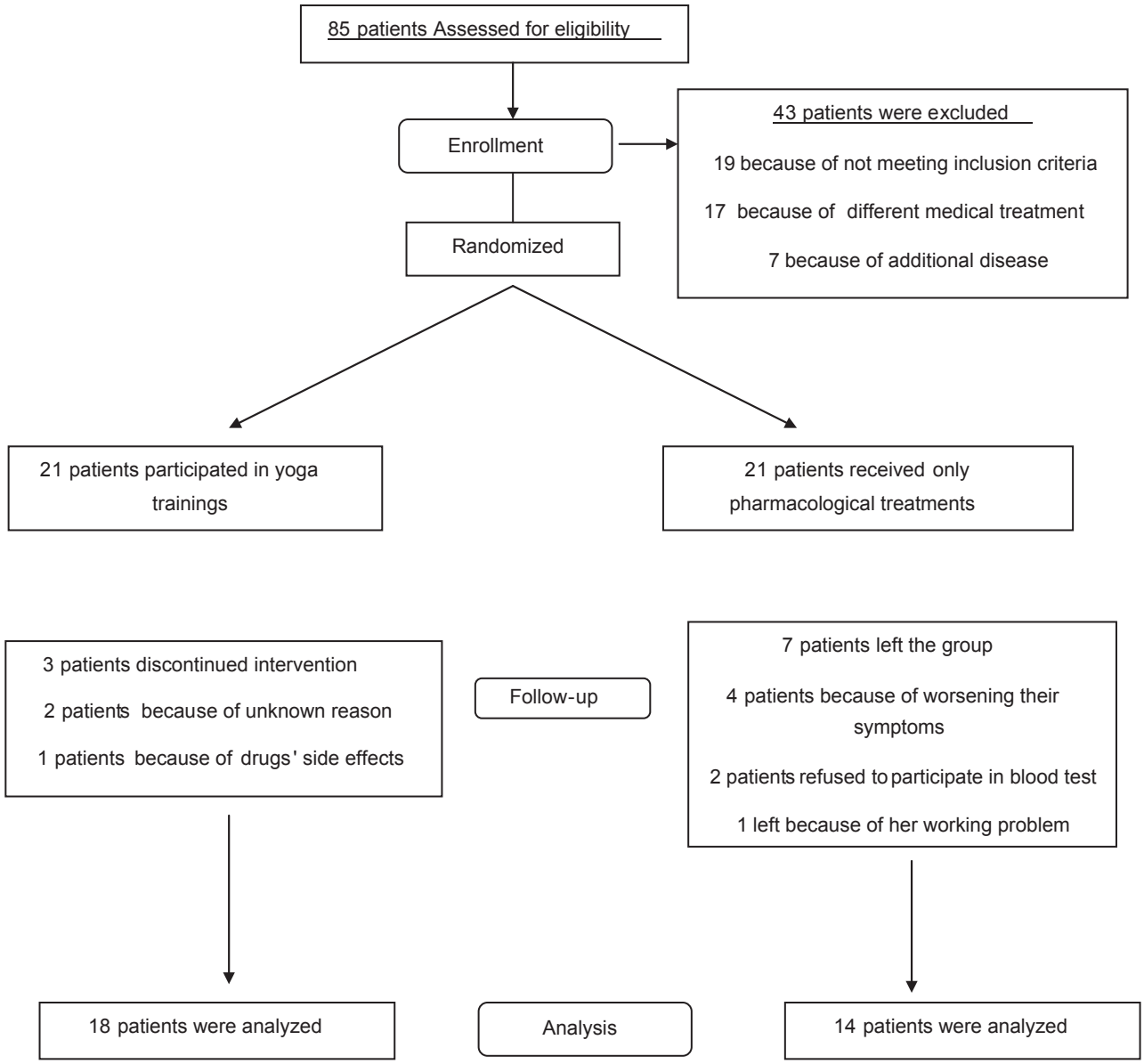

Figure 1: Flow diagram of patient participation through the study

well-known.[21] The underlying mechanisms of the observed beneficial effects of yoga on vascular function remain speculative; however are likely to happen through at least two pathways.[22]

Despite this fact that yoga cannot prevent or treat diseases itself, it relaxes muscles, regulate blood circulation and help patients feeling better in general. Yoga exercises reduce diastolic blood pressure and resting heart rate. It may be largely because of the reduction of sympathetic nervous system activity. Pranayama also seems to be an efficient method for balancing the autonomic nervous system and has a powerful influence on stress release,[20] as a significant risk factors of vascular dysfunctions.

Other important causes of vascular dysfunctions may be high blood pressure and loss of oxygen.[23] Pranayama leads to more oxygen delivery into the whole body including heart, brain and cells.[24] It is a commonly held belief that doing exercises consciously seems to play a key role. It reduces peripheral vascular resistance and regulates vessels' tone, the event which may help vessel walls related disorders. In addition, yoga asanas also improve

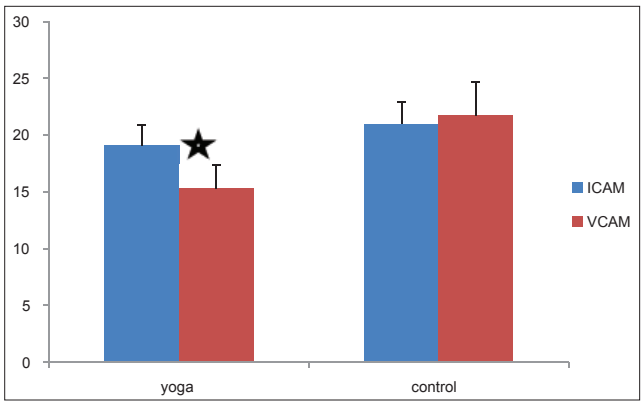

Figure 2: The comparison of serum levels of intercellular adhesion molecule (ICAM) and vascular cell adhesion molecule (VCAM) between yoga and control groups. Serum level of VCAM is significantly lower in yoga than the control group; however there is no significant difference between serum level of ICAM in two groups. (*$P < 0.05$ in compare with VCAM concentration in the control group)

the body's strength and flexibility which may help control blood pressure, respiration and heart and metabolic rates.[25] On the other hand, yoga training helps patients to cope with stress and Anxiety, the factors which are known to be the common causes of CAD.[26] Furthermore, it gives patients a deeper knowledge about themselves that can often lead to a healthy life-style and the elimination of the modifiable risk factors for CAD.[27] The physical and mental activities in yoga enhance vascular health and promote a feeling of well-being.[28,29]

Expression of VCAM-1 and ICAM-1 has been consistently observed in atherosclerotic vessels. There is accumulating evidence from prospective studies for a predictive role of elevated circulating levels of sICAM-1 in initially healthy people and of sVCAM-1 in patients at high risk or with overt CAD. VCAM-1 plays a major role in the initiation of atherosclerosis and is the most important adhesion molecules involved in monocyte recruitment to inflamed regions of vessels.[30,31]

Our study's most evident limitation lies in the absence of a placebo group; we find it impossible to develop a scientifically legitimate shame yoga technique. Consequently, patient expectation well might have confounded our results; the yoga group may have felt the need to assist in recording a favorable result, whereas the control group alternatively may have wished to demonstrate an unfavorable outcome. All the outcome measures were questioner-based and subjective and yoga therapy ideally should be tested with an objective derived outcome measure as well. Finally, we obtained no long-term follow-up data which would allow us to comment upon the durability of the treatment effect.

CONCLUSIONS

In summary, this study provides preliminary evidence that integrated yoga therapy can be an effective treatment for migraine and also improve vascular function. Additional trials employing objective outcome parameters with larger sample size need to be conducted to confirm our results and to determine the long-term effect of yoga.

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