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Is Yoga Effective in Reducing Fatigue in Patients With Multiple Sclerosis?

Melissa L. Hessler
Philadelphia College of Osteopathic Medicine, Melissahe@pcom.edu

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Melissa L. Hessler, PA-S

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ABSTRACT

Objective: The objective of this selective EBM review is to determine whether or not the use of yoga helps to improve fatigue in patients with Multiple Sclerosis (MS).

Study Design: Review of three randomized controlled trials (RCTs) published between 2004-current, all in the English language.

Data Sources: Three randomized controlled trials (RCTs), all of which evaluate the effectiveness of yoga compared to a control group that was asked not to change their exercise habits as they pertain to fatigue. All studies were found using PubMed and EBSCOhost.

Outcomes Measured: Each of the three articles analyzed the effects of yoga therapy on improving fatigue. The Fatigue Severity Scale (FFS), Modified Fatigue Impact Scale (MFIS), and Multi-dimensional Fatigue Inventory (MFI) were the questionnaires used to measure fatigue.

Results: One study found that yoga significantly reduced fatigue in MS patients. One study approached statistical significance in support for yoga as an effective therapy. One study was inconclusive.

Conclusions: Evidence is inconclusive. Future studies should focus on long-term effects of yoga and include subjects with more than minimal gait impairment.

Keywords: “multiple sclerosis” “yoga” “fatigue”

INTRODUCTION

Multiple Sclerosis (MS) is a demyelinating autoimmune disease of the central nervous system that results in many symptoms including mobility limitation, bowel and bladder dysfunction, and fatigue. MS is the most common disabling neurological disease of young adults.[1] Fatigue is a common symptom of MS, occurring in about 80% of people.[2] The patient with MS-related fatigue may feel constantly tired or may be easily fatigued from mental or physical exertion. Fatigue is one of the major barriers restricting people with MS from working.[2] Since MS affects approximately 400,000 people in the US with a prevalence of approximately 90 per 100,000, addressing fatigue may have a large impact on quality of life for MS patients.[3]

Multiple sclerosis is often an expensive disease and financial problems are compounded if the patient is no longer able to work due to fatigue. Total average costs are estimated at $47,215 per patient per year for those using disease modifying drugs (DMDs) to treat MS.[4] It is unknown how many healthcare visits per year MS patients make to manage their MS, but it is thought that patients with MS require more visits per person than all but a handful of other diagnostic groups.[5] This can be attributed to the multi-disciplinary approach that must be taken when treating a patient with MS. Most patients require more than DMDs alone to manage their symptoms. Other therapies include complex and expensive pharmacological agents, multidisciplinary medical and rehabilitation services, and assistive technology.[5]

While there are still many unknowns about MS, it is widely believed to be an autoimmune attack on the body's own cells. The myelin sheath, the fatty protective covering that surrounds nerves and aids in nerve signal conduction, is damaged, causing nerve signals to slow down or stop. The exact cause of the disease is still unknown but there appears to be genetic and environmental factors, like viruses, involved. MS is diagnosed by ruling out other conditions.[6]

Symptoms vary because nerves in any part of the brain or spinal cord can be damaged, causing the location and severity of each attack to be different. Common presenting symptoms include muscle weakness, problems moving arms or legs, numbness, tingling, or burning sensation, loss of balance, incontinence, double vision or vision loss, painful muscle spasms, dizziness, depression, erectile dysfunction, or fatigue.[6]

Typically MS is treated using disease modifying drugs (DMDs). For acute exacerbations ("attacks"), corticosteroids may be used. Other medications are taken on a regular basis to lower the rate of relapses and reduce the rate of formation of new lesions in relapsing-remitting MS. These include beta interferons, glatiramer acetate (Copaxone), dimethyl fumarate (Tecfidera), fingolimod (Gilenya), teriflunomide (Aubagio), natalizumab (Tysabri), and mitoxantrone (Novantrone). Physical therapy, muscle relaxants, and medications to reduce fatigue are often used to manage symptoms.[7]

Fatigue is often a difficult symptom to treat. Medications such as amantadine and modafinil are commonly prescribed to treat MS-related fatigue. Yoga is being proposed as an alternative therapy to medication for the reduction of fatigue due to MS. Yoga can be less expensive than medication and carries the added benefit of potentially improving other deficits caused by MS such as impaired balance and mobility limitations.

OBJECTIVE

The objective of this selective EBM review is to determine whether or not "Is yoga effective in reducing fatigue in patients with Multiple Sclerosis?"

METHODS

The studies in this systematic review included only adults with multiple sclerosis (MS). Each of the studies compares yoga therapy to participants' normal exercise routines in adults with MS and analyzed yoga's effects on improving fatigue. Included in this analysis was a randomized controlled trial comparing yoga three times per week for eight weeks to a control group in which subjects' followed their own routine treatment/exercise program. The second randomized controlled trial compared yoga once per week for ten weeks to a control group that was asked not to change their regular exercise habits. The third randomized controlled trial compared yoga once per week for six months to a waiting list control group who was asked to maintain their usual exercise program if they had one. The outcomes measured the efficacy of yoga in reducing fatigue using subjective questionnaires including the Fatigue Severity Scale (FFS), the Modified Fatigue Impact Scale (MFIS), and the Multideminensional Fatigue Inventory (MFI).

The data sources collected for this EBM review were found through researching PubMed and EBSCOhost from December 2013 through December 2014. The keywords used in the searches included "yoga" and "fatigue" and "Multiple Sclerosis." All articles were written in English and published in peer-reviewed journals. The articles were chosen based on their relevant outcomes to the topic and the importance of their information for patients. Each article was carefully selected to ensure it addressed a POEM (patient oriented evidence that matters), in this case fatigue, and was within the Physician Assistant scope of practice. Articles were also selected based on type of study (randomized controlled trial). Included in these studies were subjects with physician-diagnosed Multiple Sclerosis over the age of 18 who scored 6.0 or less on the Expanded Disability Status Scale, in other words, those who required at most unilateral

support to walk outdoors. Persons with MS were excluded if they had a previous relapse or began steroid therapy in the 12 weeks prior to participating in the first assessment, were pregnant, or had a comorbidity that severely impacted their ability to safely participate in exercise. Specifically, those who had cardiovascular disease, liver or kidney failure, symptomatic lung disease, diabetes, thyroid disorders, gout or orthopedic limitations, or were addicted to cigarettes, alcohol, or drugs were also excluded. The summary of statistics reported or used included p-values, mean change from baseline, paired t-tests, Turkey test, and analysis of variance (ANOVA). The demographics of each study can be found in Table 1 below.

Table 1: Demographics and characteristics of included studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Ahmadi (2013)[8]	RCT	21	19-54	Physician diagnosed MS with a Expanded Disability Status Scale (EDSS) score of 1.0-4.0	Cardiovascular disease, liver or kidney failure, symptomatic lung disease, diabetes, thyroid disorders, gout, orthopedic limitations, pregnant, or addicted pts (cigarettes, drugs, alcohol)	0	60-70 minute yoga class, three times per week for 8 weeks
Garrett (2013)[9]	RCT	148	>18	Pts had clinically diagnosed MS and used at most unilateral support to walk outdoors	Pts with previous relapse or began steroid therapy in the 12 weeks prior to the first assessment, were pregnant, or had a comorbidity that severely impacted their ability to safely participate in exercise.	36	60 minute yoga class, once per week for 10 weeks
Oken (2004)[10]	RCT	42	>18	Pts had clinically diagnosed MS, and EDSS less than or equal to 6.0	Insulin-dependent diabetes, uncontrolled hypertension, liver or kidney failure, symptomatic lung disease, alcoholism/drug abuse, symptoms or signs of CHF, ischemic heart disease, symptomatic valvular disease or corrected visual acuity worse than 20/50 binocularly.	6	90 minute yoga class, once per week for 6 months

OUTCOMES MEASURED

The outcome measured is improvement in fatigue. Ahmadi et al[8] measured improvement in fatigue using a 9-item self-reported questionnaire called the Fatigue Severity Scale (FFS) which is designed to assess the severity of fatigue and its effects on a person's activities and lifestyle. Garrett et al[9] measured fatigue using the 21-item Modified Fatigue Impact Scale (MFIS), which is a modified version of the Fatigue Impact Scale, designed based on interviews with MS patients concerning how fatigue impacts their lives. Oken et al[10] measured fatigue outcomes using the Multi-Dimensional Fatigue Inventory (MFI), a 20-item self-reported questionnaire designed to measure fatigue. Questionnaires were completed at baseline and after the yoga intervention. The fatigue measurements were analyzed using p-values, mean change from baseline, paired t-tests, independent t-tests, Turkey test, and analysis of variance (ANOVA).

RESULTS

Results of three randomized controlled trials are evaluated in this systematic review. All studies provided continuous data that could not be converted to dichotomous format. Test statistics reported included p-values, confidence intervals, and mean change from baseline.

Ahmadi et al[8] compared an 8 week program of Hatha yoga (n=11) to a control group where participants followed their routine exercise program (n=10). Included in the yoga group were female patients with physician-diagnosed Multiple Sclerosis over the age of 18 who scored 1.0 to 4.0 on the Expanded Disability Status Scale. Patients using MS disease modifying drugs were also included. Additionally, participants were required to be able to walk on the treadmill with or without hand support (without human assistance) and be able to walk at a constant speed on a treadmill for five minutes. See Table 1 for exclusion criteria. The yoga classes were 60-70

minutes in duration and three sessions per week. The yoga teacher was familiar with problems common to those with MS so breathing techniques and supported poses were utilized. Attrition rate was 0%. Paired t-tests were used to determine within-group differences in fatigue. Fatigue levels were significantly lower during post-test than pre-test in the yoga group by 38.69% (p=0.01) with a negligible increase of 1.43% (p=0.82) in the control group. The mean difference in FFS score between the yoga and control groups was 1.59 (p = 0.03), determined using Turkey Test. See Table 2 below for the results.

Table 2. Interventional Baseline Changes in FFS Score at 8 weeks

	Yoga group (n=11)	**Control group (n=10)**
Mean difference in FFS score between pre- and post-intervention	38.69% decrease (p = 0.01*)	1.43% increase (p = 0.82)
Mean difference in FFS score between groups (yoga vs. control)	1.59 (p=0.03*)	

The Garrett et al[9] study was an assessor-blind RCT that assessed the effects a 10 week yoga program (n=77) had on fatigue compared to a control group (n=71) asked not to change their exercise habits. Participants were physician-diagnosed MS patients over the age of 18 who used at the most unilateral support to walk outdoors. Participants were excluded if they had a previous relapse or began steroid therapy in the 12 weeks prior to participating in the first assessment, were pregnant, or had a comorbidity that severely impacted their ability to safely participate in exercise. The yoga classes were conducted in groups of eight subjects for 60 minutes per week, once per week, for 10 weeks. Yoga classes included breathing exercises, range of motion or stretching exercises, and relaxation. Adherence was fair, with participants allocated to the yoga intervention attending a mean of 7.8 of the 10 classes. This study had an

attrition rate of 22.93% but the reasons for attrition were similar across groups and those who dropped out were not significantly different from those who remained in the trial. Fatigue levels were measured using MFIS score (0-84). Paired t-tests were used to determine within-group changes. Fatigue levels in the yoga intervention group decreased by 5.8 with a 95% CI (-9.2 – -2.4) p value <0.01 from pre-test to post-test on MFIS. Comparatively, in the control group, fatigue levels decreased by 1.1 (-4.4, 2.3) p = 0.512. Change in fatigue between the yoga and control groups was analyzed using independent t-tests on the change scores. The change in fatigue was shown to approach statistical significance in the yoga group compared to the control group (p=0.05). See Table 3 below for the results.

Table 3. Interventional Baseline changes in MFIS Total Score at 12 weeks

	Yoga group (n=63)	Control group (n=49)
Mean difference (95%CI) in MFIS score between pre- and post-intervention	-5.8 (-9.2 – -2.4)	-1.1 (-4.5, 2.3)
P-value (within group)	<0.01*	0.512
P value (yoga vs. control)		0.05*

*p < 0.05

The study conducted by Oken et al[10] compared a six-month yoga intervention (n=22) to a waiting-list control group (n=20). The waiting list group was told they could enroll in either a yoga or exercise class after that 6-month period at no cost. A neurologist reviewed medical records for diagnostic criteria for MS. Only subjects with an EDSS score of 6.0 or less (i.e., able to walk 100 meters with at most unilateral support) were allowed to enroll. Subjects were excluded if they had insulin-dependent diabetes, uncontrolled hypertension, liver or kidney failure, symptomatic lung disease, alcoholism/drug abuse, symptoms or signs of CHF, ischemic

heart disease, symptomatic valvular disease or corrected visual acuity worse than 20/50 binocularly. Also excluded were those who performed yoga or tai-chi in the last 6 months or were regularly performing aerobic exercise more than 30 minutes per day. The yoga classes were 90 minutes in duration once per week for 6 months. Iyengar yoga was performed. Yoga classes included supported poses and relaxation. Daily home practice was strongly encouraged. Attendance rate for weekly yoga class was 68% and home practice occurred on 51% of non-class days. Fatigue was assessed using the Multidimensional Fatigue Inventory (MFI) at baseline and 6 months. The authors calculated mean within-group MFI scores with standard deviation for each group. Change from baseline or between-group differences were not calculated, causing the study to be inconclusive in answering if yoga is effective in treating fatigue. Despite this, the MFI score at the end of the yoga intervention was significantly lower than at baseline ($p<0.01$). See Table 4 for results.

Table 4: MFI Scores Measuring General Fatigue

	Yoga (n=22)	Wait list (n=20)
Pre-intervention MFI score (SD)	14.7 ± 3.3	15.1 ± 3.4
Post-intervention MFI score (SD)	13.0 ± 2.9*	14.9 ±3.0

* $p < 0.01$

No adverse events related to the intervention were reported. Oken et al[10] was the only study that discussed adverse events, which included three for unrelated surgeries; one MS exacerbation in the yoga group; and one low back pain related to an auto accident. Yoga is a very safe intervention with few to zero adverse events associated with its practice.

DISCUSSION

Multiple Sclerosis is the most common disabling neurological disease of young adults.[1] Disease modifying drugs are often helpful in slowing the progression of the disease and reducing exacerbations but they do not improve the potentially debilitating fatigue that often accompanies MS. Medications such as amantadine (Symmetrel) and modafinil (Provigil) are the most commonly prescribed medications used to treat MS-related fatigue.[2] Many patients have begun to shift away from using medication to manage their symptoms, looking instead for alternative therapies such as yoga. Ahmadi et al[8] showed yoga to significantly improve fatigue compared to control group. The data approached statistical significance in Garrett et al[9] so we are unable to say the study conclusively supported yoga as an effective treatment for fatigue. Oken et al[10] did not directly compare the yoga group to the control group so it is inconclusive. Despite the inconclusive evidence, yoga is widely accessible and the expenses may be reimbursed or discounted by some insurance companies.[11]

All three of the studies limited enrollment to persons with mild gait impairment. Ahmadi et al[8] was forced to limit their study to women due to the exclusion criteria and the limited number of men available to participate. Ahmadi et al[8] was also limited by a small sample size – only eleven participants in the yoga group and ten in the control group. The study by Garret et al[9] may have included a selection bias because subjects were asked to self-refer to the study, so the results may not be valid for those who are not as positively predisposed to health-promoting exercise behaviors. Oken et al[10] was limited by the mostly female group of participants and acknowledges other potential mechanisms of action that could account for the improvement in fatigue such as socialization during yoga classes, placebo effect, and self-efficacy effect.

There are barriers to MS patients practicing yoga. Some aspects of a typical yoga class are not designed with MS patients in mind and may even be contraindicated in MS. For instance, MS symptoms can be exacerbated by heat.[12] Ahmadi et al[8] kept the yoga practice room around 23-26 °C (73.4 – 78.8 °F) so that MS symptoms would not be aggravated. Also, two of the three studies reviewed used supported poses during yoga practice to aid with balance but most community yoga classes do not employ supported poses. MS patients attending a regular yoga class may have difficultly with some of the unsupported poses due to impaired balance and fatigue. It is important for patients with MS to find an instructor who is well educated in pose modifications.

CONCLUSIONS

This systematic review of three randomized controlled trials comparing yoga therapy to a control group asked not to change their exercise habits shows that the effects of yoga are inconclusive in reducing MS-related fatigue. The Ahmadi et al[8] and Oken et al[10] studies were fairly small so larger studies and studies analyzing long-term effects of yoga therapy on fatigue may be more generalizable and advantageous to patients with MS. Also, all three studies reviewed were limited to those with minimal gait dysfunction. Future studies should include patients with increased gait dysfunction to broaden the spectrum of patients able to benefit from yoga therapy.

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