

Yoga Intervention for Patients with Systemic Lupus Erythematosus- A Research Protocol

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ABSTRACT

Introduction: Systemic Lupus Erythematosus (SLE) is one of the most common systemic autoimmune diseases with a wide range of clinical manifestations. SLE patients experience periods of exacerbation or flare and quiescent disease activity. An increase in the frequency of exacerbations or flares causes permanent organ damage, increased morbidity, and early mortality, which are mainly due to the increased activity of immune-mediated inflammatory reactions. Yoga interventions have an immunomodulatory potential that regulates the psycho-neuro-immune axis, moderates disease activity, and improves the Quality of Life (QOL) for patients.

Aim: To report the methodology for the six months specified yoga interventions to reduce the inflammatory markers and enhance health-related QOL among SLE patients.

Materials and Methods: A randomised controlled trial will be conducted with a sample size of 128 SLE participants. Newly diagnosed and treatment-resistant SLE participants, patients

more than 18 years of age, will be recruited. Participants will be divided into three groups: newly diagnosed, treatment-resistant SLE, and control; patients diagnosed with SLE within six months, unresponsive to “standard therapy” will be placed in the respective groups. Participants in the newly diagnosed and treatment-resistant groups will be given yoga sessions, and the effects will be compared with controls.

Results: A baseline and postintervention (after six months) assessment will be performed for all the patients. Primary outcomes like anti-double stranded Deoxyribonucleic Acid (anti-dsDNA), complements-C3, C4, and inflammatory markers like Interleukin 6 (IL-6), 10, 17, Interferon-gamma, and plasma micro-RNA will be measured and quantified. The secondary outcome will include measurement of health-related QOL using the Lupus-QoL questionnaire.

Conclusion: Yoga integration, along with conventional treatment for SLE, as adjunctive therapy might enhance physical functioning and improve psychological health.

Keywords: Autoimmune diseases, Inflammatory markers, Plasma micro-ribonucleic acid, Quality of life

INTRODUCTION

The SLE is an autoimmune disorder characterised by immune dysfunction, causing inflammation and tissue damage in various organs [1,2]. The overall global incidence of SLE ranges between 1.5-11 per 100,000 person-years, and the global prevalence ranges from 13 to 7,713.5 per 100,000 individuals [3]. In India, SLE affects one in every 1,000 people, out of which the majority are women [4]. Auto-antibodies are formed against the body's own tissues with the deposition of immune complexes in various organs like the skin, brain, lungs, kidney, and blood vessels [5]. The course and presentation of the disease vary with time [2].

Clinical manifestations of SLE vary due to the influence of various factors like genetics, hormones, and environmental factors [6,7]. SLE has both short- and long-term consequences in a person's life, limiting their physical, mental, and social functioning [8,9]. SLE does not have a cure, but the symptoms can be improved by medications like corticosteroids and immunosuppressants with inherent side-effects [10]. Despite the fact that SLE mortality has decreased, it remains high [11]. Cardiovascular disease, renal disease, and infections remain the most common causes of death in SLE [12,13]. The risk of developing complications can be decreased by reducing the frequency of flares and remissions [14]. The signs and symptoms of SLE mimic other diseases, which complicate the diagnosis further [15].

Of late, research has been focused primarily on the assessment of reliable biomarkers for early diagnosis and assessing the prognosis of the disease [16]. However, none has achieved the status of a surrogate endpoint to assess the outcome.

Yoga interventions that are intended to be given to the subjects have been practised for decades, with no known harmful effects

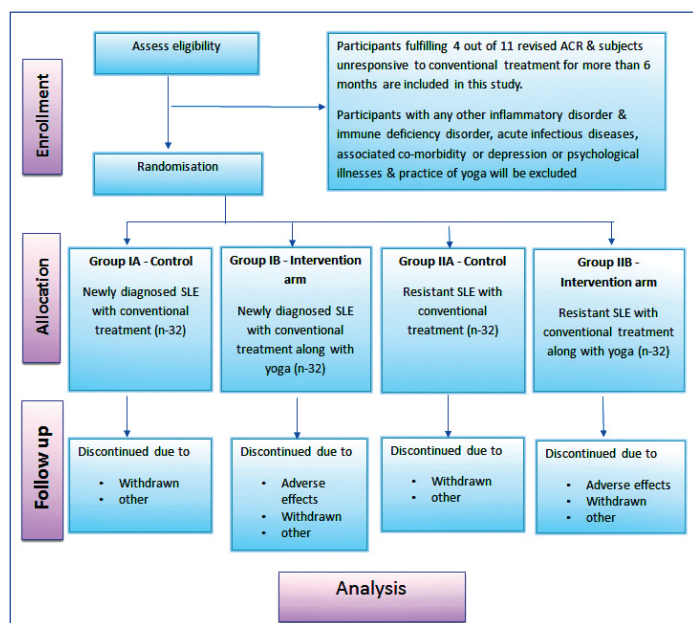
[17]. Efforts are made to ensure that protocols are suitable for the study population as well as accepted by yoga experts. A study by Middleton KR et al., which found that patients who practised yoga regularly reported less pain and could handle stress. There has been little research into the effects of yoga on SLE [18]. Patients also have experienced fewer lupus symptoms as yoga practise caused vagal dominance with subsequent inhibition of release of pro-inflammatory cytokines like IL-17 and Tumour Necrosis Factor (TNF)-alpha [19].

The intervention goals in SLE will minimise patient exposure to excessive corticosteroids and other immunosuppressive therapies and decrease the frequency of flare recurrence. There are very limited studies on the effects of yoga on the management of SLE. Conventional diagnostic tests like Antinuclear Antibodies (ANA), anti-ds DNA [20], and complement levels are used to diagnose and monitor disease activity. So, this study will be conducted with an aim to analyse the effect of yoga on inflammatory biomarkers such as IL-6, 17, and TNF-alpha and QOL in both newly diagnosed and resistant cases of SLE. The hypothesis is that yoga as a complementary therapy for patients with SLE will decrease the frequency of relapse and remission by diminishing the pro-inflammatory markers, stress markers, antibodies and reversing the damage observed in DNA.

MATERIALS AND METHODS

The present study, which will be a randomised controlled trial, which will be conducted on patients from Sri Ramachandra Medical College (SRMC) and ACS Medical College. The study is planned to start from January 2022 and completed by February 2023. Institutional Ethical Committee (IEC) approval from both the

institutes has been taken, vide letter numbers IEC-NI/21/FEB/77/39 (from SRMC), and 335/2021/IEC/ACSMCH (ACS Medical College and Hospital). The Clinical Trial registration: Ref/2021/03/041865. Outcome variables will be performed at baseline and after six months as depicted in [Table/Fig-1].



[Table/Fig-1]: Time plan.

Sample size: The sample size calculation will be based on a similar study that was conducted on 48 male participants [21]. With 80% power, two-tailed significance, an expected drop-out rate of 20%, and a 1:1:1 allocation, a total sample of 128 participants is estimated.

Randomisation and blinding: A confidential list of randomisations will be prepared either using computer-generated random numbers or coin tossing. The categorisation of allocation will be kept in a sealed cover for the research assistant to open following the assessment of baseline parameters. The allocation of participants can be unblinded as a result of participant withdrawal or adverse outcomes.

Selection of Participants

Inclusion criteria: Participants fulfilling 4 out of 11 revised American College of Rheumatology (ACR) classification criteria will be included in this study [22]. SLE subjects unresponsive to conventional treatment for more than six months will be involved in this study.

Exclusion criteria: Participants with a severe form of SLE (based on flares presenting with significant kidney disease, brain disease, very low platelet or red blood cell count, vasculitis) [23], any other inflammatory disorder or immune deficiency disorder, acute infectious diseases, associated co-morbidity or depression, or psychological illnesses will be excluded from this study. Participants practising yoga in the past 3-6 months will be excluded.

STATISTICAL ANALYSIS

All the data set will be assessed for normality using Shapiro-Wilk Test and based on the distribution parametric test or non parametric test of preference will be performed to find the intra and inter group variation using R statistical software version 4.0.2.

RESULTS

A total of 128 participants will be selected based on criteria and grouped into Group I: newly diagnosed SLE patients (n=64), Group II: resistant SLE patients, i.e., unresponsive to conservative treatment

(n=64). The participants will be randomised and subjected to the allocated intervention. Both newly diagnosed Group I and resistant SLE patients Group II are divided into two groups, A- control and B- intervention, with 32 participants in each. Yoga intervention details are shown in [Table/Fig-2].

Yoga practice	Duration	Target symptoms
Suryanuloma-viloma pranayama (right nostril breathing)	10 rounds of three cycle	Depressed mood, anorexia, weight gain
Bhramari Pranayama (humming bee breathing)	10 rounds of three cycle	Easy fatigability/loss of energy, frustration, anxiety and psychomotor agitation
Ujjayi pranayama	10 rounds of three cycle	Depressed mood, anorexia, insomnia, easy fatigability/loss of energy and psychomotor agitation
Pranava Japa (OM chanting)	5 min	Depressed mood, diminished memory, thinking and concentration, depressive ideation
Savasana (corpse pose)	5 min	Insomnia, easy fatigability/loss of energy. Psychomotor agitation
Deep Relaxation Technique (DRT)	20 min	Insomnia, depression and joint pain.
Yogic counselling	Weekly once	Depressive ideation, suicidal ideas, impairment in social and occupation functioning

[Table/Fig-2]: Details of yoga module proposed in the protocol for SLE patients.

Yoga technique: The yoga protocol will be adjusted according to the needs of SLE participants. Repetitive substantiations of the yoga protocol will be done by yoga experts to maintain the uniqueness and holistic approach of the yoga techniques [24]. The yoga sessions will be conducted at least three times a week, with each session lasting about 45-60 minutes. Daily home practises will be complemented either through online yoga sessions or with handouts on video recordings of yoga instructions and yoga practice. The participants who are willing to undergo online yoga sessions to practise at their homes will either join through online sessions or they can practise using the handout video. The intervention period will be for six months.

Components of the yoga intervention: Yoga interventions will be given in the form of asanas (postures), pranayama (breathing techniques), relaxation, and meditation. The participants will be given a video recording containing modules on yoga practises with instructions given by the yoga teacher to be practised at their convenience in their homes. This yoga intervention will take place over the next six months.

Sequences of specific classes: The sessions start with a prayer, then the participants will be subjected to mild stretching exercises, postures (asana), breathing practises (pranayama), relaxation techniques, and chanting with meditation. The yoga instructor will address the queries of the participants before the start of the session and also look into the physical status of every individual during and after the session is completed.

The aim of the intervention will be to decrease the stress, fatigue, and rate of relapse, thus reducing the complications associated with it. Though yoga can be customised for each individual, a standard protocol for everyone is needed. The present protocol is anticipated not to have many risks that could be associated with the intervention since the activities selected in this protocol are mild and are performed in comfortable supine posture.

Selection and instructors: Yoga trainers with certification will be identified and confirmed based on their experience in teaching yoga to people with chronic diseases. The selected instructor will be guided to teach the specific yoga practise to the participants.

Measurement of intervention fidelity over time: A manual checklist will be developed for the participants so as to document the practise session. A video recording of self-yoga practised at home will be entrained and brought with them to the direct contact session for further evaluation or modification.

Outcome Variables

Primary outcomes: Quantitative measurement of autoantibodies- Anti-dsDNA, ANA, Anti-cardiolipin; complements- C3, C4; Plasma micro-RNA; and pro-inflammatory markers- IL-6, IL-17, TNF-alpha, Interferon-gamma; anti-inflammatory markers- IL-10.

Secondary outcomes: Subjective health related QOL will be measured by lupus-QoL questionnaire containing 34 questions across eight domains i.e., on physical health, emotional health, body image, pain, planning, fatigue, intimate relationships, and burden to others [25].

All the parameters will be checked 'before' and 'after' six months of yoga intervention.

DISCUSSION

The positive effects of yoga on inflammation and immune response have been reported [26]. Regular yoga practice decreases the level of the pro-inflammatory cytokine IL-1 beta, which in turn enhances the immune response among individuals [27]. However, no such convincing evidence was reported for other cytokines such as IL-6, TNF-alpha, and C-reactive protein. Yoga practice increases the level of the anti-inflammatory cytokine IL-10, with a medium effect size [27]. In addition, yoga interventions help to maintain the oxidative stress and antioxidant levels among individuals, which would improve their immune function [28]. Furthermore, yoga has the potential to inhibit inflammatory processes at the transcriptional level as well. The mechanism of action of yoga intervention is vagal stimulation, which improves baroreflex sensitivity and lowers inflammatory cytokines and parasympathetic activation, which is associated with antistress mechanisms [29]. So, yoga could be recommended for immunocompromised people and could be implemented as a complementary and integrative therapy for effective management.

A study, conducted among 57 SLE patients, showed a better QOL with a reduction in stress, pain score, and sleep disturbance after yoga intervention [30]. The researchers used 60-minute yoga practises, including 16 sessions over a period of eight weeks at home. After completion of the study, the majority of the patients showed hesitation about incorporating the common yoga protocol, which is not designed for SLE specifically. So it shows the importance of developing a unique yoga protocol for patients with SLE. While developing a protocol for SLE patients, special consideration may be advised to include specific yoga poses that play an important role. Some yoga poses or techniques should be avoided and you should be cautious because they may damage or aggravate the inflamed joints. For these reasons, yoga interventions can be framed with an expert's opinion to meet the prime needs and care of the patients.

CONCLUSION(S)

The present study findings will provide high-quality clinical evidence on the efficacy and safety of the yoga protocol in the treatment of SLE patients. If the observations of this study ascertain the improvement in biomarkers and QOL among SLE patients, it could be recommended as an adjuvant therapy for better care and management for the patients along with conventional care.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Nov 16, 2021
- Manual Googling: Feb 07, 2022
- iThenticate Software: Mar 01, 2022 (6%)

ETYMOLOGY: Author Origin**AUTHOR DECLARATION:**

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Nov 12, 2021**Date of Peer Review: **Dec 23, 2021**Date of Acceptance: **Feb 08, 2022**Date of Publishing: **May 01, 2022**