



Original Research Article

A Randomized Controlled Trial: Evaluation of Yoga with IL6 as Biomarker in the Management of Knee Osteoarthritis

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ABSTRACT

Background: A proportion of people leading a sedentary and moderate lifestyle suffer from major chronic diseases like Osteoarthritis knee. Initially it was considered as degenerative disease only but now new data is emerging in favor of inflammation as a causative factor. Several non-pharmacological interventions are effective in bringing down the inflammation as well as relieving the symptoms of osteoarthritis. Yoga is a physical, mental and spiritual discipline originated in ancient India to improve or develop one's inherent power of healing in a balanced manner.

Materials and Methods: One hundred and twenty Patients of knee Osteoarthritis were randomized in the two groups' i.e. Group A with Conventional treatment of OA with adds on Yoga and Group B with conventional treatment of Osteoarthritis Knee only. They were assessed by measurement of inflammatory biomarker Interleukins 6 (IL-6) and WOMAC score (Western Ontario and McMaster University Osteoarthritis Index questionnaire) for clinical parameters of severity of Osteoarthritis knee before and after giving the Add on intervention of Yoga (follow up at the interval of 6 month). The assessments of means were compared and Significance of Chance calculated.

Results: There was a statistically significant fall in Interlukines-6 levels in Intervention group. Further, there was a significant reduction in doses of Analgesic drugs, being given to patients of Group A. Inflammation level increased significantly in those patients who left practicing yoga. Thus, with use of yoga therapy of Knee Osteoarthritis, requirement of analgesic drugs may be significantly decreased and in some cases may be withdrawn altogether, and it may be a useful adjunct in treatment of Osteoarthritis. Assessment by WOMAC had shown that Severity of pain was 3.267 times lower ($p=0.001$), Physical functions were 3.414 times Improved ($p=0.00$).

Conclusion: These results indicate that an intensive yoga therapy in Osteoarthritis Knee can help to improve inflammatory biomarkers and physical functions. Yoga is beneficial as an adjuvant when combined with the conventional therapy of Knee Osteoarthritis.

Keywords: Yogic asana, Osteoarthritis knee, Inflammation, Inflammatory marker, Physical symptoms, IL-6 (Interleukins 6)

INTRODUCTION

Osteoarthritis (OA), characterized by gradual loss of articular cartilage in the joint, is a leading cause of disability among the elderly people Altman, 2011;Ding *et al*, [1] Though the etiology and pathogenesis of OA is largely unknown, Osteoarthritis (OA) is the most widespread joint-affecting disease characterized by articular cartilage degeneration, subchondral sclerosis, osteophyte formation, and synovial inflammation. [2] It is also chronic degenerative condition of mobile joints, primarily a non-inflammatory disorder characterized by an imbalance between the synthesis and degradation of articular cartilage leading to classic pathological change of wearing away and destruction of cartilage Brandt *et al*, [3] It has been observed that about 80% of population has radiographic evidence of OA by the age of 65 years, although only about 60% of these were symptomatic. [4] Epidemiological profile of OA in India is not very clear but it is estimated that more than 30-40% of our population suffer from osteoarthritis beyond the age of 50 years. [5] Hip and knee OA represent a huge healthcare burden to society and a personal burden to individuals affected by the disease, in addition to being the main cause of the increasing need for joint replacements. [6] Though the mechanism underlying the development of OA is yet to be understood, several biochemical pathways have been found to be associated with the development of OA. [7] Joint pain is a primary clinical symptom with OA, with Knee pain being prominent in daily living with Knee OA. New data has shown that in OA the level of pro inflammatory markers is raised suggesting the involvement of inflammation as co factor in causation of Yoga. Regular physical activity is associated with lower levels of IL-6 and other pro-inflammatory cytokines, acute exercise transiently boosts production and release of IL-6 from skeletal

muscles; the IL-6 that is released during physical activity inhibits TNF- α production and can induce IL-10 production, one mechanism underlying exercise's anti-inflammatory function. [8] In addition to exercise and obesity, behavior affects inflammation through other pathways; even relatively modest levels of anxiety and depressive symptoms can raise pro-inflammatory cytokine production. [9] Additionally, psychological stressors can directly provoke transient increases in pro-inflammatory cytokines [10,11] and chronic stressors have been linked to sustained overproduction of IL-6. [12,13] Obesity is a primary risk factor for OA of the Knee. OA may lie in part with inflammation, because obesity and OA both are associated with high levels of biomarkers of inflammation including interleukins 6 (IL-6). [14] Relieving pain and stiffness and improving physical function are the important goals of present day therapy for OA. [15] There are many Non-opioid analgesics such as acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs), including cyclo-oxygenase II inhibitors the mainstay of drug treatment. [16] They reduce both pain and inflammation quite effectively, but their long-term use is associated with increased risk for gastrointestinal bleeding, [17] hypertension, [18] congestive heart failure, [19] renal insufficiency and other adverse effects. [20] Before deciding on specific non-pharmacologic and pharmacologic options, it is significantly elevated with exercise, and precedes the appearance of other cytokines in the circulation. During exercise, it is thought to act in a hormone-like manner to mobilize extracellular substrates or augment substrate delivery. [21] IL-6 is one of the most important mediators of fever and of the acute phase response of inflammation. The cellular effects of mechanical and fluid pressure on structures such as cartilage suggest that yoga postures might alter joint function. In experimental

settings, joint motion preserves cartilage that can be lost by immobilization. Correctly supervised yoga may be one way to provide the motion and forces on joints needed to preserve integrity,^[22] with this background; the current study was designed to analyze the serum cytokine (IL-6) to evaluate the effect of add on yoga asana with conservative management of OA knee.

Yoga is an ancient Indian science and way of life which talks about the origin of diseases.^[23] A growing body of evidence supports that yoga helps in attaining physical and mental health via down regulation of the hypothalamic–pituitary–adrenal (HPA) axis and sympathetic nervous system (SNS). This Mechanism is more important in young individuals. Alyson et al,^[24] Yoga therapy involves asana which not only strengthen quadriceps muscles but also relieves stress Elaine et al, hence may be effective in controlling hypertension.

Several studies point to the psychological benefits of yoga during health and disease. In a study on healthy adults, Vempati et al, .showed that the yoga-based guided relaxation can reduce the sympathetic activity as measured by autonomic parameters, oxygen consumption and breath volume.^[25]

MATERIALS AND METHODS

Study Subjects

One hundred and twenty Patients with osteoarthritis Knee were randomized in the two groups i.e. Group A with conventional treatment with add-on Yoga and Group B with conventional treatment of Knee Osteoarthritis only. They were assessed by measurement of inflammatory biomarker (IL-6) Level measured by ELISA-kit method and WOMAC score for clinical parameters of severity of Osteoarthritis knee before and after giving the Add on intervention of Yoga (follow up at the interval for 6 months).This

Randomized control Trail study consisted of men and women ≥ 40 years that fulfilled American College of Rheumatology (ACR) clinical and radiographic criteria for KOA Group A (60) and equal no of Group B were recruited from the outpatient clinic of the Department of Orthopedics Surgery of King Georg's Medical University, Lucknow. The patients A and Group B were matched for age and sex. These patients were profiled for demographic, clinical and radiological features. Age and sex were self reported. Patients were weighed with a calibrated balance beam scale to the nearest 0.1 kg in minimum possible clothing and standing height was measured (without shoes and shocks) with a Stadiometer in centimeters (cm). Body Mass Index (BMI) was recorded by Quetelet index. Among the 40 male and 80 female (including both groups) ages range from 40-72, mean age 54.49 ± 9.24 and 53.75 ± 8.47 years respectively. In the controls were male with mean age 54.50 ± 7.61 years and female with mean age 55.65 ± 8.59 years. The protocol for research work was approved by the human ethics committee of King Georg's Medical University, Lucknow. The protocol conforms to the provisions of the declaration of Helsinki in 1995. Informed consent was obtained from the study subjects for inclusion in the study before intervention. The both group patients were asked to fill up the detailed questionnaire regarding their occupation, socioeconomic status, medical history, life style habits.

In our study the patient's data were recorded immediately then they will be randomly allocated into two groups, based on computer generated random table Baseline parameters first visit at OPD then follow up at 6 months interval for the biochemical testing of inflammatory cytokines and WOMAC.

The selected interleukin-6 Level was analyzed in the enrolled patients at following intervals i.e. at 1st visit and at 6th

month. The peripheral venous blood (2 ml) was collected into E.D.T.A coated vials between 9.00 AM to 11.00 AM by using a sterile needle and then the biochemical examination was done by ELISA technique. The samples stored in the vials provided and store at -20 degree.

The Kellgren-Lawrence grade represents disease severity, as reflected on radiographs, Radiographic findings of OA were classified into mild (K-L grade 2), moderate (K-L grade 3) severe (K-L grade 4). Average BMI was 25.52 ± 3.58 . Symptoms related to KOA were assessed with the knee-specific WOMAC index (Bellamy, 1989), which assess pain (five items), stiffness (two items), Physical function (17 items), Social function, Emotional function and interpretation response in terms of a 5-point scale (0, none; 1- slight; 2- moderate; 3-severe; 4- extreme). The assessments of means were compared and significance of chance calculated.

Intervention for Yoga Group

Patients who met our inclusion criteria were randomized into two groups A & B. Group -A, All patients were given 45 min of integrated yoga therapy practice for five days in a week upto 6 months (120 days) along with conventional clinical treatment including physiotherapy and Group-B patients were given only conventional treatment including physiotherapy. The integrated yoga therapy practice included Virbhadrasan Supta Tadasan, Uttanpadasana, Dandasana, Paschimotasana, Traditional treatment in form of strengthening exercise Quadriceps drill, hot fomentation and paraffin wax bath to knee were given to both group. Tab-Paracetamol, orally in divided doses were given in both groups for initial ten days of treatment to relieve the initial pain. Clinical outcomes were assessed in terms of WOMAC (Western Ontario and McMaster Universities) score before and after giving the treatment at interval of 6th months.

Statistical Tools Employed

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean \pm SD. Wilcoxon signed rank test was used to evaluate the within group change.

RESULTS

The mean age of subjects in both study group A and B was 53.47 ± 9.98 and 53.73 ± 12.76 respectively.[Table 1]. When we compare the data after 6 months from base line data in Group-A We notice that there was significant decrease in IL6 values, Decrease in WOMAC Stiffness and Pain and Increase in WOMAC social functions. The change in WOMAC physical function was not statistically significant. The WOMAC Emotional function was decrease and found significant statistically. In group B there was decrease in IL6, WOMAC stiffness, Pain and emotional function but this difference was not significant statistically, there was an increase in WOMAC social function but it was again not significant statistically. The change in WOMAC Physical function was increased and it was statistically significant.

Table 1: Demographic and Anthropometric characteristics of patients in two groups

Characteristic	Group A	Group B	Significance of difference
Mean Age \pm SD (Range) in years	53.47 \pm 9.98 (40-70)	53.73 \pm 12.76 (40-70)	p=0.951
Occupation			
Business	0 (0.0%)	4 (26.7%)	p=0.185
Housewife	10 (66.7%)	6 (40.0%)	
Professor	1 (6.7%)	0 (0.0%)	
Retired	2 (13.3%)	2 (13.3%)	
Service	2 (13.3%)	3 (20.0%)	
Sedentary activity	11 (73.3%)	7 (46.7%)	p=0.136
BMI (kg/m ²)			
18.0-25.0	4 (26.7%)	3 (20.0%)	p=0.904
25.0-29.9	8 (53.3%)	9 (60.0%)	
\geq 30	3 (20.0%)	3 (20.0%)	

Table 2: Group-A: Comparison of Baseline and After 6 months of Add on yoga Treatment

SN	Parameter	Baseline		After 6 months
		Mean	Mean	p-Value
1.	Interleukin-6 (pg/mL)	4.26±0.58	1.18±0.97	0.001
2.	WOMAC Pain	10.53±3.66	3.73±1.67	0.001
3	WOMAC Stiffness	3.67±2.16	0.53±0.92	0.001
4	WOMAC Physical	11.53±3.70	25.27±7.69	0.005
5.	WOMAC Social	10.87±3.94	4.40±1.76	0.001
6.	WOMAC Emotional	9.80±4.26	2.73±1.83	0.001

Table 3: Group-B: Comparison of Before and After given the Traditional Treatment

SN	Parameter	Baseline		After 6 th months
		Mean	Mean	p-value
1.	Interleukin-6 (pg/mL)	3.89±1.67	3.38±0.28	0.002
2.	WOMAC Pain	7.80±3.38	6.60±2.80	0.002
3.	WOMAC Stiffness	2.87±1.88	2.73±1.22	0.660
4.	WOMAC Physical	11.53±3.70	15.20±2.02	0.001
5.	WOMAC Social	10.20±4.31	8.67±3.77	0.002
6.	WOMAC Emotional	9.27±5.26	7.87±5.48	0.020

DISCUSSION

In this study, a sequence of body postures was used specifically as an add-on intervention to existing therapeutic management of primary Osteoarthritis of knee. The results of this study indicate that 120 days course of yoga can be beneficial in reducing pain and stiffness in symptomatic knee OA patients. The intervention was safe; with no injuries experienced by participants. In this study we included five set of asana as well as pranayam practices which work on clinical parameters of OA knee. Kolasinski *et al*, [26] used a specific sequence of asana based on the teachings of Iyengar for eight weeks. They measured only the pain and physical functions by WOMAC and reported a significant reduction in pain by 46.7%. We also found in our pilot study on yoga for OA knees similar results and obtained the significant reduction ($P=0.01$) in pain and stiffness. Ranjita *et al*, [27] used a set of integrated yoga therapy program in a non-residential

camp set up for one week without any physiotherapy intervention and showed a 40% reduction in resting pain after yoga but In our study, we added yoga with standard treatment which showed a reduction in resting pain scores by 71.8% after 6th months. Haslock *et al*, [28] showed the beneficial effects of specific integrated yoga practices in patients with rheumatoid arthritis who had secondary OA in several joints. They observed better increase in hand grip strength (63%, left, 66% right) in yoga group than non yoga controls (8% left and 5% right) indicating reduced stiffness. Our study showed a reduction in early morning stiffness scores ($P=0.01$) after 6th months. Physical stressors activate immune and endocrine pathways that can enhance pro-inflammatory cytokine production. This study, designed as an initial investigation to address the mechanisms underlying yoga's potential inflammation-reduction benefits, Another randomized controlled study in patients with chronic neck pain, observed a reduction in Pain by add -on IAYT for neck pain and in present study too, we observed similar reduction of pain and 16% reduction in IL-6 after 6th months of intervention. A significant correlation observed in this study between pain and early morning stiffness after yogic intervention. None of the other yoga studies have noted morning stiffness as an outcome variable.

CONCLUSION

On the basis of result of this study we can conclude that Yoga can serve as an adjuvant with existing conventional treatment of osteoarthritis and prolong add on of yoga can even augment certain path physiological processes involved in progression of Osteoarthritis

Competing Interests: Authors have declared that no competing interests exist.

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