Therapeutic Potential of Curcumin with and without Strengthening Exercises in Improving Rheumatoid Arthritis

Maliha Khalid Khan[1], Imran Ahmad Khan[1] and Ammara Liaquat[2]

[1]*Department of Rehabilitation Sciences, Ali-Ul-Murtaza Muhammad Institute of Medical and Allied Sciences, Multan, Pakistan*
[2]*Department of Radiology, Govt. Shahbaz Sharif DHQ Hospital, Multan, Pakistan*

ABSTRACT

This study aimed to assess the synergistic effects of curcumin with and without strengthening exercises in rheumatoid arthritis (RA). Randomised controlled trial study was conducted from May 2021 to December 2021. Ninety patients were randomised into two groups. Group A was treated with strengthening exercises and curcumin. Group B was given curcumin only. Curcumin dosed at 180 mg/day was given orally to both groups. The treatment regimen was distributed as 3 sessions/week; each session lasted 45 minutes for group A. Serological findings and X-rays of the joints were also done for assessment. Pain, morning stiffness, and functional activities were assessed using the WOMAC and NPRS scale at baseline, 12th week, and 24th week. There was higher significant ($p<0.000$) reduction in quantitative values of RF, ESR and CRP, WOMAC pain, ADLs, and stiffness readings in group A. This study will project to a screening of newer and more effective interventions to treat RA.

Key Words: *Curcumin, Rheumatoid arthritis, Strengthening exercises.*

How to cite this article: Khan MK, Khan IA, Liaquat A. Therapeutic Potential of Curcumin with and without Strengthening Exercises in Improving Rheumatoid Arthritis. *J Coll Physicians Surg Pak* 2022; **32(12)**:1640-1643.

An autoimmune disease such as rheumatoid arthritis (RA) is a persistent, chronic inflammatory disease affecting many tissues, mainly joints. A systemic disease of unknown aetiology principally attacks the joints causing swelling, pain and loss of function.[1] The age of onset is mainly 45-60 years, but no age is immune to it.[1-3] Signs and symptoms of RA include pain, stiffness, and fatigue in the early morning, low-grade fever with increasing severity in the reduction of body. Functional and mechanical limitations include decreased range of motion (ROM) and muscle strength mainly affecting smaller joints of hands, feet, and wrists and larger joints are also involved.[1] Extra-articular signs might rarely appear. This leads to progressive biomechanical limitation. Swan-neck deformity (SND) and boutonniere deformity (BND) are the two most commonly seen digital deformities in RA. Therapeutic management of RA includes corticosteroids, NSAIDs, synthetic agents (DMARDs), and biological agents.[1] DMARDs (Disease-modifying antirheumatic drugs) are the most commonly used therapy for treating RA. These are expensive, and it is essential to switch or add other low-cost and effective treatments.

Correspondence to: Dr. Imran Ahmad Khan, Department of Rehabilitation Sciences, Ali-Ul-Murtaza Muhammad Institute of Medical and Allied Sciences, Multan, Pakistan
E-mail: imranahmadkhandurrani@gmail.com

Received: June 29, 2022; Revised: November 05, 2022; Accepted: November 07, 2022
DOI: https://doi.org/10.29271/jcpsp.2022.12.1640

Curcumin decreases muscle damage, thus reducing muscle pain and increasing muscle performance. Curcumin has anti-inflammatory activity, reduces oxidative stress by modulating the effect of pro-inflammatory cytokines such as TNF- and IL-6, and has antioxidant activity, all of which are beneficial in the treatment of RA.[2,3] Physical therapy intervention, mainly strengthening exercises, exerts immunomodulatory effects in managing RA. Strengthening exercises are essential in the rehabilitation programme of a patient suffering from RA.[1] The patient is subjected to muscle work against the resistive force during these exercises. So, the muscles can improve their power under external pressure and enable the person to move more effectively with less pain. These exercises are used for muscle strength and endurance and maintain these factors. It is highly effective for people suffering from RA. These factors will ultimately enhance the quality of life by increasing the functional ability of the patient and decreasing dependency on others.

A double-blinded, randomised controlled trial was conducted at Muhammad Physical Therapy and Rehabilitation Clinic and Rehabilitation Centre, Multan from May to December 2021. The trial was approved and registered in the Iranian Registry of Clinical Trials (IRCT20220401054388N1).

The study was completed in eight months after the approval of the institute's ethical committee, the Board of Advance Studies and Research (MIMAS/28/IBR/Imran). The sample size was calculated using the Burkoof formula with a 5% level of significance.

$n=2\sigma^2(Z1-\alpha+Z1-\beta)^2/(\mu o-\mu\alpha).^2$

Table I (a): Intragroup comparison of group-A and B for the improvement in serological parameters, pain, stiffness and activities of daily living with respect to baseline and 18th session of the treatment in both groups.

Parameters	n	Baseline Mean±SD	12th week Mean±SD	24th week Mean±SD	p-value
Group-A					
RF (IU/mL)	42	34±6.7	21.1±4.2	15.6±2.1	<0.001
ESR (mm/hr)	42	92±22.9	70.52±12.8	41±4.8	<0.001
CRP (mg/d)	42	11.2±6.1	6.31±3.0	1.1±0.7	<0.001
WOMAC pain score	42	16.78±2.31	11.52±5.40	5.16±3.52	<0.001
WOMAC stiffness score	42	7.09±1.03	5.33±2.19	2.83±1.76	0.005
WOMAC ADLs score	42	57.33±12.99	34.59±23.71	12.69±8.91	<0.001
NPRS	42	8.30±1.07	6.07±2.86	3.00±2.03	<0.001
Group-B					
RF (IU/mL)	42	35.16±7.75	27.85±5.95	21.34±4.40	0.002
ESR (mm/hr)	42	91±20.9	80±15.2	59±6.1	0.002
CRP (mg/d)	42	10.1±7	7±4.1	5±3.4	0.002
WOMAC pain score	42	16.16±2.75	13.85±3.95	11.34±2.40	0.01
WOMAC stiffness score	42	6.90±1.17	5.8±0.97	4.70±0.62	0.08
WOMAC ADLs score	42	47.66±20.17	40.60±20.83	35.56±16.47	0.001
NPRS	42	7.85±1.69	6.09±1.30	5.38±1.34	0.001

SD: Standard deviation, RF: Rheumatic factor, ESR: Erythrocyte sedimentation rate, CRP: C-reactive proteins, WOMAC: Western Ontario and McMaster Universities Arthritis Index NPRS: Numerical pain rating scale, ADLs: Activities of daily living.

Table I (b): Intergroup comparison of group A and B for the improvement in serological parameters, pain, stiffness and activities of daily living with respect to baseline and 18th session of the treatment in both groups.

Parameters		n	Mean±SD	Mean difference	SD error mean	Significance (2-tailed)
RF (IU/mL)	Group-A	42	15.6±2.1	-5.74	0.3	<0.001
	Group-B	42	21.34±4.40	-5.74	0.67	
ESR (mm/hr)	Group-A	42	41±4.8	-18	0.74	<0.001
	Group-B	42	59±6.1	-18	0.94	
CRP (mg/d)	Group-A	42	1.1±0.7	-3.9	0.10	<0.001
	Group-B	42	5±3.4	-3.9	0.52	
WOMAC pain score	Group-A	42	5.16±3.52	-5.74	0.54	<0.001
	Group-B	42	11.34±2.40	-5.74	0.51	
WOMAC stiffness score	Group-A	42	2.83±1.76	-1.87	0.27	<0.001
	Group-B	42	4.70±0.62	-1.87	0.22	
WOMAC ADLs score	Group-A	42	12.69±8.91	-22.87	1.37	<0.001
	Group-B	42	35.56±16.74	-22.87	1.4	
NPRS	Group-A	42	3.00±2.03	-2.38	0.27	<0.001
	Group-B	42	5.38±1.34	-2.38	0.31	

SD: Standard deviation, RF: Rheumatic factor, ESR: Erythrocyte sedimentation rate, CRP: C-reactive proteins, WOMAC: Western Ontario and McMaster Universities Arthritis Index NPRS: Numerical pain rating scale, ADLs: Activities of daily living.

Patients of all ages, diagnosed with RA, of both genders, and patients with swelling in their joints and pain were included. Patients with vascular neoplasia, fibromyalgia, radiculopathy, neuropathy, tumours, joint fractures, and vestibular problems were excluded. Written consent was taken from the diagnosed RA patients referred by a rheumatologist. Patients were evaluated using an X-ray of their joints and serological findings (RF, ESR, and CRP). The physical assessment was carried out under the supervision of a senior physical therapist, a rheumatologist and a senior radiologist.

The American College of Rheumatology Criteria for diagnosing RA was used.[4] Patients were classified into functional - classes (FC I-IV). One hundred patients were selected, out of them, ten were excluded, three for not giving consent and seven were excluded because they did not meet the inclusion criteria. Ninety patients who met the inclusion criteria were randomly assigned to two groups. A treatment group (group A) and the control group (group B). The lottery method was used for randomisation. On the initial day, there were 45 patients in each group. Treatment group A was treated with curcumin and strengthening exercises, and control group B was treated with curcumin only. A dosage of 180 mg/day of curcumin followed by European Food Safety Authority (EFSA) recommendations for humans was given to patients of both groups under the strict supervision of a pharmacologist and registered medical practitioner.[2]

The strengthening exercises given to group A were upper extremity resistive exercises, resistive hand training with the medicine ball, and elbow and shoulder resistive training with dumbbells. Lower extremity exercises, resistive knee training by pressing soft rollers and ankle weights, upper extremity theraband strengthening exercises and lower extremity theraband strengthening exercises.

The treatment regimen for group A was distributed as three sessions/week; each session lasted 45 minutes. Moreover, the treatment duration was eight months. Furthermore, curcumin was given 180 mg/day orally. Patients were assessed at baseline, 12th week, and 24th week by X-ray findings including erosion, nodules, and degeneration of

bones in the involved joints and by serological findings including RF, ESR, DAS, and CRP. These values were compared with standard values, and at the end 42 patients were left in each group as 3 patients in each group were lost to follow-up. Pain, morning stiffness, and functional activities were assessed using Western Ontario and McMaster Universities Arthritis Index (WOMAC)[5] and numerical pain rating scale (NPRS).[6]

By using SPSS version 22 data were analysed using an independent t-test for intergroup comparisons and repeated measures of ANOVA for intragroup analysis. The level of significance was set at $p<0.05$ and $p<0.001$ were considered. For quantitative variables mean and standard deviations were calculated, and for qualitative variables, like gender, occupation, functional class, frequencies, and percentages were calculated.

Group A, treated with curcumin and strengthening exercises, showed significantly better results when assessed posttreatment by X-ray and serological findings, WOMAC scale and NPRS scale than group B when treated with curcumin only. There was also a significant reduction in the quantitative values of RF, ESR, DAS score and CRP, WOMAC pain, ADLs, and stiffness scale readings of group A with higher significance ($p<0.001$). There was a noteworthy change in joint disruption as there was decreased swelling around the joint, decreased synovial inflammation and progressive changes in joint cartilage when assessed by x-ray findings. These changes are more prominent in group-A than in group B values of the same scale. NPRS scale reading of group A was also significant ($p<0.001$). These values are more effective than group B. Statistical data analysis has been shown in Table I (a & b).

This study demonstrates that curcumin, when given with strengthening exercises in patients with rheumatoid arthritis, was found to be more effective in improving ADLs, pain, and stiffness, also reduces the quantitative values of RF, CRP, ESR and tenderness of joints than curcumin when given alone.

Many studies have been conducted, and many research papers have been published, highlighting the management of RA. Previously a study was conducted on the immunomodulatory effects of curcumin in RA patients.[1] The interventions include hand and knee resisted training, upper and lower limb strengthening, dynamic whole-body exercises, *etc*. The result of the study showed that besides taking DMARDs, exercise patients are subjected to practices for better management of RA.[1]

The synergistic effects of two immunomodulators, curcumin and strengthening exercises were screened to minimise the impact of RA. In this study, both the curcumin and strengthening exercises show synergistic effects by causing changes in the quantitative values of parameters related to RA. Curcumin modulates the cytokines and inflammatory biomarkers by decreasing their quantity in the body. Strengthening exercises showed their activity by stimulating the cellular immune response. Muscle contraction causes the release of anti-inflammatory cytokines.[2] Thus, when given in combination, curcumin and strengthening exercises cause the modulation of immune response in the body. The results were significantly justified by improving the serological findings (RF, ESR, and CRP) by X-rays of the affected joints (marked reduction in synovial thickening and decrease in the size of nodules). These parameters affect the pain and morning stiffness causing their reduction and increasing patients' physical activity by increasing muscular strength and range of motion. So, strengthening exercises and curcumin should be combined to manage RA more effectively. These interventions are less expensive as curcumin is a traditional herbal product readily available, and strengthening exercises can be done at home once taught by a physiotherapist. Both are safe to use for the better management of patients with RA.

ETHICAL APPROVAL:

Approval from the Institute's Ethical Committee, Board of Advance Studies and Research (MIMAS/28/IBR/Imran).

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

MKK: Conceived the idea, analysed the data, and drafted the manuscript.

IAK, AL: Analysed the data and supervised the case.

All the authors have approved the final version of the manuscript to be published.

REFERENCES

1. Stenstrom CH, Minor MA. Evidence for the benefit of aerobic and strengthening exercise in rheumatoid arthritis. *Arthritis Care* Res 2003; **49(3)**:428-34. doi: 10.1002/art.11051.
2. Fernández-Lázaro D, Mielgo-Ayuso J, Calvo SJ, Martínez AC, García AC, Fernandez-Lazaro CI. Modulation of exercise-induced muscle damage, inflammation, and oxidative markers by curcumin supplementation in a physically active population: A systematic review. *Nutrients* 2020; **12(2)**:501. doi: 10.3390/nu12020501.
3. Javadi M, Khadem Haghighian H, Goodarzy S, Abbasi M, Nassiri-Asl M. Effect of curcumin nanomicelle on the clinical symptoms of patients with rheumatoid arthritis: A randomized, double blind, controlled trial. *Int J Rheum Dis* 2019;**22(10)**:1857-1862. doi: 10.1111/1756185X.13688.
4. Dahmen R, Buijsmann S, Siemonsma P C, Boers M, Lankhorst G J, Roorda LD. Use and effects of custom-made therapeutic footwear on lower extremity related pain and activity limitations in patients with rheumatoid arthritis: A prospective observational study of a cohort. *J Rehabil Med*

2014; **46(6):**561-7. doi: 10.2340/16501977-1807.

5. Karcioglu O, Topacoglu H, Dikme O, Dikme O. A systematic review of the pain scales in adults: Which to use? *Am J Emerg Med* 2018; **36(4):**707-14. doi:10.1016/j.ajem.2018.01.008.

6. Singh JA, Saag KG, Bridges SL, Akl EA, Bannuru RR, Sullivan MC, *et al*. American college of rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol* 2015; **68(1):** 1-26. doi: 10.1002/art.39480.