

Efficacy of Flaxseed and Fish Oils on Adults with Rheumatoid Arthritis

Safeena Amjad¹, Nighat Ahmad², Asma Afreen³, Shazia Ashraf⁴, Zaheer Ahmed⁵

Abstract

Objective: To assess the relative efficacy of flaxseed and fish oils in the management of rheumatoid arthritis.

Methods: The comparative study was conducted in the outpatient department of Rheumatology at Fatima Memorial Hospital, Shadman, Lahore, Pakistan, from July to December 2017, and comprised rheumatoid arthritis patients who were divided into group A receiving 3g/day of flaxseed oil and group B receiving 3g/day of fish oil for 90 days. Blood samples were taken at baseline and post-intervention to note the difference on biochemical parameters. Data was analysed using SPSS 21.

Results: Of the 60 patients, there were 30(50%) in each of the two groups. Overall, there were 8(13.3%) males and 52(86.7%) females. Both groups showed significant change in all biochemical parameters compared to baseline values ($p < 0.05$). Intergroup comparison showed that flaxseed oil treatment was significantly more effective than fish oil treatment ($p < 0.05$).

Conclusion: While both forms of intervention were found to be effective, flaxseed oil was significantly more effective than fish oil in reducing the inflammation of joints in rheumatoid arthritis patients.

Keywords: Rheumatoid arthritis, Synovial joints, Flax, Fish oil, Omega 3 fatty acids. (JPMA 71: 22; 2021)

DOI: <https://doi.org/10.47391/JPMA.02-290>

Introduction

The term rheumatoid arthritis, (RA) is defined as an autoimmune ailment categorised by infection of the synovial joints in the body.^{1,2} RA has a mean occurrence of $0.5 \pm 0.2\%$ and the majority of patients happen to be females. RA indicates the most mutual chronic systemic autoimmune rheumatism.³ RA was more common in northern England and the incidence noted was similar to that in citizens of Pakistani origin living in England. However, the origin of such gender-oriented insight regarding RA is yet not known.⁴⁻⁷ RA causes a person's immune system to mistakenly attack healthy tissue. When left untreated, RA can have wide-ranging effects. Along with the joints, RA can affect many of the body's organs, including heart, eyes, brain and the skeleton. Medication for RA can also cause side-effects across the body.⁸

The omega-3 polyunsaturated fatty acid (Ω -3 PUFA), particularly the n-3 abundant unsaturated fatty acid (FA), docosahexaenoic acid (DHA) (22:6 n-3) and eicosapentaenoic acid (EPA) (20:5 n-3) have several health benefits, but the role in human subjects is not very clear since few studies have been conducted on the subject.⁹ *Linum usitatissimum*, commonly called 'flaxseed', 'Jawas', 'Aksebija' and 'Alsi ke Beej' in Hindi and Urdu languages, is a blue flowering 'rabi' crop and a member of linaceae.

^{1,4}Department of Clinical Nutrition, NUR International University - Fatima Memorial System, Lahore, Pakistan; ²Department of Rheumatology, National Hospital and Medical Centre, Lahore, Pakistan; ^{3,5}Department of Environmental Design Health and Nutritional Sciences, Allama Iqbal Open University, Islamabad, Pakistan.

Correspondence: Zaheer Ahmad. e-mail: zaheer.ahmed@aiou.edu.pk

Among all lipids present in flaxseed (around 30%), 17% are linoleic acids (LAs), 53% are α -linolenic acids (ALAs), 19.5% oleic acids, 2.5% stearic acids and 5% palmitic acids, which supplied excellent n-6: n-3 fatty acid proportion of around 0.3:1. Thus, the seed may be an option for providing this fatty acid to populations in parts of the world where there is no great consumption of sea-food which is the best source of n-3 fatty acids.^{10,11} There are variety of healthy nutrients, such as lignin, fibre and essential fatty acids, present in linseed. Most individuals are not aware of the possible health benefits of flaxseed. The overall recommendation for consumption has been 1-3 tablespoons per day of ground flaxseed or one tablespoon of linseed oil. Flaxseed is going to be one of the functional and nutritive elements in food crops as scientific outcomes have favoured flaxseed intake.¹²

Fish oil is also a good source of long-string Ω -3 PUFAs containing 18% EPA and 12% DHA derived from marine fish. The consumption of Ω -3 PUFAs at dosages of 2.7g/day for three months reduced nonsteroidal anti-inflammatory drugs (NSAIDs) intake by RA patients.¹³ Oily fish and fish oil supplements contain the long-chain (LC) Ω -3 PUFAs EPA and DHA.¹⁴ A few studies have found that fish oil at a minimum of 3g per day considerably reduced morning stiffness and also the number of tenders, swollen joints in patients with autoimmune diseases, while one study used a dose of 18g per day.¹⁵ Effects of flaxseed on inferior chronic inflammation are still conflicting. A study showed that inflammatory markers as well as the C-reactive protein (CRP) levels were reduced with the intake of flaxseed and its bioactive compounds.¹⁰

The current study was planned to assess the relative efficacy of flaxseed and fish oils in RA management.

Patients and Methods

The comparative study was conducted in the outpatient department (OPD) of Rheumatology at Fatima Memorial Hospital, Shadman, Lahore, Pakistan, from July to December 2017. The total sample size in this study had been calculated keeping in view following facts as described in literature:¹⁶

- Significance level= 5%
- P = Prevalence of desired outcome was at least 0.2 (20%)
- q = 0.8
- Probability level or confidence level (1- α) =95%

So the sample size was;

$$\begin{aligned} n &= Z^2 P (q) \div (ME)^2 \\ &= (1.96)^2 \times 0.2 \times 0.8 / (0.1)^2 \\ &= 3.84 \times 0.2 \times 0.8 / 0.01 \\ &= 0.61/0.01 \end{aligned}$$

$$n = 61.44$$

After approval from the institutional ethics review board, the sample of sixty (60) subjects was collected using simple random sampling technique from among patients of either gender aged 34-69 years with RA according to the American College of Rheumatology (ACR) criteria.¹⁷ The subjects had uncontrolled RA and were taking medications. Those having any other chronic illness, like diabetes, renal failure, liver disease and cancer, as well as patients undergone any surgery, having advanced RA stage, and allergic to medication were excluded. After taking written informed consent from the subjects, they were separated into group A receiving 3g of flaxseed oil capsule per day orally for 90 days, and group B receiving 3g fish oil capsule per day orally for 90 days.

All participants went through baseline nutritional assessment with the help of standard methods.¹⁸ These included height and weight measurements to estimate the body mass index (BMI). As per the World Health Organisation (WHO) South Asian criteria, subjects <18.5kg/m² BMI were considered underweight, 18.5-22.9kg/m² normal weight, 23-24.9 kg/m² overweight and ≥ 25 kg/m² obesity.¹⁹

Biochemistry assessment included complete blood-cell count (CBC), erythrocyte sedimentation rate (ESR), CRP and rheumatoid factor (RF). Sysmex XN-1000 (Sysmex Co., Kobe, Japan) automatic analyzer was used for haematological analyses (CBC) and erythrocyte sedimentation rate was measured (ESR) by using Vesmatic method. CRP and

rheumatoid factor (RF) were analyzed by Roche Cobas c 311 analyzer (Roche, Mannheim, Germany). The original kits provided by the manufacturer were used for all analysis.

The Disease Activity Score comprising 28 joints (DAS28) was applied to assess the number of swollen and tender joint numbers, while the patients' inclusive evaluation of health was assessed using the visual analogue scale (VAS) as described previously in literature.²⁰ DAS28 score ranges from 0 to 10 points, with 2.6 to 3.2 indicating low disease activity, 3.2 to ≤ 5.1 moderate and >5.1 high disease activity. VAS had a range of 0-100.

The evaluations were done at baseline (Level-1), after 45 days of intervention (Level-2) and at the end of intervention (Level-3). The variations in results, assessed using the ACR criteria¹⁷ were taken as the effect of the intervention.

Data was analysed using SPSS 21. Multivariate analysis of variance and general linear regression were carried out for inter-group comparisons. P<0.05 was considered statistically significant.

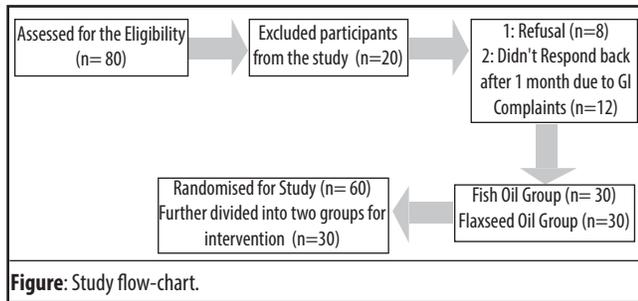
Results

Of the 80 individuals approached, 8(10%) refused to participate, while 12(15%) were excluded in the first month of intervention because of gastrointestinal (GI) complaints and indigestion. The final sample, as such, comprised 60(75%); 30(50%) in each of the two groups (Figure).

Table-1: Demographic profile of the sample.

Description	Fish Oil	Flaxseed oil
	n (%)	n (%)
Gender		
Male	3 (5)	5 (8.3)
Female	27 (45)	25 (41.7)%
Age (years)		
21-30	5 (8.3)	5 (8.3)
31-40	15 (25)	16 (26.7)
41-50	3 (5)	3 (5)
51-60	5 (8.3)	3 (5)
61-70	2 (3.3)	3 (5)
Marital status		
Married	19 (31.7)	21 (35)
Unmarried	11 (18.3)	9 (15)
Profession		
House Wife	20 (66)	24 (80)
Tailor	3 (10)	2 (7)
Shopkeeper	4 (13)	3 (10)
Teacher	3 (10)	1 (3)
BMI (kg/m²)		
Normal	9 (30)	11 (37)
Overweight	13 (43)	10 (33)
Obesity	8 (27)	9 (30)

BMI: Body mass index.

**Table-2:** Comparative effect of fish oil and flaxseed oil.

Variables	Fish oil (Mean ± SD)	p-value (Within group)	Flax Seed Oil (Mean ± SD)	p-value (Within group)	p-value (After Intervention Between group)
ESR					
Pre-test	45.47±20.06	0.000	45.20±22.06	0.000	0.000
Post-test	32.43±16.19		30.23±15.40		
Intervention effect	13.033±10.43		14.97±13.61		
CBC					
Pre-test	11.797±1.54	0.023	11.97±1.89	0.072	0.000
Post-test	12.14±1.12		12.27±1.45		
Intervention effect	-0.34±0.78		-0.31±0.89		
RF					
Pre-test	19.20±2.99	0.000	17.18±1.05	0.000	0.000
Post-test	15.30±1.49		14.53±3.18		
Intervention effect	3.90±2.71		2.65±3.35		
CRP					
Pre-test	2.15±0.96	0.000	2.11±0.96	0.000	0.000
Post-test	1.43±0.96		1.39±0.96		
Intervention effect	0.72±0.77		0.72±0.80		

SD: Standard deviation, ESR: Erythrocyte sedimentation rate, CBC: Complete blood count (CBC), RF: Rheumatoid factor, CRP: C-reactive protein.

Overall, there were 8(13.3%) males and 52(86.7%) females. Age, marital status, profession and BMI values were also noted, and RA was found to be more prevalent in the female married population (Table-1).

Both groups showed significant change in all biochemical parameters compared to baseline values ($p<0.05$) except CBC in group A ($p=0.072$). Intergroup comparison showed that flaxseed oil treatment was significantly more effective than fish oil treatment ($p<0.05$) (Table-2).

Discussion

Inflammation is intricate in the pathophysiology of many long-lasting ailments, such as rheumatoid arthritis and neurodegenerative diseases.²¹ The current study was planned to estimate the relative effect of flaxseed oil and fish oil in adults with uncontrolled RA. Several studies have discovered that EPA and DHA comparatively hinder some inflammatory progressions and, as a consequence, they might be helpful in provocative conditions, for example, rheumatoid joint pain.²² The present study found that RA was more prevalent among females compared to males.

Among the RA patients, there was a high frequency of co-morbidities and risk factors. The age range of subjects in the current study was 21-70 years, while an earlier study had mentioned 22-65 years.²³ The subjects in the current study were treated with Ω -3 FA sources. The suggestive benefit of fish oil in RA is well proven.²⁴ It was observed in a study that fish oil supplementation reduced inflammatory symptoms in chronic RA.²⁵ The influence of Ω -3 fish oil capsule, on CRP as an inflammatory indicator, was also investigated in the current study, and the results

indicated a major decrease in CRP levels after therapy with Ω -3 FAs. These findings were in line with earlier findings.²⁶ The ESR levels were considerably decreased in our patients compared to the baseline value, and the finding was in line with earlier studies.²⁷ One study reported uncertain but substantial decrease in ESR and CRP levels in a study of RA patients.²⁸ Studies have also explored ω -3 PUFAs in various oils, such as borage oil and evening primrose oil, to support a better steadiness of PUFA constituents.²⁹ Additionally, soy and rest of the plants have been naturally altered to contain higher levels of Ω -3 PUFAs.^{29,30} Although marine creatures are the major source of Ω -3 PUFAs, some plant seeds also contain them. For example, flax, chia, and canola seeds are some of the richest source of ALA, which works as a precursor to the synthesis of LC PUFAs in the human body. Clinical nutritionists globally recommend combination of Ω -3 FA food sources in the diet. Linseed helps as the best Ω -3 FA source to those who don't consume fish.³¹ In a study with a six-month follow-up, modifications in NSAID dosage were endorsed. A considerable decrease of NSAID requirement was perceived in patients who consumed Ω -3 FAs at 3 ($p<0.05$) and 6 months ($p<0.01$).³² Earlier studies have reported that flaxseed/ *Linum (L.) usitatissimu* revealed significant role in reducing inflammation, treating arthritis and also exhibited antiulcer properties.³³ Flaxseeds provide abundant amount of fatty acids. Flaxseed contains 18% of monounsaturated FAs, 16% Ω -6 FAs, 9% saturated FAs and 57% Ω -3 FAs.³⁴

Fish oils seem to improve RA indications, which is, perhaps, unsurprising as n-3 FAs are believed to be affected in the prohibition of the production of inflammatory eicosanoids. Numerous studies have revealed that really LC n-3 FAs decrease pain and morning stiffness and decrease the requirement for NSAIDs.^{35,36} A meta-analysis of 10 double-blind, placebo-controlled, comparative study in 395 patients showed that fish oil for three months was significantly associated with reduction in joint tenderness and morning stiffness. There were no substantial improvements in joint swelling, grip strength or ESR.³⁷

Previously, a study on albino rats observed anti-arthritis action of linseed/flaxseed oil against turpentine oil-induced joint oedema and adjuvant induced arthritis. It has been observed that daily intake of linseed oil aids in reducing the inflammation of RA patients.³¹ An anti-inflammatory property of various plant lipids has been reported and findings showed that lipids consists of ALAs, like linseed oil, had significant anti-inflammatory action. Regardless of the evidence of total low quality of trials, ingesting of Ω -3 FAs was found to considerably improve disease activity inflammatory markers.²³ Flaxseed can be used in food, skin care, hair care and other healthcare products rather than in flaxseed oil supplements.³¹ Various studies discovered that the flaxseed components supply disease defensive and therapeutic aids which helps in the expansion of new labelled healthy and functional foods utilising flaxseeds, oil and cakes.³⁸

More studies are required to explore if a substitute is needed to NSAIDs in definite conditions.

Conclusion

Flaxseed oil supplementation significantly decreased ESR levels in uncontrolled RA patients compared to fish oil supplementation. Nutritional supplementation rich in Ω -3 FAs, such as flaxseed and fish oil, are linked with clinical improvement in RA patients.

Acknowledgement: We are grateful to all the study participants for cooperation.

Disclaimer: The text was presented at the 1st International Conference on Health and Environment which was held at the Allama Iqbal Open University Islamabad, Pakistan, on March 22, 2018.

Conflict of interest: None.

Source of Funding: None.

References

- Athar M, Khokhar SA, Shakeel A, Abbas A. A brief outlook of rheumatoid arthritis RA patients in health facilities of Karachi, Pakistan. *Med Sci.* 2014; 15:34-8.
- Imran MY, Khan EAS, Ahmad NM, Raja SF, Saeed MA, Haider II. Depression in Rheumatoid Arthritis and its relation to disease activity. *Pak J Med Sci.* 2015; 31:393.
- Lemerle J, Arleevskaya MI, Brooks WH, Renaudineau Y. Effects of environmental factors and omega-3 fatty acids on rheumatoid arthritis. *Ann Joint.* 2016:1-4.
- Alam SM, Kidwai AA, Jafri SR, Qureshi BM, Sami A, Qureshi HH, et al. Epidemiology of rheumatoid arthritis in a tertiary care unit, Karachi, Pakistan. *J Pak Med Assoc.* 2011; 61:123.
- Khalil Z, Salim B, Nasim A, Malik S. Patients' knowledge on Rheumatoid Arthritis—A study at a tertiary care hospital. *J Pak Med Assoc.* 2017; 67:256-60.
- Rennie K, Hughes J, Lang R, Jebb S. Nutritional management of rheumatoid arthritis: a review of the evidence. *J Hum Nutr Diet.* 2003; 16:97-109.
- Ullah Z, Ullah MI, Hussain S, Kaul H, Lone KP. Determination of serum trace elements (Zn, Cu, and Fe) in Pakistani patients with rheumatoid arthritis. *Biol Trace Elem Res.* 2017; 175:10-6.
- Nie Y. Completeness of rheumatoid arthritis prevalence estimates from administrative health data: comparison of capture-recapture models, 2014.
- Bell JG, Henderson RJ, Tocher DR, Sargent JR. Replacement of dietary fish oil with increasing levels of linseed oil: modification of flesh fatty acid compositions in Atlantic salmon (*Salmo salar*) using a fish oil finishing diet. *Lipids.* 2004; 39:223-32.
- Cardoso Carraro JC, Dantas MIdS, Espescht ACR, Martino HSD, Ribeiro SMR. Flaxseed and human health: reviewing benefits and adverse effects. *Food Rev Int.* 2012; 28:203-30.
- Singh K, Mridula D, Rehal J, Barnwal P. Flaxseed: a potential source of food, feed and fiber. *Crit Rev Food Sci.* 2011; 51:210-22.
- Ganorkar P, Jain R. Flaxseed—a nutritional punch. *Int Food Res J.* 2013;20.
- Lee YH, Bae SC, Song GG. Omega-3 polyunsaturated fatty acids and the treatment of rheumatoid arthritis: a meta-analysis. *Arch Med Res.* 2012; 43:356-62.
- Abdulrazaq M, Innes JK, Calder PC. Effect of ω -3 polyunsaturated fatty acids on arthritic pain: A systematic review. *Nutrition.* 2017; 39:57-66.
- Covington M. Omega-3 fatty acids. *Am Fam Phys.* 2004; 70:133-40.
- Borm GF, Franssen J, Lemmens WA. A simple sample size formula for analysis of covariance in randomized clinical trials. *J Clin Epidemiol.* 2007; 60:1234-8.
- Anderson J, Caplan L, Yazdany J, Robbins ML, Neogi T, Michaud K, et al. Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice. *Arthrit Care Res.* 2012; 64:640-7.
- Gibson RS. Principles of nutritional assessment: USA: Oxford university press, 2005.
- Consultation W E. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet (London, England).* 2004;363:157-163.
- Van der Heijde D, van't Hof MA, Van Riel P, Theunisse L, Lubberts EW, van Leeuwen MA, et al. Judging disease activity in clinical practice in rheumatoid arthritis: first step in the development of a disease activity score. *Ann Rheum Dis.* 1990; 49:916-20.
- Jalil F, Arshad M, Bhatti A, Jamal M, Ahmed M, Malik JM, et al. Progression pattern of rheumatoid arthritis: A study of 500 Pakistani patients. *Pak J Pharm Sci.* 2017; 30:1219-23.
- Gioxari A, Kaliora AC, Marantidou F, Panagiotakos DP. Intake of ω -3 polyunsaturated fatty acids in patients with rheumatoid arthritis: A systematic review and meta-analysis. *Nutrition.* 2018; 45:114-24.
- Dougados M, Soubrier M, Antunez A, Balint P, Balsa A, Buch MH, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). *Ann Rheum Dis.* 2014; 73:62-8.
- Cleland LG, Caughey GE, James MJ, Proudman SM. Reduction of cardiovascular risk factors with longterm fish oil treatment in early rheumatoid arthritis. *J Rheumatol.* 2006; 33:1973-9.
- Cleland LG, James MJ, Proudman SM. The role of fish oils in the treatment of rheumatoid arthritis. *Drugs.* 2003; 63:845-53.
- Berbert AA, Kondo CRM, Almendra CL, Matsuo T, Dichi I. Supplementation of fish oil and olive oil in patients with rheumatoid arthritis. *Nutr.* 2005; 21:131-6.
- Rajaei E, Mowla K, Ghorbani A, Bahadoram S, Bahadoram M, Dargahi-Malamir M. The effect of omega-3 fatty acids in patients with active rheumatoid arthritis receiving DMARDs therapy: double-blind randomized controlled trial. *Glob J Health Sci.* 2016;8:18.

28. Rosal MC, Ockene IS, Restrepo A, White MJ, Borg A, Olendzki B, et al. Randomized trial of a literacy-sensitive, culturally tailored diabetes self-management intervention for low-income Latinos: Latinos en Control. *Diabetes Care*. 2011; 34:838-44.
 29. Shahidi F, Ambigaipalan P. Omega-3 polyunsaturated fatty acids and their health benefits. *Annu Rev Food Sci T*. 2018; 9:345-81.
 30. No Author Listed. fatty acids in human nutrition. Report of an expert consultation. Rome: FAO; 2010. FAO Food Nutr Pap. 2010; 91:1-166.
 31. Gutte KB, Sahoo A, Ranveer RC. Bioactive components of flaxseed and its health benefits. *Int J Pharm Sci Rev Res*. 2015; 31:42-51.
 32. Ariza AR, Peralta MM, Cardiel MH. Omega-3 fatty acids in rheumatoid arthritis: an overview. *Semin Arthritis Rheum*. 1998; 27:366-70.
 33. Kaithwas G, Majumdar DK. Effect of *L. usitatissimum* (flaxseed/linseed) fixed oil against distinct phases of inflammation. *Int Sch Res Notices*. 2013; 2013:735158.
 34. Paez V, Barrett WB, Deng X, Diaz-Amigo C, Fiedler K, Fuerer C, et al. AOAC SMPR® 2016.002. *J Aoac Int*. 2016; 99:1122-4.
 35. Küllenberg D, Taylor LA, Schneider M, Massing U. Health effects of dietary phospholipids. *Lipids Health Dis*. 2012; 11:1-16.
 36. Fattori V, Amaral FA, Verri Jr WA. Neutrophils and arthritis: role in disease and pharmacological perspectives. *Pharmacol Res*. 2016; 112:84-98.
 37. Mason P. Fish oils-an update. *Acute pain*. 2019; 10:12-34.
 38. Raghuvanshi V, Agrawal R, Mane K. Flaxseed as a functional food: A review. *J Pharmacogn Phytochem Res*. 2019;8:352-4.
-