World Nutrition Journal |eISSN 2580-7013

CASE REPORT

Effect of omega-3 supplementation on osteoarthritis: An evidence-based case report

Jessica Ferdi[1], Diana Sunardi[1]

1. *Department of Nutrition, Faculty of Medicine, Universitas Indonesia – Dr. Cipto Mangunkusumo General Hospital Jl Salemba Raya no 6, Jakarta 10430, Indonesia*

Received 28 July 2023
Accepted 8 December 2023
Published 29 February 2024

Link to DOI:
10.25220/WNJ.V07.i2.0003

Citation: Ferdi J, Sunardi D. Effect of omega-3 supplementation on osteoarthritis: An evidence-based case report. World Nutrition Journal.2024 February 29,7(i2): 9-17.

Website :
http://www.worldnutrijournal.org/

Abstract

Background: Osteoarthritis is marked by mild inflammation, causing cartilage damage that leads to bone remodelling and potentially reduces the quality of life. Omega-3 has anti-inflammatory properties, which can help mitigate cartilage damage.

Objective: This research aims to determine the role of omega-3 in relieving pain in patients with osteoarthritis.

Methods: A literature search was conducted using advanced searching on three large databases: PubMed, Cochrane, and Scopus. The search used Mesh terms according to the criteria. After assessing the relevance and suitability of the literature, two articles were selected and critically evaluated based on Oxford Center for Evidence-Based Medicine.

Results: Two systematic review-meta-analyses that meet the PICO and eligibility criteria were found. One of the literature sources does not demonstrate the effect of omega-3 supplementation on joint pain, while the other literature source shows the beneficial effects of omega-3 in reducing joint pain in osteoarthritis.

Conclusion: Omega-3 supplementation can alleviate joint pain in individuals with osteoarthritis. Providing omega-3 may be worth considering.

Keywords: omega-3, osteoarthritis, joint pain

Corresponding author:
Dr. dr. Diana Sunardi, MGizi, SpGK(K)
Department of Nutrition, Faculty Medicine, Universitas Indonesia-Dr. Cipto Mangunkusumo Hospital, Jakarta 10430, Indonesia
Email: diana_sunardi@yahoo.com

Case scenario

A 56-year-old woman came to the nutrition clinic for consultation. The patient is actively working and has been suffering from osteoarthritis for the past 5 years. Her complaints include stiffness and pain in the hands and knees, along with occasional cracking sounds during certain movements. She also experiences frequent muscle fatigue in the neck and waist area. The patient is currently taking Arcoxia 60 mg once daily, Myonal 50 mg twice daily, and Neurobion 1 tablet once daily. She is overweight and frequently consumes fast food. The patient wants to start a healthy diet and exercise routine. She inquires if taking omega-3 supplements can help reduce the joint pain she is experiencing?

Introduction

Musculoskeletal health encompasses bones, cartilage, tendons, ligaments, muscles, and connective tissues. Balanced metabolism is crucial for maintaining musculoskeletal system homeostasis. Osteoarthritis (OA) is one of the common musculoskeletal disorders, with a global prevalence of 15%, projected to reach 35% by 2030.[1] Currently, there are 303 million people worldwide suffering from osteoarthritis.[2] The estimated number of osteoarthritis patients in the United States will reach 78 million by 2040.[3] The prevalence of joint diseases is around 7.3% in Indonesia.[4]

Osteoarthritis is a degenerative joint disease characterized by the damage to cartilage tissue, ligaments, synovial inflammation, osteophyte formation, and bone remodeling.[1] This condition is caused by low-grade inflammation, which subsequently disrupts the homeostasis of cartilage synthesis and degradation.[5] Osteoarthritis commonly affects the hands, hips, and knees, gradually leading to cartilage deterioration and bone changes, resulting in pain, stiffness, and swelling, which can lead to decreased function and disability.[6] Osteoarthritis patients are susceptible to experiencing depression, memory loss, and even suicidal thoughts.[7] Risk factors include being above 50 years of age, genetics, female gender, bone or joint structural disorders, joint injuries, muscle weakness, obesity, physical activity, and diet.[6,8]

Assessment of OA diagnosis relies on clinical symptoms and physical examination. If OA is suspected, it is important to conduct a medical history, perform a physical examination, and employ an approach to rule out other possible diagnoses, along with using supplementary tests. Basic radiological examinations can help confirm the presence of OA and exclude other conditions.[6,8] Preventing osteoarthritis can be achieved by adopting a healthy lifestyle and avoiding injuries. This includes maintaining a balanced and nutritious diet, engaging in at least 150 minutes of physical activity per week, practicing good body posture, and managing weight if there is excess or obesity.

The development of OA involves various pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), IL-6, IL-8, and signaling pathways such as nuclear factor kappa B (NF-κB), protein kinase B (Akt), c-Jun N-terminal kinases (JNK), mitogen-activated protein kinase (MAPK), signal transducer and activator of transcription 6 (STAT6), and mammalian target of rapamycin (mTOR). These cytokines and signaling pathways can increase chondrocyte catabolism and inhibit anabolism, leading to disruptions in homeostasis and cartilage degradation.[9]

The fat present within articular cartilage chondrocytes can trigger inflammation, chondrocyte damage, and cartilage degradation. Omega-6 fatty acids are pro-inflammatory and accumulate in osteoarthritis joints. Conversely, omega-3 fatty acids are anti-inflammatory and are inversely related to patellofemoral cartilage damage.[10] Omega-3 includes α-linolenic acid, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). While α-linolenic acid can be converted into EPA/DHA, the amount is not significant. Through elongation and saturation processes, EPA and DHA will produce anti-inflammatory eicosanoids such as prostaglandin (PG3), leukotrienes (LTB5), thromboxane (TXA3), and resolvins (RvE1, RvE2, RvD3, RvD4). These substances can reduce pain in osteoarthritis by decreasing the production of pro-inflammatory eicosanoids, reactive oxygen

species, cytokines, and through the mediation of anti-inflammatory agents.[11]

Some studies have shown that the administration of omega-3 can reduce the symptoms of pain in osteoarthritis. The purpose of conducting the EBCR (Evidence-Based Case Report) is to conduct a thorough examination of the effects of administering omega-3 on pain in osteoarthritis, considering all available evidence and data to make informed and evidence-based.

Clinical question

P : osteoarthritis patient

I : omega-3 supplement

C : placebo

O : joint pain

Clinical question: could omega-3 supplementation reduce joint pain?

Methods

Literature search was conducted using PubMed, Cochrane, and Scopus databases on June 4, 2023. MeSH terms, title/abstract/keywords were used for the database search. The keywords used were 'osteoarthritis' AND 'omega-3 fatty acid' OR 'omega 3 eicosapentaenoic acid' AND 'joint pain' (**Table 1**) to investigate the role of omega-3 in alleviating pain in individuals with osteoarthritis. After obtaining the results from these databases, title and abstract screening were performed, followed by selection based on inclusion criteria, and checked for duplications. Literature relevant to the PICO (Population, Intervention, Comparison, Outcome) was filtered using criteria for full-text and English language. Critical appraisal of the included studies was carried out following the systematic review guidelines published by the University of Oxford Centre for Evidence-Based Medicine (CEBM).

Eligibility criteria

Inclusion criteria for the study were as follows:

1. Age ≥ 18 years.
2. Subjects diagnosed with osteoarthritis.
3. Intervention involving omega-3 fatty acids.
4. Study design: systematic review–meta analysis or randomized controlled trial (RCT).
5. Articles published within the last 10 years.
6. Articles published in the English language.

Exclusion criteria:

1. Subjects undergoing analgesic therapy.
2. Studies conducted on animals.
3. Studies with outcomes that do not assess joint pain.

Results

There are 76 literatures from Pubmed, 4 literatures from Cochrane, and 60 literatures from Scopus (**Table 1**). The literature was sorted using a search engine filter, which screened titles and abstracts based on inclusion criteria and removed duplicates. After reading the full texts, we utilized two literatures from systematic reviews and meta-analyses. The literature originates from Senftleber et al.[12] and Deng et al.[13] The flowchart of the search and selection strategy can be seen in **Figure 1**. The characteristics of the literature are presented in **Table 2**. The description of the eligible criteria can be found in **Table 3**.

Discussion

Joint pain is one of the common complaints found in osteoarthritis patients, which can cause disability and reduce long-term quality of life. The administration of omega-3 with EPA and DHA content has anti-inflammatory properties that can reduce the expression of proinflammatory genes associated with cartilage degradation.

There are two systematic reviews and meta-analyses of randomized controlled trials that can be used to address the clinical question. Senftleber et al.[12] compared the administration of omega-3 with placebo in subjects with osteoarthritis, rheumatoid arthritis, or mixed arthritis, focusing on joint pain,

function, and inflammation. The intervention involved the oral administration of marine oil containing omega-3 to reduce arthritis pain. The marine oil used in the studies included fish oil, cod liver oil, shellfish extract, krill oil, and seal oil. The results of the studies showed an effect of marine oil on joint pain. However, there was high heterogeneity in the studies (I^2 = 63%) due to variations in diagnosis, types, and dosage of supplementation. Only 5 out of 42 studies assessed the effect of marine oil on patients with osteoarthritis. The studies indicated no effect on OA patients given EPA and DHA. Conversely, there was a significant effect in the rheumatoid arthritis and mixed arthritis groups, with an 8% improvement on the visual analogue scale (VAS). The funnel plot and Egger's test results indicated low publication bias. The sensitivity analysis using the fixed-effect model showed no small study bias.

A recent study by Deng et al.[13] showed that the administration of omega-3 significantly reduces joint pain compared to placebo in patients with osteoarthritis (standardized mean difference (SMD): –0.29, 95% confidence interval (CI) –0.47 to –0.11, p = 0.002, I^2 = 60%). The assessment of joint pain used the Western Ontario-McMaster University Osteoarthritis Index (WOMAC) and Visual Analog Scale (VAS). This study analyzed OA patients given omega-3 ranging from 350 to 2400 mg. There was high heterogeneity in this study (Cochrane Q test = 0.01, I^2 = 60%).

Table 1. Search strategy

Database	Search Strategy	Hits
Pubmed	(((osteoarthritis[MeSH Terms]) AND (fatty acids, omega 3[MeSH Terms])) OR (omega 3 eicosapentaenoic acid[MeSH Terms])) AND (pain[Title/Abstract])	76
Cochrane	#1 MeSH descriptor: [Osteoarthritis] explode all trees #2 MeSH descriptor: [Fatty Acids, Omega-3] explode all trees #3 (joint pain):ti,ab,kw #4 #1 AND #2 AND #3	4
Scopus	(TITLE-ABS-KEY (osteoarthritis) AND TITLE-ABS-KEY (omega 3 fatty AND acid) AND TITLE-ABS-KEY (joint AND pain))	60

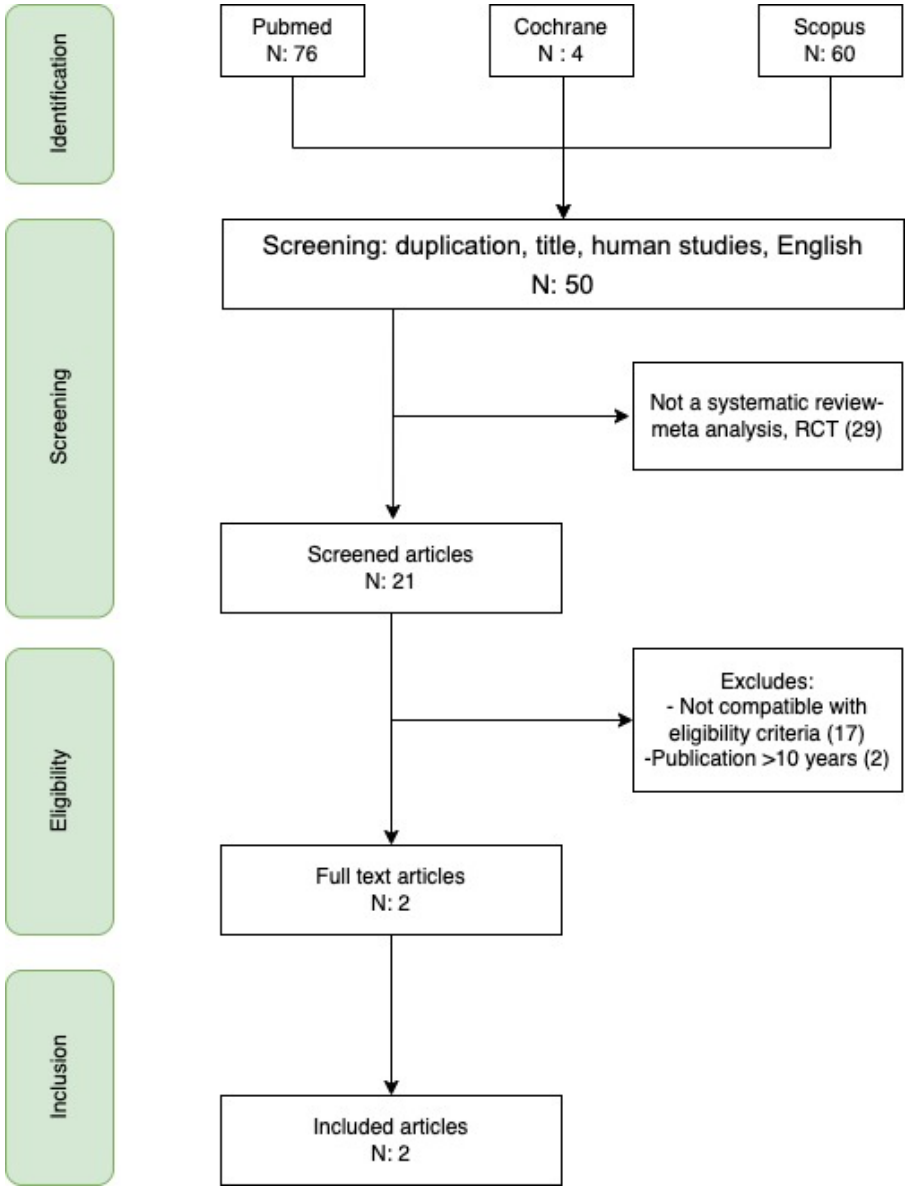

Figure 1. Prisma flow chart

Table 2. Study characteristic

Articles	Study Design	Population	Outcome	Result
Senftleber et al.[12] (2017)	Systematic review and Meta-analysis of Randomized Controlled Trials	42 studies involving 2,751 patients. These studies compared the administration of marine oil in patients with arthritis, with a minimum duration of 2 weeks of treatment. Among these, 32 studies examined rheumatoid arthritis, 6 studies examined osteoarthritis, and 4 studies examined mixed arthritis.	Joint pain was assessed using the Visual Analog Scale (VAS), inflammation was measured using C-reactive protein (CRP), and joint function was evaluated through walking tests and grip strength assessments.	There is a slight effect of marine oil in reducing joint pain in arthritis patients (SMD –0.24; 95% CI, –0.42 to –0.07; heterogeneity I^2 = 63%). However, there is no significant effect on osteoarthritis patients (SMD –0.17; 95% CI, –0.57 to 0.24).
Deng et al.[13] (2023)	Systematic review and Meta-analysis of Randomized Controlled Trials	There are 9 studies involving 2,070 patients with osteoarthritis. These studies compared the administration of omega-3 with placebo regarding the reduction of joint pain.	Joint pain and function were evaluated using the Western Ontario-McMaster University Osteoarthritis Index (WOMAC) or Visual Analog Scale (VAS).	Omega-3 supplementation significantly reduces pain compared to placebo (SMD: –0.29, 95% CI –0.47 to –0.11, p = 0.002). Subgroup analysis showed consistent pain improvement evaluated by WOMAC or VAS after n-3 PUFA supplementation, regardless of whether the dose was less than or equal to 1000 g/day, with EPA < 500 mg/day or ≥ 500 mg/day, and with DHA < 500 mg/day or ≥ 500 mg/day. The study also found an improvement in joint function with omega-3 supplementation (SMD: –0.21, 95% CI –0.34 to –0.07, p = 0.002, I^2 = 27%).

Table 3. Validity criteria

	Study design	Number of patients	Randomization	Similarity treatment and control	Blinding comparable treatment	Domain	Determinant	Measurement of outcomes	Quality of evidence*	Level of evidence**
Senftleber et al.[12]	+	+	+	+	+	+	+	+	Moderate	1A-
Deng et al.[13]	+	+	+	+	+	+	+	+	Moderate-High	1A-

* Quality of evidence according to GRADE guidelines, https://www.ncbi.nlm.nih.gov/pubmed/21208779
**Level of evidence according to Oxford Center of Evidence-based Medicine (CEBM), http://www.cebm.net.
+ clearly mentioned in the article; - not done; ? Not stated clearly
- Systematic review and meta-analysis with heterogeneity

Table 4. Criteria relevance

	Similarity Population	Similarity Intervention	Similarity Outcome
Senftleber et al.[12]	+	+	+
Deng et al.[13]	+	+	+

However, subgroup analysis found consistent reduction in joint pain with the administration of omega-3 PUFA, regardless of whether the dose was less than or equal to 1000 g/day, with EPA < 500 mg/day or ≥ 500 mg/day, and with DHA < 500 mg/day or ≥ 500 mg/day. The study also found an improvement in joint function with omega-3 supplementation (SMD: –0.21, 95% CI –0.34 to –0.07, $p = 0.002$, $I^2 = 27\%$). The results of the funnel plots and Egger's regression test indicate that this study has a low risk of publication bias. This further strengthens the potential of omega-3 in reducing joint pain.

The role of omega-3 in reducing joint pain occurs through its anti-inflammatory properties. Omega-3 produces anti-inflammatory eicosanoids, such as prostaglandins, leukotrienes, thromboxanes, and resolvins, which suppress inflammation, catabolic responses, and reduce chondrocyte apoptosis.[14] A study by Chen et al.[15] found that DHA acts as an agonist for G-protein-coupled receptor 120 (GPR120), which plays a role in homeostasis and regulation of free fatty acids, as well as inflammation prevention. Patients with OA have lower levels of GPR120, and patients given DHA showed reduced expression of proinflammatory genes. Additionally, the metabolite of DHA, called maresin-1, contributes to cartilage damage reduction and an increase in collagen in cartilage.[16] These findings further strengthen the benefits of omega-3 in reducing inflammation and pain in OA patients.

Omega-3 is obtained from foods such as salmon, tuna, mackerel, cereal, walnuts, flaxseeds, and grains.[17] Currently, there are also omega-3 supplementation forms (fish oil) available, which can enhance the effects of anticoagulant and antidepressant medications, but may also cause stomach discomfort.[18] Consuming a diet rich in omega-3 will influence the composition of fatty acids in cell membranes that can alter signaling and gene expression, leading to anti-inflammatory

effects, reduced catabolic responses, and decreased chondrocyte apoptosis.

Based on the two literatures mentioned above, there are conflicting results regarding the administration of omega-3 on reducing joint pain in patients with osteoarthritis. This discrepancy may be due to the limited number of osteoarthritis studies in Senfleber et al.'s research. On the other hand, the more specific study conducted by Deng et al., which focused on patients with osteoarthritis, showed a significant reduction in joint pain. Consistent results were also obtained in subgroup analysis. This further strengthens the benefits of omega-3 in reducing inflammation and pain in OA patients.

Conclusion

Based on the critical review conducted on two systematic reviews and meta-analyses, it can be concluded that the supplementation of omega-3 can still provide benefits to patients with osteoarthritis. Omega-3 can be administered either through dietary sources or supplements.

Conflict of interest

Authors declared no conflict of interest regarding this article.

Open Access

References

1. He Y, Li Z, Alexander PG, Ocasio-Nieves BD, Yocum L, Lin H, et al. Pathogenesis of osteoarthritis: risk factors, regulatory pathways in chondrocytes, and experimental models. *Biology (Basel).* 2020 Jul 29;9(8):194. doi: 10.3390/biology9080194
2. Kloppenburg M, Berenbaum F. Osteoarthritis year in review 2019: epidemiology and therapy. *Osteoarthr Cartil*. 2020 Mar;28(3):242–8. doi: 10.1016/j.joca.2020.01.002
3. Hootman JM, Helmick CG, Barbour KE, Theis KA, Boring MA. Updated projected prevalence of self-reported doctor-diagnosed arthritis and arthritis-attributable activity limitation among US adults, 2015-2040. *Arthritis Rheumatol*. 2016 Jul;68(7):1582–7. doi: 10.1002/art.39692.
4. Kementerian Kesehatan Republik Indonesia. Hasil Utama Riskesdas 2018. 2018. Available from: http://www.depkes.go.id/resources/download/info terkini/materi_rakorpop_2018/ Hasil Riskesdas 2018.pdf
5. Cordingley DM, Cornish SM. Omega-3 fatty acids for the management of osteoarthritis: a narrative review. *Nutrients*. 2022 Aug 16;14(16):3362. doi: 10.3390/nu14163362
6. Centers for Disease Control and Prevention. Osteoarthritis. 2020 [cited 2023 Jun 20]. Available from: https://www.cdc.gov/arthritis/basics/osteoarthritis.htm
7. Kye SY, Park K. Suicidal ideation and suicidal attempts among adults with chronic diseases: a cross-sectional study. *Compr Psychiatry*. 2017 Feb;73:160–7. doi: 10.1016/ j.comppsych.2016.12.001
8. Indonesian Rheumatology Association. Rekomendasi IRA untuk diagnosis dan penatalaksanaan Osteoarthritis. Jakarta; 2014.
9. Sun Y, Zuo Z, Kuang Y. An emerging target in the battle against osteoarthritis: macrophage polarization. *Int J Mol Sci*. 2020 Nov 12;21(22):8513. doi: 10.3390/ijms21228513
10. Baker KR, Matthan NR, Lichtenstein AH, Niu J, Guermazi A, Roemer F, et al. Association of plasma n-6 and n-3 polyunsaturated fatty acids with synovitis in the knee: the MOST study. *Osteoarthr Cartil*. 2012 May;20(5):382–7. doi: 10.1016/j.joca.2012.01.021. Epub 2012 Feb 4.
11. Saini RK, Keum YS. Omega-3 and omega-6 polyunsaturated fatty acids: dietary sources, metabolism, and significance — a review. *Life Sci*. 2018 Jun;203:255–67. doi: 10.1016/j.lfs.2018.04.049. Epub 2018 Apr 30.
12. Senftleber N, Nielsen S, Andersen J, Bliddal H, Tarp S, Lauritzen L, et al. Marine oil supplements for arthritis pain: a systematic review and meta-analysis of randomized trials. *Nutrients*. 2017 Jan 6;9(1):42. doi: 10.3390/nu9010042.
13. Deng W, Yi Z, Yin E, Lu R, You H, Yuan X. Effect of omega-3 polyunsaturated fatty acids supplementation for patients with osteoarthritis: a meta-analysis. *J Orthop Surg Res*. 2023 May 24;18(1):381. doi: 10.1186/s13018-023-03855-w.
14. Benabdoune H, Rondon EP, Shi Q, Fernandes J, Ranger P, Fahmi H, et al. The role of resolvin D1 in the

regulation of inflammatory and catabolic mediators in osteoarthritis. *Inflamm Res*. 2016 Aug 7;65(8):635–45. doi: 10.1007/s00011-016-0946-x.

15. Chen Y, Zhang D, Ho KW, Lin S, Suen WCW, Zhang H, et al. GPR120 is an important inflammatory regulator in the development of osteoarthritis. *Arthritis Res Ther*. 2018 Dec 3;20(1):163. doi.org/10.1186/s13075-018-1660-6.
16. Xie Y, Zhou W, Zhong Z, Yu H, Zhang P, Shen H. Docosahexaenoic acid inhibits bone remodeling and vessel formation in the osteochondral unit in a rat model. *Biomed Pharmacother*. 2019 Jun;114:108811. doi: 10.1016/j.biopha.2019.108811.
17. Gropper S, Smith J, Carr T. Advanced Nutrition and Human Metabolism. Boston: Cengage Learning Inc; 2020.
18. Morgovan C. Nutrivigilance: a new activity in the field of dietary supplements. *Farmacia*. 2019 May 19;67(3):537–44. doi.org/10.31925/farmacia.2019.3.24.