"Effect of the intervention with omega-3 fatty acids on nutritional and clinical aspects in patients with breast cancer receiving medical treatment."

Palma-Gutierrez Edgardo¹, Espinoza-Rado Erika¹, Zafra-Tanaka Jessica Hanae²

Affiliations:

¹ Universidad Privada Norbert Wiener, Lima, Perú
² CRONICAS Center of Excellence for Chronic Diseases, Universidad Peruana Cayetano Heredia, Lima, Peru

ABSTRACT

Background:

It is known that cancer can cause loss of body weight and muscle protein wasting, which leads to a state of malnutrition, which in turn worsens the prognosis and health of the cancer patient. It has been suggested that the promoting mechanism of this state is systemic inflammation, for which reason several clinical trials have used omega-3 fatty acids, especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), as adjuvants to antineoplastic treatment, mainly due to its anti-inflammatory effects. However, few systematic reviews and meta-analyses have analyzed the effects of omega-3s in patients with breast cancer.

Objective:

The aim of this study is to assess the effect of the supplementation with omega-3 fatty acids on nutritional and clinical outcomes in patients with breast cancer receiving medical treatment.

Methods:

A systematic review will be conducted, starting with a search in PubMed, CENTRAL and EMBASE using search terms related to omega-3 fatty acids and breast cancer. We will include only randomized controlled trials that assess the effects of omega-3 in patients with breast cancer receiving medical treatment. Data will be extracted in a spread sheet. Study selection and data extraction will be conducted by two reviewers independently and the Cochrane Risk of Bias Tool for RCT will be used for assessment of risk of bias. Discrepancies will be reviewed with a third reviewer.

Conclusion:

This systematic review aims to provide an analysis on the outcomes of the usage of the intervention with omega-3 fatty acids on nutritional and clinical aspects in patients with breast cancer receiving medical treatment.

Keywords:

Fatty Acids Omega-3, Eicosapentaenoic Acid, Docosahexaenoic Acids, Breast Neoplasms.

NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.
Conflicts of interest:

All authors declare to have no interest conflict.

Introduction

Breast cancer has one of the highest burdens of disease among cancer. In 2018, it affected around 2,261,419 women worldwide and caused the death of 684,996 patients. It is known that cancer can lead to severe malnutrition; possibly, due to the systemic inflammation that it promotes that induces loss of weight and muscle mass, which in turn worsens the prognosis of the patient. Malnutrition can be very frequent and has a high impact on these people, since it has been estimated that 10 to 20% of deaths from cancer may be due to malnutrition rather than to the neoplasia itself. In other studies, worse response rates to chemotherapy drugs were observed in patients who lost weight, including women with breast cancer.

It is known that omega-3 fatty acids could help fight malnutrition associated with cancer, due to their anti-inflammatory effects that reduce the breakdown and wasting of muscle mass and improve other nutritional aspects. The types of omega-3 most studied in antineoplastic therapy have been eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Some clinical trials have reported that omega-3 supplementation helps modulate the immune response, and improved the survival of breast cancer patients receiving antineoplastic treatment. With regards to nutritional outcomes, no significant differences were found on weight or body composition between those who received the supplementation and those who did not.

There are physiological mechanisms by which omega-3 could be part of the treatment of breast cancer. However, the effects of this intervention on nutritional and clinical outcomes remains unclear. Moreover, there is a need to further explore how the dose, the time of intervention and the characteristics of the population can modify the effects of omega-3. The objective of this systematic review and meta-analysis will be to analyze the effect of the supplementation with omega-3 fatty acids, in their form of EPA and DHA, on nutritional and clinical outcomes in patients with breast cancer receiving medical treatment.

Methods

Study design:

This systematic review will be conducted according to the preferred reporting items for systematic reviews and meta-analyses guidelines (PRISMA).

Inclusion criteria:

We will include studies that assess:

1. Participants: patients with breast cancer receiving medical treatment.
2. Intervention: omega-3 fatty acids supplementation
3. Comparison: Any control group or other treatment.
4. Types of studies: randomized controlled trials with no publication date restriction

Exclusion criteria:

1. Full-text documents not available
2. The following study designs: cross-sectional studies, case control, cohort, case reports, case series, letters to the editor, editorial, narrative review, systematic reviews, correspondence, short communications, technical notes, commentaries and pictorial essays.

3. Studies published in any language other than Spanish or English

**Literature search, data collection and coding**

We will search the following databases: 1) PubMed, 2) Central Cochrane Library, and 3) Embase. Duplicates articles will be removed using Endnote software. Two reviewers will screen titles and abstracts, and will identify potentially relevant studies inclusion and exclusion criteria. Disagreements will be discussed with another reviewer. Then, we will screen full-text in a similar fashion.

The complete search strategy for each database, the number of hits retrieved, and the reasons for exclusion of any studies at the full text stage of selection will be recorded and provided as appendices. We will record the results of included and excluded publications and show them on a PRISMA flowchart.

The data extracted from the selected articles will include:

- Study details: first author, corresponding author, article title, country, year of publication and year of data collection, duration of follow-up, disease outcome, dietary assessment, medical treatment.
- Subjects: number of participants, range of age, population source, location, inclusion and exclusion criteria of studies selected Study.
- Results: nutritional and clinical outcomes

In case we find a study in which the methodology or outcome is not clearly specified, we will try to contact the corresponding author. If we do not receive an answer, then the study will be excluded from the systematic review.

**Risk of bias (quality) assessment**

We will assess risk of bias using the Cochrane Risk of Bias Tool for RCT and present a table with the results of this assessment.

**Statistical analysis**

The results of each study will be expressed, when possible, as standardized or weighted mean difference or relative risk (RR) with corresponding 95% confidence intervals for continuous or dichotomous data, respectively.

The included studies will be grouped into sub-groups of similar population, intervention, and outcome. If a subgroup of studies appears comparable, we will investigate the possibility of pooling such data via formal meta-analysis analytical techniques.

We will assess heterogeneity using an I² statistical. In the case of finding heterogeneity, we will use a random-effects model. The data will be processed with the software Stata v14.0.
References

1. International Agency for Research on Cancer / World Health Organization. Cancer Today [Internet] France; 2020 [Consultado el 18 de enero de 2021]. Disponible en: https://gco.iarc.fr/today/home

2. Arends J, Baracos V, Bertz H, Bozzetti F, Calder P, Deutz NEP, Erickson N, Laviano A, Lisanti M, Lobo D, Mcmillan D, Muscaritoli M, Ockenga J, Pirlich M, Strasser F, De van der Schueren M, Gossum A, Vaupel P, Weimann, A. (2017). ESPEN expert group recommendations for action against cancer-related malnutrition. Clinical Nutrition. 36. 10.1016/j.clnu.2017.06.017

3. Persson C, Glimelius B. The relevance of weight loss for survival and quality of life in patients with advanced gastrointestinal cancer treated with palliative chemotherapy. Anticancer Res. 2002 Nov-Dec; 22(6B):3661-8

4. Seabra F, Estadella D, Caetano D. The role of omega 3 fatty acids in suppressing muscle protein catabolism: A possible therapeutic strategy to reverse cancer cachexia? Journal of Functional Foods 54 (2019) 1–12. https://doi.org/10.1016/j.jff.2018.12.033

5. Calder, P. C. (2006). n−3 Polyunsaturated fatty acids, inflammation, and inflammatory diseases. 1505S–1519S. Retrieved from The American Journal of Clinical Nutrition,83(6), https://doi.org/10.1093/ajcn/83.6.1505S

6. Paixão EMDS, Oliveira ACM, Pizato N, et al. The effects of EPA and DHA enriched fish oil on nutritional and immunological markers of treatment naïve breast cancer patients: a randomized double-blind controlled trial. Nutr J. 2017;16(1):71. Published 2017 Oct 23. doi:10.1186/s12937-017-0295-9

7. Darwito D, Dharmana E, Riwanto I, et al. Effects of Omega-3 Supplementation on Ki-67 and VEGF Expression Levels and Clinical Outcomes of Locally Advanced Breast Cancer Patients Treated with Neoadjuvant CAF Chemotherapy: A Randomized Controlled Trial Report. Asian Pac J Cancer Prev. 2019;20(3):911-916. Published 2019 Mar 26. doi:10.31557/APJCP.2019.20.3.911

8. de la Rosa Oliva F, Meneses García A, Ruiz Calzada H, Astudillo de la Vega H, Bargalló Rocha E, Lara-Medina F, Alvarado Miranda A, Matus-Santos J, Flores-Díaz D, Oñate-Acuña LF, Gutiérrez-Salmeán G, Ruiz García E, Ibarra A. Effects of omega-3 fatty acids supplementation on neoadjuvant chemotherapy-induced toxicity in patients with locally advanced breast cancer: a randomized, controlled, double-blinded clinical trial. Nutr Hosp. 2019 Aug 26;36(4):769-776. English. doi: 10.20960/nh.2338. PMID: 31192682

9. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009 Ju l21;6(7):e1000097.
10. Higgins JPT, Savović J, Page MJ, Elbers RG, Sterne JAC. Chapter 8: Assessing risk of bias in a randomized trial. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.1 (updated September 2020). Cochrane, 2020.

Appendix:
Search strategy

Pubmed

("Fatty Acids, Omega-3"[Mesh] OR “Omega-3”[tiab] OR PUFA[tiab] OR "Eicosapentaenoic Acid"[Mesh] OR Eicosapentaenoic[tiab] OR "Docosahexaenoic Acids"[Mesh] OR Docosahexaenoic[tiab] OR "Fish Oils"[Mesh] OR “fish oils”[tiab] OR DHA[tiab] OR EPA[tiab]) AND ("Breast Neoplasms"[Mesh] OR "Breast neoplasm”[tiab] OR "Breast cancer”[tiab])

Filter: randomized controlled trials

Embase:

(('omega 3 fatty acid'/exp OR 'omega 3 fatty acid' OR 'fish'/exp OR fish) AND ('oils'/exp OR oils) OR 'dha'/exp OR dha OR epa OR pufa OR 'omega 3'/exp OR 'omega 3' OR eicosapentaenoic OR docosahexaenoic) AND ('breast cancer'/exp OR 'breast cancer' OR 'breast neoplasm')

Filter: publication type:article

CENTRAL:

("Fatty Acids, Omega-3"[Mesh] OR "Fish Oils"[Mesh] OR Omega-3 OR PUFA OR Eicosapentaenois OR Docasahexaenoic OR fish oils OR DHA OR EPA) AND (Breast neoplasm OR breast cancer OR Breast Neoplasms[Mesh])