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Case Report

The impact of omega-3 supplementation on body weight in cancer patients: Evidence-based case report

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Abstract

Introduction: Cancer-related malnutrition affects 20-70% of patients, causing anorexia and increased energy expenditure, leading to muscle and adipose tissue decline. Omega-3 polyunsaturated fatty acid (PUFA) supplementation is believed to reduce inflammation, maintain muscle strength and weight, and improving the quality of life. This study aims to examine its effectiveness in aiding weight maintenance in cancer patients.
Case Illustration: A 23-year-old man was admitted to the hospital with a worsening headache. He had a history of craniotomy, maxillectomy, and tracheostomy due to a tumor obstructing his airway, followed by chemotherapy. Despite normal bowel and urination, he reported decreased appetite and weight loss. Physical examination revealed severe malnutrition and a left facial mass with temporal hollowing. Anemia, hyponatremia, and hypokalemia were noted. The patient was scheduled for surgery and advised dietary adjustments and omega-3 supplementation to manage inflammation and prevent further weight loss.
Discussion: A critical review revealed significant outcomes of omega-3 supplementation on cancer patients' weight. Cancer induces inflammation and metabolic changes, leading to anorexia and muscle decline. Omega-3 suppresses inflammation, improves appetite, and promotes weight gain. Studies support its efficacy in various cancer types. Concerns over chemoresistance and gastrointestinal effects exist. Nonetheless, omega-3 can be safely integrated into cancer patient management to improve treatment response and quality of life. Supplementation with at least 1 g of EPA is recommended for its anti-inflammatory benefits.
Conclusion: Omega-3 supplementation can help maintain weight in cancer patients.

Keywords: cancer, omega-3 polyunsaturated fatty acid, supplementation, weight

Abstrak

Pendahuluan: Malnutrisi terkait kanker memengaruhi hingga 20-70% pasien. Hal ini menyebabkan anoreksia dan peningkatan pengeluaran energi yang mengakibatkan penurunan massa otot dan jaringan adiposa. Suplementasi Omega-3 *polyunsaturated fatty acid* (PUFA) diyakini dapat mengurangi peradangan, mempertahankan kekuatan otot serta berat badan, dan meningkatkan kualitas hidup. Studi ini bertujuan untuk menguji efektivitas omega-3 dalam membantu menjaga berat badan pada pasien kanker.
Ilustrasi Kasus: Seorang pria berusia 23 tahun masuk ke rumah sakit dengan sakit kepala yang memberat. Pasien memiliki riwayat kraniotomi, maksilektomi, dan trakeostomi akibat tumor yang menghalangi saluran napas, diikuti dengan kemoterapi. Meski buang air besar dan buang air kecil normal, pasien melaporkan penurunan nafsu makan dan penurunan berat badan. Pemeriksaan fisik menunjukkan malnutrisi berat dan massa pada wajah kiri dengan cekungan temporal. Hasil laboratorium menunjukkan anemia, hiponatremia, dan hipokalemia. Pasien dijadwalkan untuk menjalani operasi dan disarankan penyesuaian diet serta suplementasi omega-3 untuk mengelola peradangan dan mencegah penurunan berat badan lebih lanjut.
Diskusi: Sebuah tinjauan kritis mengungkapkan hasil signifikan dari suplementasi omega-3 terhadap berat badan pasien kanker. Kanker menyebabkan peradangan dan perubahan metabolik, yang menyebabkan anoreksia dan penurunan massa otot. Omega-3 menekan peradangan, meningkatkan nafsu makan, dan membantu penambahan berat badan. Studi mendukung efektivitasnya dalam berbagai jenis kanker. Namun, terdapat risiko terhadap kemoresistensi dan efek gastrointestinal. Meskipun demikian, omega-3 dapat dengan aman diintegrasikan ke dalam manajemen pasien kanker untuk meningkatkan respons pengobatan dan kualitas hidup. Suplementasi minimal 1 g EPA disarankan untuk mendapatkan manfaat anti-inflamasi.
Kesimpulan: Suplementasi omega-3 dapat membantu menjaga berat badan pada pasien kanker.

Kata Kunci: berat badan, kanker, omega-3 *polyunsaturated fatty acid*, suplementasi

Background

Cancer-related malnutrition affects approximately 20-70% of cancer patients. The prevalence of cancer-related malnutrition varies depending on many factors, such as the type and stage of cancer, treatment modalities, and age.[1] Cancer is characterized by systemic inflammation, the production of pro-inflammatory cytokines, and tumor catabolic factors that trigger various metabolic changes.[2] This leads to anorexia and increased resting energy expenditure, ultimately causing a decline in skeletal muscle mass and adipose tissue. Consequently, the loss of muscle mass contributes to a progressive decline in muscle strength and endurance and is associated with higher levels of dose-limiting chemotherapy toxicity, reduced quality of life, and poor survival.[3]

Omega-3 PUFA, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are found in fatty fish such as salmon, sardines, tuna, and algae. Omega-3 PUFA supplementation is said to reduce systemic inflammation and may increase or maintain muscle strength and body weight by reducing the release of pro-inflammatory cytokines (e.g., IL-1, IL-6, and TNF-α) and tumor-induced factors, thereby improving the quality of life in cancer patients.[4] A more recent systematic review reported positive results in maintaining skeletal muscle mass and body weight in cancer patients using oral nutritional supplements enriched with omega-3 PUFA, but found inconsistent findings regarding the effects of omega-3 PUFA supplements on quality of life. This recent review did not consider studies using fish oil capsules or other oral delivery methods, was limited to articles published after 2014, and did not conduct a meta-analysis on muscle mass and quality of life.[1] This study aims to investigate the effectiveness of omega-3 supplementation in helping to maintain body weight in cancer patients. Omega-3 fatty acids offer promising avenues for the development of future cancer therapies aimed at helping maintain body weight in cancer patients undergoing treatment. By targeting appetite regulation, muscle preservation, metabolic modulation, inflammation management, and nutritional support, omega-3s may play a valuable role in mitigating weight loss and improving the overall well-being of cancer patients throughout the course of their illness and treatment.

Case Illustration

A 23-year-old male patient presented with chief complaint of worsening headache since one day before admission to the hospital. One year prior to admission, the patient underwent craniotomy and maxillectomy by the Neurosurgery and ENT departments. The patient also underwent tracheostomy to secure the airway due to a tumor pressing on the airway. Subsequently, the patient received chemotherapy in the Intensive Care Unit. The patient reports a decrease in appetite and weight, as well as a decline in food intake since the initiation of chemotherapy. Bowel movements (BM) and urination are normal.

On physical examination, the patient's parameters were within normal limits. The patient's weight was 28.6 kg, height was 162 cm, with a body mass index (BMI) of 10.9 kg/m2 (severe malnutrition). General examination revealed a lump on the left side of the patient's face, as well as temporal hollowing on the left side, while the neck, chest, and abdomen were within normal limits. Complete blood count showed anemia with a hemoglobin level of 10.8 g/dL, sodium level of 128 mEq/L, and potassium level of 3.2 mEq/L. The patient was scheduled for surgery and consulted with the Clinical Nutrition department for dietary adjustments to improve the patient's nutritional status. The patient was also planned to receive omega-3 supplementation to help manage inflammation and maintain the patient's weight. The patient asked the clinical nutritionist whether omega-3 supplementation would be beneficial in helping to maintain his weight and prevent further weight loss. The patient was aware that omega-3 is known to be beneficial for maintaining cardiovascular health.

Literature Review

Literature search was conducted on October 10, 2023, using advanced searching techniques in PubMed, Cochrane Library, Scopus, and Science Direct for systematic reviews or randomized controlled trials articles. The search employed a combination of MeSH Terms and Title/Abstract from each component of the PICO framework, utilizing the boolean operator “OR” to increase sensitivity and “AND” to enhance specificity (Table 1). The keywords used were “omega-3,” “n-3 fatty acids,” “ω-3,” “weight gain,” “weight increase,” and “cancer.” Critical appraisal tools and determination of the level of evidence were conducted based on the Oxford Centre for Evidence Based Medicine.

Table 1. Literature search strategy

Database	*Search Strategy*	*Hits*	*Selected Article*
Pubmed	(((omega 3[Title/Abstract])) OR (omega 3[MeSH Terms])) OR (n-3[MeSH Terms])) OR (ω-3[Title/Abstract])) AND (((((weight gain[MeSH Terms]) OR (weight increase[Title/Abstract])) OR (weight increase[Title/Abstract])) OR (weight gain[MeSH Terms])) OR (weight[MeSH Terms])) OR (gain[Title/Abstract]) AND (((cancer[Title/Abstract]) OR (cancer cachexia[MeSH Terms])) OR (cancer cachexia[MeSH Terms])) OR (cancer cachexia[Title/Abstract]))	186	1
Cochrane Library	#1 (omega 3):ti,ab,kw OR (n-3 fatty acids):ti,ab,kw OR (ω-3 fatty acids):ti,ab,kw OR (ω-3):ti,ab,kw #2 (weight gain):ti,ab,kw OR (weight gains):ti,ab,kw OR (gain):ti,ab,kw #3 (cancer):ti,ab,kw OR (neoplasma) :ti,ab,kw OR (tumour) :ti,ab,kw #4 #1 AND #2 AND #3	19	1
Scopus	(TITLE-ABS-KEY (omega) AND TITLE-ABS-KEY (3) OR TITLE-ABS-KEY (ω) AND TITLE-ABS-KEY (3) OR TITLE-ABS-KEY (n) AND TITLE-ABS-KEY (3) AND TITLE-ABS-KEY (fatty) AND TITLE-ABS-KEY (acids) AND TITLE-ABS-KEY (weight) AND TITLE-ABS-KEY (gain) OR TITLE-ABS-KEY (weight) AND TITLE-ABS-KEY (increase) OR TITLE-ABS-KEY (weight) AND TITLE-ABS-KEY (improvement) AND TITLE-ABS-KEY (cancer)) AND PUBYEAR > 2018 AND PUBYEAR < 2024 AND (LIMIT-TO (LANGUAGE , "English")) AND (LIMIT-TO (OA , "all"))	13	1
Science Direct	(omega 3 fatty acids OR ω-3 AND weigt gain OR weight increase AND Cancer OR neoplasma OR tumour)	21	1

Clinical Question:

P : Cancer patients
I : Omega-3 supplementation
C : Placebo or No medication
O : Stable or increased body weight

Clinical Question: Can omega-3 supplementation help maintain body weight in cancer patients?

Eligibility Criteria

The eligibility criteria for the study included the following inclusion criteria: subjects aged over 18 years with a diagnosis of cancer, studies utilizing a randomized controlled trial (RCT) design and systematic review/ meta-analysis of RCTs. The intervention group receiving omega-3 while the control group received placebo or no medication. Studies presenting outcomes in the form of stable/increased body weight. References reviewed were from 2018 to 2023, and articles written in English. The exclusion criteria for the study encompasses studies not conducted on humans.

Critical Appraisal Method

Critical appraisal was performed on all selected articles by assessing validity, importance, and applicability (VIA) using the CEBM (Centre for Evidence Based Medicine) criteria according to the type of therapy study.

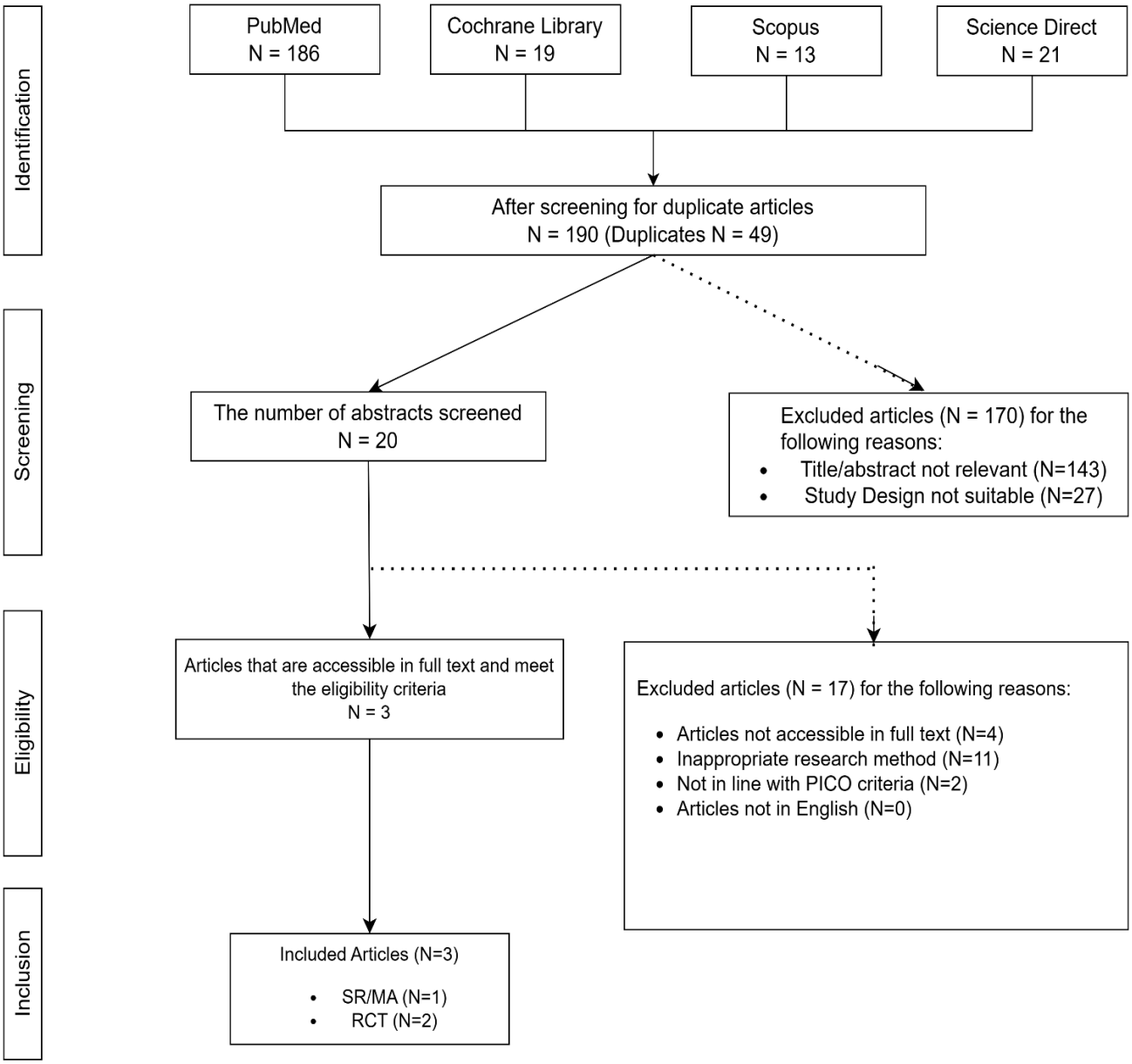

Figure 1. Prisma's flowchart

Result

Based on the search results from the databases conducted using Advanced Searching, 186 literatures were found in PubMed, 19 literatures in the Cochrane Library, 13 literatures in Scopus, and 21 literatures in Science Direct. Three research articles involved patients with cancer who received omega-3 supplementation in the intervention group, compared to the control group given a placebo or no medication to assess the outcome of weight improvement.

Table 2. Assessment of literature characteristics

Author(s)	Study Design	Population Characteristics	Intervention	Outcome	Research Findings
Lam CN, et al. (2021)[5]	*Systematic review* and Meta-analysis RCT	The subjects are: 135 adult patients with various types of cancer.	Patients with various types of cancer were given omega-3 supplementation at a dose of >600 mg/day compared to a placebo that did not receive omega-3 supplementation for more than 3 weeks.	Lean body mass (LBM), fat-free mass (FFM), mid-upper arm muscle circumferences (MUAMC) and weight gain	Potential effects of oral omega-3 were found in the intervention group compared to the control group.
Cheng M, et al. (2021)[6]	*Randomized Controlled Trial*	The subjects were 60 lung cancer patients with an NRS 2002 score > 4, randomly allocated into two groups, with one group receiving omega-3 supplements and the other group serving as the control, receiving a placebo for 12 weeks.	The patients received weekly omega-3 supplementation administered over a period of 12 weeks. Group A received omega-3 supplementation consisting of 1.6 g of EPA and 0.8 g of DHA, while Group B (the control group) received a placebo.	Anthropometry including body weight, body mass index, upper arm circumference, laboratory nutritional indicators (hemoglobin, albumin, triglycerides, and cholesterol), as well as inflammation markers (C-reactive protein, tumor necrosis factor-α, and interleukin-6) were measured.	There was an increase in body weight in the intervention group.
Feijó PM, et al. (2019)[7]	*Randomized Controlled Trial*	The subjects were 68 gastric cancer patients, randomized into two groups, one receiving an omega-3 enriched formula and the other receiving a placebo (formula without omega-3) for 30 days.	The group that received the omega-3 enriched formula and the placebo group (formula without omega-3) for 30 days.	Weight gain in the intervention group	Increased weight and reduced inflammation profile in the intervention group compared to the placebo group.

Critical Appraisal

Selected systematic review/meta-analysis (SR/MA) articles were assessed using the FAITH tools, while articles with RCT designs were reviewed using the therapy worksheet from the CEBM University of Oxford. Before conducting the critical appraisal, the relevance of the three obtained articles was evaluated with the PICO from the established clinical question. The three acquired articles were found to be highly relevant to the PICO of the established clinical question. This can be observed in Table 3.

Based on the critical review of one Systematic Review/Meta-Analysis (SR/MA) article and two Randomized Controlled Trials (RCTs), the three articles obtained show good validity and demonstrate statistically significant and meaningful results regarding the weight of cancer patients. This can be observed in Table 4.

Table 3. Relevance criteria

Authors	Population Similarity	Similar Determinants	Outcome similarity
Lam CN, et al. (2021)[5]	+	+	+
Cheng M, et al. (2021)[6]	+	+	+
Feijó PM, et al. (2019)[7]	+	+	+

Table 4. Summary of critical review validity, importance, applicability, and level of evidence (SR/MA)

	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
Lam CN, et al. (2021)[5]	+	+	+	+	+	+	+	+	Moderate	1A
Cheng M, et al. (2021)[6]	+	+	+	+	+	+	+	+	Moderate	1B
Feijó PM, et al. (2019)[7]	+	+	+	+	+	+	+	+	Moderate	1B

Discussion

Based on the critical review results, all SR/MA and RCT articles show significant outcomes of omega-3 supplementation on weight in cancer patients. Cancer is characterized by systemic inflammation, the production of pro-inflammatory cytokines, and tumor catabolic factors that trigger various metabolic changes.[2] This leads to anorexia and increased resting energy expenditure, ultimately resulting in a decrease in skeletal muscle mass and adipose tissue.[3] As a consequence, the loss of muscle mass contributes to a progressive decline in muscle strength and endurance, and is associated with higher levels of chemotherapy toxicity, decreased quality of life, and poor survival rates.[5]

Several studies have indicated that omega-3 fatty acid supplementation improves the nutritional status of cancer patients through various mechanisms. Omega-3 fatty acids are polyunsaturated fatty acids (PUFAs) characterized by the presence of a triple bond three atoms away from the methyl end group in their chemical structure.[6] Omega-3 plays a crucial role in lipid metabolism in humans. Omega-3 fatty acids have been shown to suppress systemic inflammatory and oxidative responses, enhance patients' appetite,

and promote weight gain in cancer cachexia patients.[7,8] Omega-3 fatty acids have been evaluated for their beneficial effects in various types of cancer, including colorectal cancer, oral squamous cell carcinoma, breast cancer, and hematological cancer, with promising results.[8] In addition to the mentioned evidence, there is not yet sufficient definitive evidence to support the use of omega-3 fatty acid supplementation in these patients, and more randomized controlled clinical trials considering relevant outcomes, adequate sample sizes, and appropriate dosages are recommended.[9]

Lam et al. conducted a systematic review/meta-analysis (SR/MA) of RCT studies, including 31 research studies, of which 18 studies compared the administration of omega-3 to cancer patients with a placebo. The results of the SR/MA indicated that omega-3 supplementation did not significantly help maintain or increase the body weight of cancer patients, with a mean difference of 0.98 kg, p<0.33, and a 95% confidence interval. However, after analyzing subgroups, where the intervention provided was in the form of Oral Nutritional Support (ONS) and compared with omega-3 capsules, a positive trend was found in the body weight of the group with omega-3 capsule intervention compared to ONS.[10]

The RCT study conducted by Cheng et al involved research on 60 lung cancer patients with Nutritional Risk Screening 2002 (NRS 2002) scores > 4 between May 2019 and September 2020, observed over 12 weeks. The study found that supplementation in the form of omega-3 capsules containing eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) was effective. The omega-3 capsules administered contained 1.6 g/day of EPA and 0.8 g/day of DHA. After the intervention, the patients experienced a significant increase in body weight (61.86 ± 10.02 vs. 66.71 ± 9.17, p = 0.049) without significant changes in the patients' food intake (2,067 ± 338 vs. 2,133 ± 420, p = 0.512).[11] Another RCT study conducted by Feijó et al also yielded similar results. In this study, a formula containing omega-3 was administered for 30 days. The results showed an increase in body weight and a decrease in inflammatory markers in the intervention group with a p-value of 0.001.[12] The results of both RCTs were significant both statistically and clinically.

The 2017 ESPEN guidelines on nutrition in cancer mention a weak recommendation regarding the use of PUFA omega-3 supplementation to treat cancer-related malnutrition in patients with advanced cancer undergoing chemotherapy based on low-level evidence.[13] A more recent systematic review reported positive results in maintaining skeletal muscle mass and body weight in cancer patients using oral nutritional supplements enriched with PUFA omega-3, but these findings were inconsistent regarding the effects of PUFA omega-3 supplements on quality of life.[1] This recent review did not consider studies using fish oil capsules or other oral delivery methods, was limited to articles published after 2014, and did not conduct a meta-analysis related to muscle mass and quality of life.[1,13]

Cancer has been proven to alter the body's metabolism. Glucose, lipid, and protein metabolism change to support the growth of cancer cells. This process is known as metabolic reprogramming. These changes involve rapid cell replication or growth, cell resistance to apoptosis, genetic mutations in cells, and invasion and migration to distant tissues from the cancer cell. These metabolic alterations cause cancer cells to require larger amounts of nutrients.[14] The rapid growth of cancer cells increases the cell's demand for oxygen. If this is not balanced with an increased oxygen supply, tumor hypoxia can occur. This will induce hypoxia-inducible factor (HIF)-1, which increases glucose transcription via GLUT-1. Increased GLUT-1 will enhance glucose usage in the cell, resulting in the production of more pyruvate.[15] Hypoxia-inducible factor-1 induces pyruvate dehydrogenase kinase (PDHK), an enzyme that inactivates pyruvate dehydrogenase, thereby inhibiting the conversion of pyruvate to acetyl Co-A in the mitochondria. The accumulation of pyruvate is then converted to lactate by the enzyme lactate dehydrogenase (LDH). The conversion of glucose to lactate is an inefficient energy/ATP-generating process because it requires up to 40 times more glucose than needed in the TCA cycle (glucose addiction).[16]

Muscle wasting is a common occurrence in cancer patients. Cancer cells can stimulate the innate immune system, including macrophages and dendritic cells, to stimulate NF-$_k$β, which will trigger the release of TNF-α. TNF-α will induce the release of proteolysis-inducing factor (PIF), which will induce proteolysis, mainly via the ubiquitin pathway. Additionally, the high levels of pro-inflammatory cytokines in cancer will contribute to the decrease in protein synthesis. This process leads to muscle mass degradation and consequent weight loss and muscle wasting.[17]

Supplementation of omega-3 fatty acids has been proposed as a therapy to counter the observed catabolism in most cancer patients and cachexia by reducing the inflammatory response. This supplementation helps to reduce the formation of pro-inflammatory cytokines, improve metabolic tolerance of energy substrates, and decrease protein catabolism, aiming to improve the prognosis of cancer patients.

Due to these anti-inflammatory properties, omega-3 supplementation has the potential to improve the health condition of cancer patients and cachexia. The anti-inflammatory effects of omega-3 are achieved through daily supplementation with EPA, helping to stabilize the unintentional weight loss in cancer patients.[13]

Foods rich in omega-3 fatty acids are commonly found in fatty fish such as trout, salmon, tuna, and mackerel, as well as in algae. Omega-3 is widely found in natural edible seed oils and marine products, and it plays a significant role in human lipid metabolism. Omega-3 fatty acids have been shown to suppress systemic inflammatory and oxidative responses, improve the appetite of patients, and promote weight gain in cancer cachexia patients. Omega-3 fatty acids have been evaluated for their beneficial effects in various types of cancer, including colorectal cancer, oral squamous cell carcinoma, breast cancer, and hematological cancer, with promising results.[6]

There are concerns about PUFA omega-3 supplements causing chemoresistance, as well as the potential gastrointestinal side effects such as diarrhea and reflux. Therefore, it is important to monitor the effects of PUFA omega-3 on treatment-related toxicity. However, none of the studies included in the studies reported significant treatment-related toxicity in patients using PUFA omega-3 supplements.[18]

Based on the critical review above and several studies regarding the effectiveness of omega-3 on the weight of cancer patients, omega-3 supplementation can be part of the nutritional management of cancer patients that is not contraindicated. The administration of at least 1 g of EPA has become a nutritional medical management that can help address inflammation due to cancer, as well as help improve and maintain the weight of patients. Optimal nutritional status of cancer patients can support a good response to therapy, minimize side effects, reduce the risk of morbidity and mortality, and improve quality of life.[5]

Conclusion

Based on the review of the journals conducted, the administration of omega-3 to cancer patients significantly, both statistically and clinically, can help maintain and increase body weight. The administration of omega-3 to cancer patients can be considered, especially in cancer patients with high inflammatory markers. The duration of omega-3 supplementation in the three critical reviews above ranged from 3 to 12 weeks, with doses ranging from 600 mg to 2 g of EPA.

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