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EVIDENCE BASED CASE REPORT: AN EFFECTIVENESS OF OMEGA 3 SUPPLEMENTATION ON CLINICAL SYMPTOMS IMPROVEMENT AND CLINICAL PARAMETERS OF COVID-19

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Abstract

Background: Coronavirus disease 2019 (COVID-19) infection is a disease with high morbidity and mortality rates worldwide. This viral infection can cause metabolic and clinical changes that affect the patient's condition. Omega 3 polyunsaturated fatty acids (ω3-PUFAs) are important mediators of anti-inflammatory and immune response. Thus, it can reduce clinical symptoms of COVID-19 patients.
Objective: To know the effect of omega 3 supplementation in improving clinical symptoms and clinical parameters of COVID 19.
Methods: Article searches were conducted using advanced searching by combining MesH Terms and abstracts/titles in the Pubmed, Cochrane Library, and Scopus databases. The search found two selected literatures to further conduct a critical assessment.
Results: Two articles were selected based on the eligibility criteria and conformity with the Problem Intervention Comparison Outcome (PICO). Study conducted by Sedighiyan et al.,[1] showed that there were significant changes in clinical symptoms of COVID-19 patients such as pain, fatigue ($p< 0.001$), increased appetite ($p=0.003$), decreased Erythrocyte Sedimentation Rate (ESR) values ($p < 0.002$), and decreased C-reactive protein (CRP) values ($p<0.001$). Study conducted by Doaei et al.,[2] showed that there was significant decrease in pH ($p=0.001$), HCO_3 ($p = 0.001$), Be ($p = 0.001$), and creatinine ($p = 0.002$), thereby improving clinical symptoms of COVID-19 patients.
Conclusion: Omega 3 supplementation can improve clinical symptoms and clinical parameters of COVID 19. However, further research is needed with a larger sample, a longer duration, and with dose adjustment of omega 3 supplementation.

Keywords: COVID-19, omega 3 fatty acids, clinical symptoms and clinical parameters improvement

Introduction

Since being declared a global pandemic by the World Health Organization (WHO) on March 11, 2020, coronavirus disease 2019 (COVID-19) has infected more than 300 million individuals worldwide. Increasing cases continue to occur every day, with a total of 5,560,718 deaths.[3]

According to WHO data, the total number of positive confirmed COVID-19 cases in the world as of January 21, 2022 was 169,118,995 people, with 3,519,175 deaths.[3] Until January 21, 2022, there were 4,280,248 confirmed COVID 19 cases in Indonesia, with 144,201 deaths.[4]

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Coronavirus infection is a disease with high morbidity and mortality worldwide. The novel coronavirus 2019 (nCoV 2019) is known as an acute respiratory syndrome coronavirus 2 (SARS CoV2). This viral infection can cause metabolic and clinical changes that affect the patient's condition. COVID-19 infection in humans can be asymptomatic or symptomatic.[5] COVID-19 infection can cause mild, moderate, or severe symptoms. Fever (temperature >38°C), cough, and difficulty breathing are the most common clinical symptoms. Furthermore, it can be accompanied by severe shortness of breath, fatigue, myalgia, gastrointestinal symptoms such as diarrhea, and other respiratory symptoms. Shortness of breath can develop as soon as one week after a patient is infected with the COVID-19 virus. In extreme cases, such as Acute Respiratory Distress Syndrome (ARDS), septic shock, metabolic acidosis, and bleeding or coagulation system failure, a rapid and gradual worsening can occur within a few days. Some people have mild symptoms that aren't even accompanied by a fever.[6]

Omega 3 polyunsaturated fatty acids (ω3-PUFAs) are an important mediator in inflammatory process and immune response, thereby functioning as an anti-inflammatory substance. Study conducted by Zhao et al.,[7] demonstrated that omega 3 PUFA including eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and α-linoleic acid (ALA) can increase cell membrane stability, regulate immune function, inhibit inflammatory reactions, reduce the incidence of systemic inflammatory response syndrome (SIRS), multiple organ dysfunction and infectious complications.[7]

Omega 3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) can inactivate viruses by modulating the ideal host lipid conditions for viral replication. Furthermore, EPA and DHA inhibit the cyclooxygenase (COX) enzyme, which aids in the suppression of prostaglandin (pro-inflammatory) production.[8] Despite the numerous beneficial effects of Omega 3, one of which is its anti-inflammatory properties, few studies have been conducted to evaluate its effectiveness in reducing the clinical symptoms of COVID-19 patients. Therefore, the purpose of this EBCR is to determine the efficacy of omega 3 in improving clinical symptoms and clinical parameters of COVID-19 patients.

Clinical Question

A 41-year-old female patient came to the Emergency Room (ER) with complaints of fatigue, pain, decrease appetite, fever,

cough with phlegm, runny nose and feeling a little short of breath since three days ago. The patient's blood pressure was 120/80 mmHg, pulse 98 times per minute, respiratory rate 22 times per minute, temperature 39◦C, weight 50 kg, height 155 cm and Body Mass Index (BMI) 20.8 kg/m^2. In addition, the patient was also subjected to a PCR swab examination and the results was positive for COVID-19. The patient was treated in the isolation room of the hospital for seven days. The patient was interested in trying omega 3 supplementation after reading an article about the benefits of omega 3 on COVID-19. The patient asked the doctor whether omega 3 supplementation could reduce the complaints such as fatigue, pain that she was currently experiencing?

Methods

Article searches were conducted using advanced searching by combining MesH Terms and abstracts/titles in the Pubmed, Cochrane Library, and Scopus databases. The search was carried out on December 26, 2021. Keywords were entered in the MeSH Terms and title/abstract categories. The articles included in the search were systematic reviews, meta-analyses, and randomized controlled trials within the last 5 years. Studies on animals, studies that were not fully available, and studies other than in English, were not included in the search. Titles and abstracts were reviewed, articles that did not meet the eligibility criteria and PICO were excluded and duplication screening was carried out. A critical study was carried out using tools from the Center for Evidence-Based Medicine, Oxford Center for Evidence-Based Medicine.

Research Results

The search results yielded 4 articles from Pubmed database, 7 articles from Cochrane Library, and 21 articles from Scopus. After the search results were obtained, a screening of duplicated articles was conducted using EndNote X9 program. Subsequent screening test was carried out by comparing the title and abstract to the suitability of the PICO. Eligibility criteria such as full text and limitations on the publication of articles within the last 5 years were applied before conducting a critical review of the articles obtained. After screening duplication and selecting articles according to eligibility criteria, 2 literatures from Sedhigiyan et al.,[1] and Doaei et al.,[2] were found to be relevant and could be analyzed to answer clinical question.

Discussion

Individuals infected with severe acute respiratory syndrome coronavirus 2 (SARS CoV2), the virus that causes COVID 19, may

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experience mild to severe symptoms. Symptoms of COVID 19 can be experienced with or without fever, weakness, cough, anorexia, muscle aches, sore throat, nasal congestion, headache, shortness of breath, nausea, vomiting, and diarrhea. Severe symptoms of COVID-19 include signs of pneumonia with respiratory distress, septic shock, and multi-organ failure that ultimately leads to death.[6]

Omega 3 polyunsaturated fatty acids (ω3-PUFAs) is an important mediator in inflammatory process and immune response, thereby functioning as an anti-inflammatory substances. Study conducted by Zhao et al.,[7] demonstrated that omega 3 PUFA including eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and α-linoleic acid (ALA) can increase cell membrane stability, regulate immune function, inhibit inflammatory reactions, reduce the incidence of systemic inflammatory response syndrome (SIRS), multiple organ dysfunction and infectious complications.[2] Omega 3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) can inactivate viruses by modulating the ideal host lipid conditions for viral replication. Furthermore, EPA and DHA inhibit the cyclooxygenase (COX) enzyme, which aids in the suppression of prostaglandin (pro-inflammatory) production.[8]

Sedhigiyan et al.,[1] conducted a study on 30 COVID-19 patients. The study showed that there was a significant effect on improving clinical symptoms and clinical parameters. Complaints of pain decreased after giving omega 3 in the intervention group. Before supplementation of omega 3, a pain score of 8.6 ± 0.25 was observed, after omega 3 supplementation, a score of 4.3 ± 0.21 was obtained, with a p value of < 0.001. Complaints of fatigue were assessed with a score of 1-10, there was a decrease after giving omega 3 from 9.13 ± 0.19 to 4.06 ± 0.16 with a p<0.001.The study demonstrated that supplementation of omega 3 can improve clinical symptoms except for olfactory disturbances. Omega 3 supplementation can reduce pain complaints due to the ability of DHA to increase serotonergic and glutaminergic synaptic activity which can inhibit deacetylation and worsen pain complaints.[9] In addition, omega 3 also has an analgesic effect by reducing the resolving type D and E, which can suppress pain receptors such as TRPV1.[1] Administration of omega 3 can improve complaints of fatigue, this is because omega 3 supplementation in COVID-19 patients can improve muscle function by increasing membrane fluidity, acetylcholine sensitivity thereby increasing protein catabolism.[1]

Omega 3 supplementation had a

significant effect in decreasing the value of ESR and CRP, which are markers of inflammation. The CRP value in the intervention group after administration of omega 3 was 25.1 ± 1.39 compared to before administration with a value of 92.8 ± 4.74 with p value < 0.001. The administration of omega 3 also gave significant results by reducing the ESR value from 59.3 ± 3.16 to 26.3 ± 2.4 with p value = 0.002. Supplementation of omega 3 aims to reduce the inflammatory reaction that often occurs in viral infections and can cause an increase in inflammatory markers. Omega 3 can suppress Interleukin 6 (IL-6), (Interleukin 1) IL-1, and Tumor Necrosis Factor- (TNF-α) by producing anti-inflammatory lipid metabolites.[1]

The strength of the study conducted by Sedhigiyan et al.,[1] with the administration of 2 g of omega 3 for 2 weeks was well tolerated and provided a beneficial effect with reduced complaints of fatigue, pain all over the body, and an increase in appetite. The limitations of the study conducted by Sedhighiyan et al.,[1] include the small number of samples, the subjective method used in measuring clinical variables, and not using a standardized questionnaire to determine the severity of clinical symptoms experienced by patients.

The second study conducted by Doaei et al.,[2] showed that there were significant results after supplementation of omega 3. There was an improvement in the pH value in the intervention group, which was 7.3 after being given omega 3 compared to the control group with a pH value of 7.26, with a p value of 0.001. There was an improvement in the HCO3 value after giving omega 3 in the intervention group, which was 22 compared to before giving omega 3, which was 18.17, with a p value of 0.001. There was a decrease in the value of Be in the intervention group, which was -3.59 compared to the control group, which was -7.09, with a p value of 0.001. There was an improvement in creatinine value after giving omega 3 to the intervention group with a value of 1.29 compared to 1.68 in the control group. Several studies have shown that omega 3 supplementation improves endothelial function and microcirculation. Vasil'ev et al.,[2] reported that omega 3 PUFAs increase tissue hemoperfusion, capillary blood flow, and tissue blood flow which can improve microcirculation. Trevor et al.,[2] demonstrated the effect of DHA and EPA supplementation on vascular and microcirculation reactivity, in which DHA significantly increased vasodilator mechanisms, and improved endothelial and microcirculatory reactivity. This is consistent with impaired renal function that often occurs

in patients with COVID[19]. A diet high in PUFAs can also improve creatinine clearance and maintain good kidney function.[2] The strength of this study is that, this is the first study conducted to assess the effect of omega 3 supplementation on patients with COVID-19. The limitations of this study include the short study time and the use of only dose of omega 3 which makes it difficult to interpret the effectiveness of omega 3 according to the dose response given.

Conclusion

Based on the result of the critical review, omega 3 supplementation can provide benefits in reducing clinical symptoms and clinical parameters of COVID-19 patients. Two weeks treatment with 2 g omega 3 reduce symptoms of fatigue, pain, and increase appetite in COVID-19 patients. Omega 3 can also reduce CRP values, ESR values, improve kidney and respiratory function thereby reducing clinical symptoms. However, further studies are needed to assess clinical symptoms using a more objective questionnaire to obtain better results. The research duration should be longer so that it can assess the success of omega 3 therapy in improving clinical symptoms and clinical parameters of COVID-19 patients. Furthermore, a larger sample size is needed in this study to give good results and omega 3 can be used as additional therapy for COVID-19 patients.

Competing Interest

The authors have no conflict of interest in this study.

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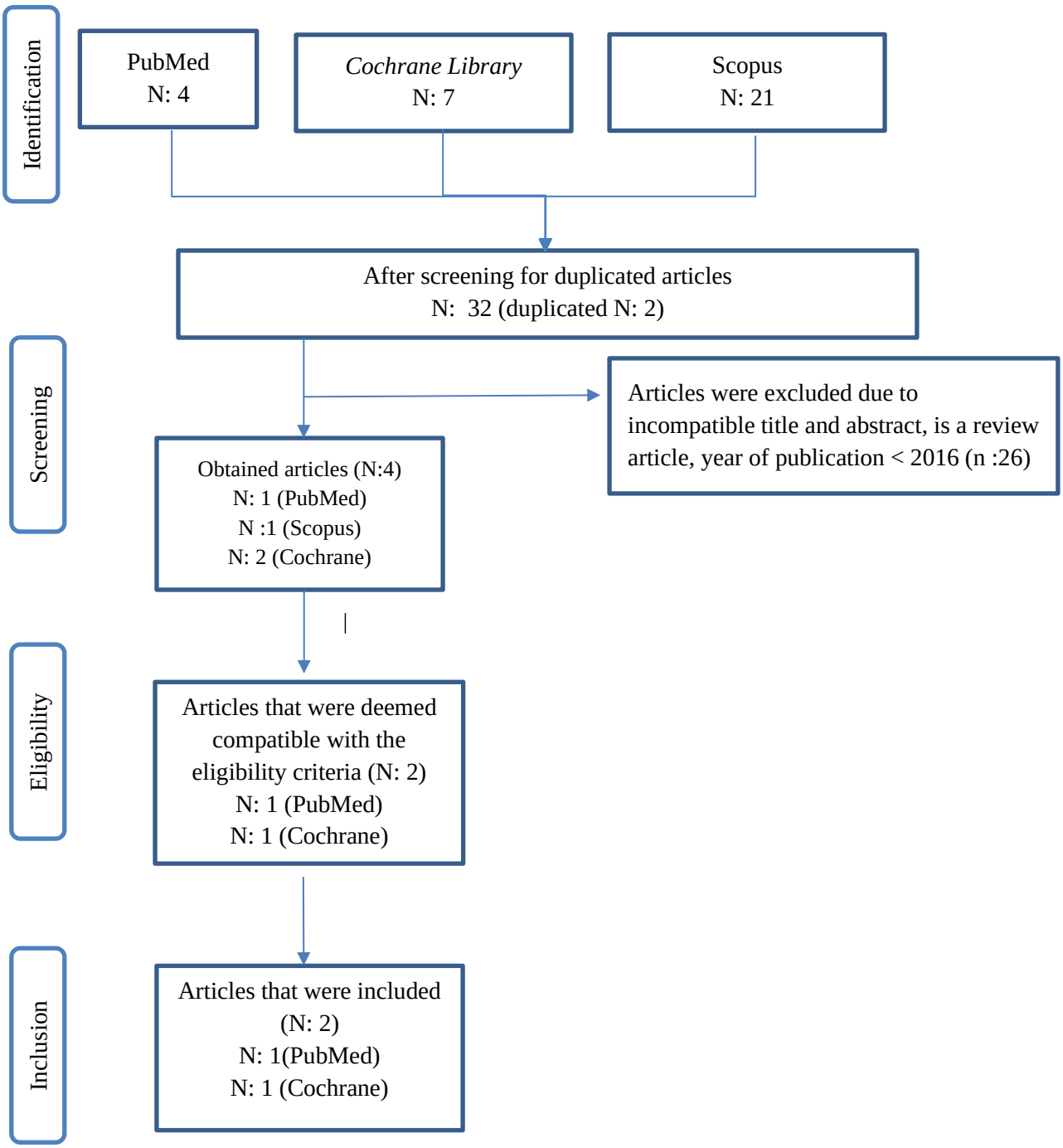

Figure 1. Prisma flow diagram on literature searching

	Study design	Number of patients	Randomization	Similarity of groups	Blinding	Groups treated equally	Measurement of outcome	Level of Evidence*
Sedhigiyan, et al	RCT	30	+	+	+	+	+	2A
Doaei, et al	RCT	128	+	+	+	+	+	2A

Table 1. Critical research assessments of randomized control trial

Parameters	Question	Sedhigiyan et al.	Doaei, et al
Validity	Was the assignment of patient to treatments randomized?	Yes	Yes
	And was the randomization list concealed?	Yes	Yes
	Were the groups similar at the start of the trial?	Yes	Yes
	Aside from the allocated treatment, were groups treated equally?	Yes	Yes
	Were all patients who entered the trial accounted for?	Yes	Yes
	And were they analyzed in the group to which they were randomized?	Yes	Yes
	Were measures objective or were the patients and clinicians kept "blind" to which treatment was being received?	Yes	Yes
Importance	How large was the treatment effect?		
	There was reduced clinical symptoms such as fatigue, pain all over the body (p<0.001).	p<0,001	
	There was an increase in appetite in the intervention group compared to the control group (p <0.003).	p<0,003	
	There was a decrease in CRP value		p 0,001
	There was a decrease in ESR value		Not explained
	There was an improvement of pH value, HCO_3, Be	p<0,001 p 0,002	
	How precise was the estimate of the treatment effect?	Not explained	
Applicability	Is my patient so different to those in the study that the results cannot apply?	No	No
	Is the treatment feasible in my setting?	Yes	Yes
	Will the potential benefit of treatment outweigh thepotential harms of treatment for my patient?	Yes	Yes