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Research Article

Effectiveness of Fish Oil Containing Omega-3 in Improving Symptoms and Lung Function in Asthma Outpatient in Surabaya, Indonesia

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ABSTRACT

Indonesia as a potential maritime country in fish production, can be processed into fish oil containing omega-3. Based on previous libraries, omega-3 fish oils can be used to improve asthma control and improve lung function. The effects of a drug are individualized depending on genetic and environmental factors. The aim of the study was to investigate the effect of fish oil containing omega-3 on improving asthma symptoms and improving lung function. The research method used is pre-post test design, using data collection technique with asthma control test questionnaire to see clinical symptoms of asthma and measure lung function with peak flow meter. Intervention given is a fish oil product with once daily doses, then follow up every week for 4 weeks. The subject of research is adult age. Pulmonary function data and asthma symptoms will be tested for normality with shapiro-wilk test and followed by anova one way. The research was conducted in 2016-2017 in Surabaya and the data obtained 28 respondents. At the control level of asthma and total ACT score ($P < 0.05$) it can be concluded that there was significant difference between before and after omega-3 fish oil therapy for 4 weeks. In the improvement of lung function there is a significant improvement of lung function starting from before therapy until the increase every week until the 4th week. Fish oil containing omega 3 for 4 weeks may decrease asthma symptoms in the asthma control level category and total ACT score. In addition, fish oil can also improve lung function significantly in every week.

Keywords: asthma, fish oil contains omega-3, asthma symptoms, lung function.

INTRODUCTION

Asthma is a heterogeneous disease in the form of chronic respiratory tract inflammation characterized by respiratory symptoms such as wheezing, shortness of breath, feeling depressed in the chest and cough. Despite the low level of fatality but the number of cases is quite common in the community. The World Health Organization (WHO) estimates that 100-150 million people worldwide suffer from asthma. Even this number is expected to continue to grow to reach 180,000 people every year[1-2]. Adverse effects of asthma include decreased quality of life, decreased productivity, school absenteeism, increased healthcare costs, hospital care risks and even death[3]. Increases in the prevalence of asthma in Asia such as Singapore, Taiwan, Japan or South Korea are also striking. The incidence of asthma has increased over fifteen years, both in developing and developed countries. In Indonesia, the prevalence of asthma is not known for certain, but it is estimated that 2-5% of Indonesia's population suffers from asthma. The Department of Health estimates that asthma is among the top 10 causes of illness and mortality in hospitals and an estimated 10% of Indonesia's 25 million people suffer from asthma. The prevalence of asthma in urban areas is generally higher than in rural areas, as urban lifestyle increases the risk of asthma. According to RISKESDAS (2013) asthma prevalence in Indonesia reached 4.5% with asthma prevalence in East Java 5.1%[4-5].

In Indonesia, which is a maritime country, has great potential in fish production and even the government also launched GEMARIKAN in 2014, to popularize fish consumption. Fish has been known to be processed into fish oil containing high omega-3. Fish consumption can prevent asthma in adult patients. Research has shown that fish consumption at least once a month can reduce the risk of asthma[6]. In the meantime, several fish oil-related studies, including omega-3s as Aprizayanti (2011)[7] and Santoso et al. (2013)[8]. Omega-3 has been used only as a supplement in helping the child's growth process, help lower cholesterol, heart disease. High intake of fish oil has protective effect against asthma and or allergies[9]. Omega-3 polyunsaturated fatty acids (n-3 PUFAs) consisting of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are found primarily in

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Table 1: Frequency Distribution of Respondent Characteristics.

Characteristics		Number (n: 26)	Percentage (%)
Gender	Male	7	27,00
	Female	19	73,00
Age (years)	Youth end (17-25)	25	96,15
	Early adult (26-35)	1	3,85
	Late adult (36-45)	0	0,00
History of Asthma Treatment based on Global Initiative for Asthma (2016)[1]	Oral agonist beta-2 short acting	8	21,05
	Inhaled agonist beta-2 short acting	10	26,31
	Oxygen	1	2,63
	Not taking any medication	3	7,89
	Oral corticosteroids (used only when symptoms worsen)	1	2,63
	Oral methylxanthine (used only when symptoms worsen)	3	11,53

Table 2: Frequency Distribution Assessment of Asthma Symptoms Based on ACT.

Asthma Assessment Category		Number of Respondents	
		ACT_0	ACT_4
Asthma Control Based on Activity Limitations	Every now and then	1	0
	Too often	0	0
	Often	2	4
	Not too often	14	16
	Never	9	6
Asthma Control Based on Frequency of Shortness of Breath	More than once a day	0	0
	Once a day	0	0
	3-6 times a week	5	3
	Once or twice a week	14	14
	Not a week at all	7	9
Asthma Control Based on Symptoms Symptom Asthma At Night or Morning	4 or more nights per week	2	2
	2-3 nights per week	3	1
	once a week	4	0
	Once or twice	6	14
	not at all	11	9
Asthma Control Based on Frequency of Asthma Drug Use	3 or more per day	1	0
	1 or 2 times per day	2	3
	2 or 3 times per week	4	5
	Once a week or less	5	4
	not at all	14	14
Asthma Control Based on Asthma Control Level	Not controlled at all	8	3
	Less controlled	6	5
	Simply controlled	6	8
	Well controlled	4	6
	Full controlled	0	4
ACT Total	Uncontrolled (total value of ACT: <19)	17	11
	Partially controlled (total value ACT: 20-24)	5	13
	Full controlled (total value ACT: 25)	4	2

fish oil. Epidemiological studies show that omega-3 has a protective effect against cardiovascular disease myocardial infarction or cerebral infarction, hypertension, and hyperlipidemia. In addition, omega-3 has beneficial effects on chronic inflammatory diseases including chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, and inflammation of the intestine. Atopic sensitization and allergies can also be prevented with fish intake during pregnancy[10].

In Indonesia has conducted several studies related to fish oil, which among others contain omega-3. Omega-3 is used as a supplement in helping the child's growth process, help lower cholesterol, heart disease[7,8,10,11,12]. But there has been no research related to the effect of omega-3 on the improvement of asthma in Indonesia. The anti-inflammatory effect on omega-3 is due to the content of EPA which is a competitive substrate with arachidonate so it has the potential to reduce inflammation of the respiratory tract and bronchoconstriction. This has led to a new understanding over the last 30 years that fish oil deficiency can aggravate asthma[13].

This study aims to determine the effect of omega-3 on the control of asthma in patients with asthma in Surabaya who

Table 3: ACT Normality Assessment Test Group Intervention

Asthma Assessment Category	P value		
	ACT_0	ACT_4	Conclusion
Activity Limitations	0,00	0,00	Distribution of data is not normal
Frequency of Shortness of Breath	0,00	0,00	Distribution of data is not normal
Asthma Symptoms At Night or Morning	0,00	0,00	Distribution of data is not normal
Frequency of Asthma Drug Use	0,00	0,00	Distribution of data is not normal
Level of asthma control	0,001	0,044	Distribution of data is not normal
ACT Total	0,558	0,460	Distribution of data is normal

P> 0.05 means normal distribution; P <0.05 means the distribution is not normal

Table 4: Changes in ACT Value as Asthma Symptoms

Asthma Assessment Category	Number of Respondents		
	Change the value of ACT_0 to ACT_4		
	Up	Constant	Down
Activity Limitations	5	15	6
Frequency of Shortness of Breath	6	18	2
Asthma Symptoms At Night or Morning	6	17	3
Frequency of Asthma Drug Use	4	17	5
Level of asthma control	16	9	1
ACT Total	15	6	5

Table 5: ACT Differences Test Before and After Omega-3 Fish Oil Therapy.

Asthma Assessment Category	Average		Test the Difference		
	ACT_0	ACT_4	P value	Type of Test Used	Conclusion
Activity Limitations	3,81	4,08	0,763	Friedman Test	There is no significant difference
Frequency of Shortness of Breath	4,08	4,23	0,157	Friedman Test	There is no significant difference
Asthma Symptoms At Night or Morning	3,81	4,04	0,317	Friedman Test	There is no significant difference
Frequency of Asthma Drug Use	4,12	4,12	0,739	Friedman Test	There is no significant difference
Level of asthma control	2,08	3,12	0,00	Friedman Test	There is a significant difference
ACT Total	17,89	19,58	0,041	Anova One Way	There is a significant difference

P> 0.05, Ho accepted means there is no significant difference
P <0.05, Ho rejected means there is a significant difference

will be given fish oil. During this treatment asthma focuses on therapy with long-term synthetic drugs, which can cause problems such as: the use of aminophylline which is a drug with a narrow range of therapy so that the risk of causing side effects[14,15,16], single use of long-acting beta-2 agonist that can aggravate Exacerbation of asthma[17], or the use of inhaled corticosteroids that may cause oropharyngeal candidiasis and even lung infections[1].

This study aims to determine the effect of fish oil containing omega-3 to improve asthma symptoms and improve lung function. Patients with a high level of education influence self evaluation so that it can affect the patient's asthma control level. This study uses research subjects with a minimum education level of high school with the hope that the level of asthma control is good, and is expected this study can also increase knowledge related to the influence of nutrition on asthma, in the role of pharmacist to support the handling of asthma by motivating patients to be obedient in treatment, Provide information, counseling, and education so that they better understand the treatment regimen provided so that patients can be more actively involved in their treatment which can improve their adherence to drug use. Treatment of asthma is a long-term treatment and adherence to medication and treatment is desirable. It is expected that good patient compliance will affect the number of drugs used less, fewer doses per day, the incidence of drug side effects is less common[3].

METHOD

This research uses pre-post test design method. This study used data collection techniques with Asthma Control Test questionnaire to see clinical symptoms of asthma and measure lung function with peak flow meter tool. Each sample of the study was given fish oil. Intervention given is a fish oil products circulating in Indonesia. Fish oil is given to patients with once daily doses, then follow up every week for 4 weeks. Dosage of fish oil containing

Tabel 6: Average PEF Value and Normality Test for Lung Function Data

Group	Average PEF Value (L/sec)	Test Data Normality		
		Type of Test Used	P value	Conclusion
PEF_0	217,96	Shapiro wilk	0,002	No normal
PEF_1	273,15	Shapiro wilk	0,131	Normal
PEF_2	295,56	Shapiro wilk	0,109	Normal
PEF_3	298,89	Shapiro wilk	0,209	Normal
PEF_4	325,00	Shapiro wilk	0,089	Normal

P> 0.05 means normal distribution; P <0.05 means the distribution is not normal

omega-3 recommended by 1 gram to 5.4 gram per day[18], then in this study selected fish oil with dose of 1.0 gram.

The independent variable of this research is fish oil. While the dependent variables of this study are symptoms of asthma and lung function, with controlled variables according to inclusion and exclusion criteria.

Symtoms of asthma: Symptoms of asthma were measured by using the Asthma Control Test (ACT) questionnaire. ACT is one of the specific instruments in assessing asthma control in patients with chronic asthma. Consisting of 5 questions that include activity limitation, shortness of breath, asthma symptoms at night, frequency of reliever drug use, and asthma control rate counted for 4 weeks. Each question is given a choice of 5- Likert [1,19]. Symptoms of asthma were measured 2 times, ie, at week 0 (before intervention) and at week 4 (after intervention). Initials to use:

ACT_0: The value of ACT at week 0, ie before getting fish oil therapy contains omega-3

ACT_4: The value of ACT at week 4, ie after getting fish oil therapy containing omega-3 for 4 weeks (one month)

Lung function: Pulmonary function is measured from the Peak Expiratory Flow (PEF) value. PEF is the maximum ability to expel air in the lungs from the maximum inspiratory state through the mouth in liters per minute units measured by peak flow meter which is a simple and easy to apply tool [1]. Pulmonary function is measured 5 times, ie once before the intervention and 3 times During intervention (after 1 week, 2 week, and 3 week intervention), and after intervention. Initials to use:

PEF_0: PEF value at week 0, ie before getting fish oil therapy contains omega-3

PEF_1: PEF value at week 1st, after getting fish oil therapy containing omega-3 for 1 week

PEF_2: The value of PEF at week 2nd, ie after getting fish oil therapy contains omega-3 for 2 weeks

PEF_3: PEF value at week 3rd, ie after getting fish oil therapy containing omega-3 for 3 weeks

PEF_4: PEF value at week 4th, ie after getting fish oil therapy containing omega-3 for 4 weeks (one month)

The population of this study were adult asthma patients (> 18 years) in Surabaya. The sample (subject) of the study were adult asthma patients who were willing to engage in research and meet the requirements, namely: (1) no chronic diseases that can affect respiratory function (such as chronic respiratory illness, heart disease, chronic renal failure, etc.); (2) No smoking or consuming alcohol; and (3) not taking routine asthma medication.

Pulmonary function data and asthma symptoms will be tested the normality of data distribution by using shapiro-wilk test. If p> 0,05 then it can be concluded that normal distribution data and then proceed with one way anova to know the improvement of lung function and clinical symptoms among respondents Before and after using fish oil.

RESULT

The research was conducted in 2016-2017 in Surabaya. The data used in this study were obtained through the asthma control test (ACT) questionnaire given at the beginning of the first week and the end of the 4th week, peak expiratory flow (PEF) measured weekly for 5 weeks. Based on the data obtained 28 respondents, but 2 people dropped out due to allergy to fish oil and resigned because out of town, then only 26 people who can follow the research.

Characteristics of Respondents

Respondents in this study were grouped by sex, age, and medical history. The number of respondents based on the characteristics of respondents includes age and gender. In the age category, the largest number is the final adolescent (17-25 years old) that is equal to 96.15% or a number of 25 people and the largest number of female respondents is 73% or 19 respondents from the total of 26 respondents. The largest number was in the respondents who used a group of agonist beta-2 short inhalation work of 26.31% in step 1 (Table 1).

Improvement of Asthma Symptoms with Fish Oil Therapy Containing Omega-3

Characteristics of respondents can be seen in table 2 with the depiction of each category ACT. Most of the symptoms of respondent asthma in three categories, namely: based on activity limitations, frequency of shortness of breath, frequency of asthma drug use, showed no change. But in most asthma symptoms based on asthma symptoms appearing in the evening or morning shows a decrease from the point "not at all" to "once up to two times". While asthma symptoms based on the level of control of respondents asthma increased. Based on the total of the overall ACT score, it showed improvement of most respondents with uncontrolled asthma symptoms being partially controlled (Table 2).

Normality tests across all ACT categories show all data not normally distributed, except for the total ACT values showing normal distributed data (Table 3).

The change in the value of asthma symptoms was divided into 3, ie "up" (there was an increase in ACT values after 4 weeks of fish oil), "fixed" (no change in ACT values after 4 weeks of fish oil) and "down" There was a decrease in ACT value change after being given fish oil for 4 weeks).

Table 7: Changes in PEF Value and Pef Value Differences Test Before and After Omega-3 Fish Oil Therapy.

Compared groups	Jumlah Responden			Uji Perbedaan		
	Changes in PEF Value (L/sec)			P value	Type of Test Used	Conclusion
	Up	Constant	Down			
PEF_0 and PEF_1	20	2	5	0,014	Friedman Test	There is a significant difference
PEF_0 and PEF_2	21	1	5	0,003	Friedman Test	There is a significant difference
PEF_0 and PEF_3	20	1	6	0,009	Friedman Test	There is a significant difference
PEF_0 and PEF_4	24	1	2	0,00	Friedman Test	There is a significant difference
PEF_1 and PEF_2	20	0	7	0,00	Anova One Way	There is a significant difference
PEF_2 and PEF_3	16	2	9	0,013	Anova One Way	There is a significant difference
PEF_3 and PEF_4	21	0	6	0,017	Anova One Way	There is a significant difference

P> 0.05; Ho rejected means there is no significant difference
P <0.05; Ho accepted means there is a significant difference

From table 4, it can be concluded that most improvements in asthma symptoms are seen only in the asthma level control category, whereas other categories show a fixed value. However, when viewed from the total value of ACT, showed most respondents experienced improvement (Table 4).

Test the difference of asthma symptoms based on ACT value before and after fish oil therapy in table 5. At the control level of asthma and total ACT value (P <0,05) it can be concluded that there was significant difference between before and after fish oil therapy containing omega-3 For 4 weeks (Table 5).

Improvement of Lung Function with Omega-3 Fish Oil Therapy

The Difference Test describes the average PEF score obtained once a week after the respondents get a fish oil intervention for 4 weeks. The largest number was in the intervention group at week 4 with an average of 325,00 (Table 6).

Based on the normality test from table 6 indicating that there is data showing abnormal distribution (PEF0 data), the difference test using Friedman Test (Table 7). Based on the difference test, it was concluded that there was a significant improvement on every week (Table 7).

DISCUSSION

Discussion of Asthma Symptoms Improvement

The results showed changes in ACT values that increased from uncontrolled conditions before treatment were then partially controlled after therapy. This is consistent with existing libraries that the omega-3 content of fish oil containing fatty acids has a beneficial effect on chronic inflammatory diseases including chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, and inflammatory diseases[18]. Fish oils containing omega 3 comprising EPA and DHA suppress the production of arachidonic acid through the ALOX5 pathway. Arachidonic acid is a substrate for eicosanoid synthesis that produces an inflammatory mediator consisting of CYS-LT, prostaglandin, and thromboxane. This mediator is involved in the bronchoconstriction process and improves the respiratory tract mucus in asthma patients. EPA-enriched fish oil can inhibit the competitive production of LTC4 with arachidonic acid that acts as an ALOX5 substrate. EPA can also suppress an allergic response to asthma by inhibiting arachidonic acid that produces leukotrienes. Leukotriene and prostaglandin E2 contribute to the formation of immunoglobulin E (IgE), an antibody that contributes to the occurrence of an allergic response. This is usually increased in patients with asthma[13]. Although the respondents experienced an improvement in ACT scores, there were several factors that could affect the value of ACT, among others:

Gender and age: In table 1, shows the largest number of samples are women than men. In boys have a greater risk in infancy and this risk decreases as they mature. While in women have a risk of staying in childhood and adulthood. The prevalence of women is higher than men, but the reason for the difference is not clear. However, at birth, men's lung size is smaller than women but as adults are larger. The risk of asthma in boys decreases as they grow older. While in women, the influence of estrogen and progesterone hormones can cause high asthma risk in women during and after puberty[20]. Similarly, the National Center for Health Statistics (NCHS) (2011)[21], which says by sex 7,2% of men and 9,7% of women that the prevalence of women is higher than men. Respondents in this study were mostly in the final adolescent category with age 17-25 years.

Genetic Factors: There is a relationship between ALOX5's genetic polymorphism and the severity of asthma, whereas ALOX5 is the code of the enzyme that produces leukotriene, which plays the role of the severity of asthma. Genetic polymorphisms of ALOX5 as well as 5-lipoxygenase-activating protein (FLAP) are associated with excessive production of leukotrienes. ALOX5 and FLAP are increased RNA messenger in peripheral blood leukocytes in asthmatics and leukotriene concentrations in

sputum are greater in asthma patients compared with non-asthma[13].

Environmental factors (eg trigger exposure): To minimize the influence of environmental factors in this study respondents will always be required to report their activities during fish oil therapy, as factors such as contact with triggers, diet, excessive physical activity, etc. may affect the control of asthma symptoms.

Other therapies used. In the treatment history, most of the samples used inhaled beta-2 agonist drug inhalation group and all respondents were at step 1 treatment. Asthma treatment is divided into controller and reliever. Controller is a daily-used treatment in the long term to keep asthma under clinical control through its anti-inflammatory effects. While reliever is a treatment that is used when necessary and quickly to reduce bronchoconstriction and reduce the acute symptoms that accompany it. In this study, all respondents were at step 1, which means that none of the respondents used controller asthma medication to maintain their daily asthma control, and all respondents only used asthma medications when experiencing worsening symptoms (reliever). The main choice in this type of reliever is a short action beta-2 agonist which is generally salbutamol with inhalation route. Inhalation routes are preferred because they are topical, so side effects tend to be smaller and can work directly to the target site in the bronchioles. However, from the data of treatment used by respondents there are some respondents who use corticosteroids (oral or inhalation) and methylxanthine group which is actually an asthma therapy in the controller group[1].

Discussion of Lung Function Repair

From the research results can be seen that there is an increase in PEF value between the data before and after the patient get therapy. This indicates a potential effect after the respondents are given intervention in the form of fish oil. Improvement of asthma function may be influenced by other uncontrollable factors in research such as psychological (stress)[22,23], unpredictable weather changes (such as cold or windy air)[24,25] and daily activities[26]. During the measurement of PEF values, Which can be minimized the activity of respondents because it is done at the same time. The factors that affect the value of PEF but can be controlled in this study include food and drugs consumed. Foods such as fish that contain high protein can cause bias research results. And drugs like asthma medication can increase the value of PEF. However, it can be controlled from the presence of a log book given to the patient to be filled daily containing the activities carried out, drugs and food consumed, and adherence during the consumption of fish oil.

Limitations of Research

Criteria for inclusion of respondents such as heart and kidney history data were not accurately obtained. Because when respondents say that no history of heart and kidney is not supported by the results of checking the doctor first by using electrocardigram (ECG)

In this study using fish oil from a particular brand, which does not rule out the possibility that fish oil with other types can provide effects or not on research related asthma. Researchers use this type of fish oil because the dose corresponds to the desired dose of fish oil is 1.0 grams. Therefore, respondents feel less comfortable to consume fish oil that is considered quite large because some respondents commented on soft capsule large enough.

Increased prevalence of asthma occurs due to genetic and environmental factors. Asthma is a complex disease resulting from the interaction between genetic predisposition and environmental factors. Both of these factors not only affect the inflammatory process but also affect the complex and interactive phenotype.

The number of samples in this study were 26 people. Researchers have difficulty in finding a large number of samples to get valid results. Researchers should be able to work with health centers or other health agencies so that the number of samples can be reproduced.

Researchers cannot control racial factors that can affect genetic outcomes. Therefore it is necessary to do further research related to genetic influence (polymorphism of ALOX5) on therapeutic effect of fish oil containing omega-3.

CONCLUSION

Fish oil containing omega-3 for 4 weeks may decrease asthma symptoms in the asthma control level category and total ACT score. In addition, fish oil can also improve lung function significantly in every week.

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