Journal of Biosciences and Medicines, 2023, 11, 208-219
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

# The Effects of Omega-3 Fatty Acids Supplementation in Bronchial Asthma

**Uttam Kumar Barua[1], Pranab Karmaker[2], Arup Kumar Saha[3], Md. Merazul Mostofa[4], Dilip Kumar Ghosh[5], Kamal Krishna Biswas[6*]**

[1]Department of Respiratory Medicine, Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh
[2]Bangladesh Reference Institute for Chemical Measurements (BRiCM), Dhaka, Bangladesh
[3]Department of Dental Public Health, City Dental College and Hospital, Dhaka, Bangladesh
[4]Department of Genetic Engineering and Biotechnology, University of Rajshahi, Rajshahi, Bangladesh
[5]Department of Gastroenterology, Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh
[6]Department of Biochemistry and Molecular Biology, University of Rajshahi, Rajshahi, Bangladesh
Email: *kkbiswas@ru.ac.bd

**How to cite this paper:** Barua, U.K., Karmaker, P., Saha, A.K., Mostofa, M.M., Ghosh, D.K. and Biswas, K.K. (2023) The Effects of Omega-3 Fatty Acids Supplementation in Bronchial Asthma. *Journal of Biosciences and Medicines*, **11**, 208-219.
https://doi.org/10.4236/jbm.2023.114015

**Received:** December 7, 2022
**Accepted:** April 20, 2023
**Published:** April 23, 2023





## Abstract

Bronchial asthma is a chronic inflammatory disease. Allergies are intensely related to bronchial asthma and to other respiratory diseases such as chronic sinusitis, middle ear infections, and nasal polyps. Treatment can vary from inhalers to oral medications to drugs delivered in a nebulizer or breathing machine. Besides, dietary involvement was a significant tool to reduce the severity of many chronic inflammatory diseases including asthma. Randomly assigned, double blind, and placebo controlled 290 adults with mild to moderately persistent bronchial asthma concluded in this study, were subjected to alternating phases of supplementation with omega-3 fatty acids, vitamin C and Zn either singly or in combination. Subjective symptom improvement, pulmonary function, and biochemical tests were carried out at the beginning of the study and at the end of each therapeutic phase. The study findings showed that nearly half of the cases were in age between 18 years to 40 years followed by 29.6 of the cases that fall in age range between 40 years and 60 years. It was clear that all the four supplements (ogema-3 fatty acids, vitamin C and Zn, and combination) contributed more than placebo in reducing the severity of bronchial asthma. However, omega 3 fatty acids and combined supplement significantly contributed in symptomatic improvement ($p < 0.05$). There was a significant improvement of pulmonary function and sputum inflammatory markers with diet supplementation ($p < 0.05$). So, the subjects with mild and moderately persistent bronchial asthma may get benefit from their dietary supplementation with omega 3 fatty acids, Zinc and vitamin C. It is evident from this study that omega 3 fatty acids and combined supplementation significantly improved the severity of bronchial asthma.

**Keywords**

Bronchial Asthma, FEV1, FVC, Omega 3 Fatty Acids

## 1. Introduction

Bronchial asthma is a general illness arising in around 10% of the inhabitants globally which characterized through adjustable grade of airway impediment, airway irritation and airway hyper-responsiveness. The general signs of bronchial asthma were breathless, tussis and chest tightness. Although bronchial asthma was first defined periods before, the pathogenesis was yet not completely assumed, and deficiency of management opportunities rested a problematic for numerous subjects with bronchial asthma [1]. An occurrence of bronchial asthma could be activated by extensive variety of several stimuli varying from general cold or supplementary respiratory tract contaminations to ecological causes, such as allergens or contact to cold or dry air. The connotation among workout and bronchial asthma was identified meanwhile long since and was 1st defined by Areatus in the first period. Areatus said "if from running, aerobics workout or several different works the respiration becomes problematic, it was called bronchial asthma" [2]. Nowadays, researches had revealed that the majority of untreated bronchial asthmatic patients would experience bronchoconstriction afterwards workout [3] [4] [5]. Numerous earlier researches had shown that omega-3 polyunsaturated fatty acids source of a decrease of disease, such as contaminations, respiratory infection, bronchial asthma, and dermatologic situations [6]-[11]. Nutritional fats containing omega-3 fatty acid and omega-6 fatty acids act as an amendable immune role and inflammation [12].

Addition of nutrient by omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) acts as ambiguous part in the controlling of asthma, which has managed for more potential research to examine where there was every welfare from an omega-3 fatty acid supplemented diet in asthma [13]. Outcomes had not been dependable when measuring high dosages of nutritional $\omega$-3 fatty acids on bronchial hyper-responsiveness (BHR), important feature of asthma. Early studies administering ω-3s daily over ten weeks demonstrated no attenuation of exercise-induced bronchoconstriction (EIB) [14] while causing a small decrease of the late airway response to inhaled allergen [15]. Additional, 3 weeks of $\omega$-3 fatty acids were stated to constrain slight airway reactions to workout and eucapnic voluntary hyperventilation (EVH) in mutually leading sportspersons and characteristic patients/subjects with asthma [16] [17] [18]. That was perceived in connotation with decreases in indicators of airway inflammation, where compact cytokine levels, waned secretion of the urinary eicosanoids 11b-prostaglandin F2a (11b-PGF2a) and leukotriene E4 (LTE4), and reduced sputum eosinophil counts, proposing that the aids of a $\omega$-3 supplemented nutrition on EIB was with anti-inflammatory procedure. Taking snuff mannitol such as a trial

for BHR had been revealed for example a suitable model for EIB [19] besides entire pharmacotherapies useful at hindering EIB, impeding BHR to mannitol [20] [21] [22] [23]. Mannitol reasons bronchoconstriction by an proliferation in the osmolarity of the airway surface fluid, prominent to intermediary discharge from mast cells related to the suggested appliance for EIB [24]. Indication for intermediary discharge to mannitol was an proliferation in urinary eicosanoids 11b PGF2a and LTE 4 following a mannitol challenge related to what had been witnessed with workout and EVH [25] [26]. BHR to mannitol recognizes EIB in best sportspersons [27] and guesses the relentlessness of EIB in people with asthma [19]. In view of likenesses, we calculated whether nutritional supplement with $\omega$-3 fatty acids might hinder BHR to take snuff mannitol to measure the efficiency of $\omega$-3 fatty acids in individuals with mild to moderate BHR. Then we calculated the outcome of 3 weeks of nutritional $\omega$-3 fatty acids on BHR to mannitol, sputum eosinophil counts, spirometry, and asthma indications in patients through clinically defined steroid-naive asthma as well as in those consuming consistent take snuff corticosteroids (ICSs). Serum was aggregated for the period of the research to regulate the biochemical properties of the $\omega$-3 supplementation on mast cell mediators.

## 2. Materials and Methods

### 2.1. Participant's Selection Criteria

#### 2.1.1. Inclusion Criteria

The inclusion criteria indicates; physician diagnosed mild to moderate persistent asthma between 18 to 60+ years and bronchial asthma patients are on step care management protocol.

#### 2.1.2. Exclusion Criteria

The inclusion criteria indicates; any chronic diseases other than asthma and rhinitis, intake of antileukotrienes during the study, patient taking polyunsaturated fatty acid (PUFA) or antioxidants supplements above the levels recommended for adequate intake, or regularly consumed omega 3 containing food, manifestations of vitamin C or Zn deficiency, and allergy to fish oil/omega-3.

### 2.2. Asthma Diagnosis

The asthma diagnosis indicates; history and patterns of symptoms, measurements of lung function (Spirometer and peak expiratory flow), measurement of airway responsiveness, and allergic status to identify risk factors.

### 2.3. Patient Recruitment Procedure

The study started recruiting patients from the department of Respiratory Medicine, Shaheed Suhrawardy Medical College Hospital, Dhaka (ShSMCH) upon full filling the written informed consent form. The patients were deliberately described with the aims, procedure and benefits of participating the study and of

its refusal. The study included diagnosed mild to moderate bronchial asthma patients. The demography, anthropometry and other medical records were taken in semi-structured data collection sheet. Asthma related information and reports of serum IgE and eosinophils were recorded in the check list. In total 290 diagnosed mild and moderate bronchial asthma patients were included in the study.

### 2.4. Data Collection

The study obtained ethical clearance for the Institutional Review Board (IRB) of Institute of Biological Sciences, University of Rajshahi by this time. However, the whole study divided into 3 phases. The phases are:

#### 2.4.1. Phase-1 Case Identification and Intervention Phase

This intervention trial involved 290 adults' asthma patients. Among them, 135 asthma patients (case) had taken step care managements with omega 3 fatty acid, Zn, vitamin C, and combination. 142 asthma patients (control) taken step care managements with normal diet plus three placebo identical appearing capsules containing lactose. Baseline investigation serum IgE level, sputum eosinophil count and pulmonary function tests e.g. FEV1, FEV1/FBC ratios were done before the trial has started.

#### 2.4.2. Phase-2 Follow up Phase

After 3 months of consumption of drugs or placebo, all subjects were clinically followed up for their conditions and any adversity.

#### 2.4.3. Phase-3 Follow up Phase

At the end of 6 month all histories, clinical examinations and all laboratory investigations were done again.

## 3. Results

Table 1 shows the demographic and the socio-economic characteristics of four different selection criteria. This table clearly indicates that nearly half of the case was found in age between 18 years and 40 years followed by 29.6 of the cases that fall in age range between 40 years and 60 years. Nearly one-fifth of the subjects were elderly people. Similar situation was observed in the age pattern of control group. About 52.6 percent of case was male and remaining 47.4 percent was female. The percentages for male and female in control group were found to be 51.4 and 48.6 percent respectively. Most of the subjects were residing in urban areas and it is true irrespective of all groups. It further reveals the similar occupation structure of both groups. It is also evident from the table that about one-third of the subjects of both groups were either smoker or ex-smoker.

About 51 percent of cases and 52.1 percent of controls were found with mild bronchial asthma while the percentages of moderate bronchial asthma for case and control were 48.9 and 47.9 respectively (Table 2). Table 2 further indicated that more than 45 percent of cases were suffering from other diseases along with

bronchial asthma. Similar situation was observed for the subjects of control group too. Diagnosis further showed that about 40% of the cases and 39.4 percent of controls had been suffering from associated nasal allergy.

Table 1. Background characteristics of the subjects.

| Variables | Case % | Mean ± S.E | Control % | Mean ± S.E |
|---|---|---|---|---|
| **Age** | | | | |
| 18 - 40 | 53.3 | | 48.6 | |
| 40 - 60 | 29.6 | 41.3 ± 14.3 | 30.3 | 42.9 ± 16.4 |
| >60 | 17.1 | | 21.1 | |
| **Sex** | | | | |
| Male | 52.6 | 50.0 ± 3.68 | 51.4 | 50.0 ± 1.98 |
| Female | 47.4 | | 48.6 | |
| **Place of Residence** | | | | |
| Rural | 38.5 | 50.0 ± 16.26 | 39.4 | 50.0 ± 14.99 |
| Urban | 61.5 | | 60.6 | |
| **Occupation** | | | | |
| Housewife | 19.3 | | 16.9 | |
| Farmer | 20.7 | | 23.2 | |
| Service | 17.8 | 16.67 ± 5.76 | 19.0 | 16.66 ± 5.80 |
| Business | 22.2 | | 21.1 | |
| Retired | 13.3 | | 12.0 | |
| Others | 6.7 | | 7.8 | |
| **Smoking status** | | | | |
| Smoker | 23.7 | | 26.7 | |
| Non-smoker | 67.4 | 33.33 ± 30.41 | 66.2 | 33.33 ± 30.10 |
| Ex-smoker | 8.9 | | 7.1 | |

Table 2. Subjects by selected variables.

| Variables | Case % | Mean ± S.E | Control % | Mean ± S.E |
|---|---|---|---|---|
| **Bronchial Asthama** | | | | |
| Mild | 51.1 | 50.00 ± 1.56 | 52.1 | 50.00 ± 2.97 |
| Moderate | 48.9 | | 47.9 | |
| **Comorbidities** | | | | |
| Present | 47.4 | 50.00 ± 3.68 | 45.8 | 50.00 ± 5.95 |
| Absent | 52.6 | | 54.2 | |
| **Associated Nasal Allergy** | | | | |
| Present | 40.0 | 50.00 ± 14.14 | 39.4 | 50.00 ± 14.99 |
| Absent | 60.0 | | 60.6 | |

Table 3 shows that none of subjects were prescribed high dose of ICS. Most of subjects of case and control group were provided (66.7% vs 66.9%) moderate dose of ICS while low dose was provided to only 33 percent of each group. After receiving different doses of ICS a vast majority of the subjects of case and control reported that asthma was not fully controlled (80% vs 90.1%). Four types of supplements namely Omega 3 Fatty Acids, Zinc, Vitamin C and Combination of these supplements were used in addition to ICS to treat the cases while the control received only Placebo. The distribution of supplementation is shown in Table 4.

Table 5 shows the symptomatic assessment of subjects after prescribing the four supplementations. It is clear from the table that all the four supplements contributed more than placebo in reducing the severity of asthma. However, out of 4 only omega 3 fatty acids and combined supplement significantly contributed in controlling the severity of asthma.

The pulmonary function tests of the subjects are presented in Table 6. No significant difference was observed between placebo and vitamin C group ($p > 0.05$). However, FEV/FVC ratio showed statistically significant ($p < 0.05$) improvement but not clinically improvement in the placebo group. All four supplements showed statistical significant improvement with respect to placebo group ($p < 0.05$). It further showed that combined supplement was more effective in improving the condition of subjects than any other single supplement ($p < 0.05$).

Table 3. Subjects by Steroid dose and condition of Bronchial Asthma.

| Variables | Case % | Control % |
|---|---|---|
| **ICS Dose** | | |
| Low | 33.3 | 33.1 |
| Moderate | 66.7 | 66.9 |
| High | - | - |
| **Condition of Asthma** | | |
| Controlled | 20.0 | 9.9 |
| Partially controlled | 63.7 | 48.6 |
| Uncontrolled | 16.3 | 41.5 |

Table 4. Subjects by types of supplement.

| Supplement | Case % | Control % |
|---|---|---|
| Vitamin C | 20.8 | 20.8 |
| Zinc | 23.7 | 23.7 |
| Omega 3 Fatty Acid | 25.9 | 25.9 |
| Combination | 29.6 | 29.6 |
| Placebo | - | - |

**Table 5.** Subjects by symptomatic improvement.

| Symptoms | Placebo | | Vitamin C | | Zinc | | Omega 3 Fatty acid | | Combined | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | No. | % |
| **Wheezing** | | | | | | | | | | |
| No | 16 | 11.3[a] | 4 | 14.3 | 4 | 12.5 | 12 | 34.3 | 14 | 35.0 |
| Mild | 54 | 38.0 | 15 | 53.6 | 17 | 53.1 | 12 | 34.3 | 13 | 32.5 |
| Moderate | 72 | 50.7 | 9 | 32.1 | 11 | 34.4 | 11 | 31.4 | 13 | 32.5 |
| **Total** | **142** | | **28** | | **32** | | **35** | | **40** | |
| p-value | - | | [a]>0.05 | | [a]>0.05 | | [a]<0.05 | | [a]0.00 | |
| **Breathlessness** | | | | | | | | | | |
| No | 15 | 10.6[b] | 3 | 10.7 | 5 | 15.6 | 12 | 34.3 | 15 | 37.5 |
| Mild | 56 | 39.4 | 13 | 46.4 | 18 | 56.3 | 14 | 40.0 | 15 | 37.5 |
| Moderate | 71 | 50.0 | 12 | 42.9 | 9 | 28.1 | 9 | 25.7 | 10 | 25.0 |
| **Total** | **142** | | | | **32** | | **35** | | **40** | |
| p-value | - | | [b]>0.05 | | [b]>0.05 | | [b]0.00 | | [b]0.00 | |
| **Cough** | | | | | | | | | | |
| No | 18 | 12.7[c] | 4 | 14.3 | 7 | 21.8 | 13 | 31.4 | 15 | 37.5 |
| Mild | 50 | 35.2 | 13 | 46.4 | 15 | 46.9 | 16 | 45.7 | 16 | 40.0 |
| Moderate | 74 | 52.1 | 11 | 39.3 | 10 | 31.3 | 8 | 22.9 | 9 | 22.5 |
| **Total** | **142** | | **28** | | **32** | | **35** | | **40** | |
| p-value | - | | [c]>0.05 | | [c]>0.05 | | [c]<0.05 | | [c]0.00 | |
| **Chest tightness** | | | | | | | | | | |
| No | 14 | 9.9[d] | 3 | 10.7 | 4 | 12.5 | 13 | 37.1 | 21 | 52.5 |
| Mild | 53 | 37.3 | 14 | 50.0 | 17 | 53.1 | 14 | 40.0 | 12 | 30.0 |
| Moderate | 75 | 52.8 | 11 | 39.3 | 9 | 34.3 | 8 | 22.9 | 7 | 17.5 |
| **Total** | **142** | | **28** | | **32** | | **35** | | **40** | |
| p-value | - | | [d]>0.05 | | [d]>0.05 | | [d]0.00 | | [d]0.00 | |

**Table 6.** Subjects by improvement based on pulmonary function test.

| Parameter/ Duration | Placebo | | Vitamin C | | Zinc | | Omega 3 Fatty acid | | Combined | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | Mean ± SE | n | Mean ± SE | n | Mean ± SE | n | Mean ± SE | n | Mean ± SE |
| **FEV1 (%)** | | | | | | | | | | |
| Baseline | 142 | 76.2 ± 6.8 | 28 | 76.2 ± 6.7 | 32 | 75.8 ± 5.8 | 35 | 76.3 ± 7.2 | 40 | 76.1 ± 6.9 |
| Week 2 | 138 | 76.8 ± 2.3 | 28 | 77.0 ± 2.1 | 31 | 78.9 ± 2.9 | 35 | 78.8 ± 3.1 | 39 | 79.2 ± 2.5 |
| Week 6 | 126 | 78.9 ± 1.2 | 25 | 78.8 ± 1.3 | 26 | 80.2 ± 2.1 | 33 | 82.3 ± 4.2 | 35 | 83.5 ± 1.8 |
| Week 12 | 118 | 79.9 ± 1.5 | 20 | 80.1 ± 1.4 | 22 | 81.1 ± 2.1 | 29 | 85.1 ± 2.6 | 31 | 88.2 ± 1.1 |
| Month 6 | 105 | 76.5 ± 5.3 | 18 | 80.3 ± 1.2 | 19 | 81.3 ± 2.1 | 24 | 85.9 ± 2.6 | 26 | 88.6 ± 1.3 |
| Month 12 | 78 | 76.9 ± 2.1 | 15 | 81.1 ± 2.1 | 17 | 81.0 ± 2.2 | 21 | 86.1 ± 3.1 | 28 | 89.2 ± 1.2 |
| **FEV1/FVC** | | | | | | | | | | |
| Baseline | 142 | 76.6 ± 1.6 | 28 | 77.2 ± 2.3 | 32 | 78.2 ± 2.2 | 35 | 78.2 ± 2.1 | 40 | 77.5 ± 2.8 |
| Week 2 | 138 | 75.3 ± 2.1 | 28 | 78.2 ± 2.1 | 31 | 79.2 ± 1.9 | 35 | 80.2 ± 2.0 | 39 | 81.8 ± 1.7 |
| Week 6 | 126 | 75.9 ± 2.4 | 25 | 77.9 ± 2.4 | 26 | 78.9 ± 2.3 | 33 | 79.9 ± 2.2 | 35 | 83.2 ± 1.9 |
| Week12 | 118 | 76.6 ± 1.6 | 20 | 81.4 ± 2.5 | 22 | 82.4 ± 2.3 | 29 | 80.1 ± 1.9 | 31 | 82.4 ± 2.1 |
| Month 6 | 108 | 75.8 ± 2.5 | 19 | 81.6 ± 3.1 | 17 | 80.5 ± 1.9 | 22 | 80.3 ± 1.5 | 25 | 82.8 ± 1.5 |
| Month 12 | 74 | 76.6 ± 2.1 | 17 | 82.1 ± 2.8 | 19 | 82.8 ± 2.2 | 23 | 82.3 ± 1.4 | 20 | 83.1 ± 1.2 |

Biochemical test and improvement of subjects are presented in Table 7. Total sputum eosinophil count showed no significant difference between pre-treatment and placebo group ($p > 0.05$) while a significant decrease of the count was observed in all four supplementations ($p < 0.05$). It decreases 2.3 to 0.7 for combined supplementation ($p < 0.05$). Similar situation was observed for other three supplementations too but rate of decrease was less than that of combined supplementation.

## 4. Discussion

It was evident from the study that the omega-3 fatty acids significantly improved respiratory roles (both FEV1 parentage and FEV1/FVC ratio) compared to placebo. It also caused a decrease in the sputum eosinophil count which is an important marker of airway inflammation. Mickleborough *et al.,* showed 16 asthmatic subjects with exercise-induced bronchoconstriction (EIB) and found that fish oil might denote a theoretically advantageous non-pharmacologic intercession for asthmatic subjects with EIB [28]. Numerous researcher's backing the statement that more ingesting of oily fish, which contains higher quantities of omega-3 PUFA, protects in contradiction of juvenile asthma and improves lung function [29] [30]. Adequate omega-3 fatty acid in the food was dangerous to proper prostaglandin digestion, and therefore, insufficiencies in omega-3 fatty acid could propose that upper levels of inflammation in the body might be present. Scientific researchers had described that oral fish oil supplementation had useful effects in rheumatoid arthritis and between specific subjects with

Table 7. Subjects by improvement based on sputum analysis and serological test.

| Parameter/ Duration | Placebo | | Vitamin C | | Zinc | | Omega 3 Fatty acid | | Combined | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | Mean ± SE | n | Mean ± SE | n | Mean ± SE | n | Mean ± SE | n | Mean ± SE |
| **Serum IgE level** | | | | | | | | | | |
| Baseline | 142 | 408 ± 215 | 28 | 410 ± 218 | 32 | 288 ± 170 | 35 | 258 ± 160 | 40 | 233 ± 154 |
| Week 2 | 141 | 430 ± 232 | 26 | 411 ± 221 | 29 | 289 ± 170 | 33 | 255 ± 172 | 37 | 240 ± 149 |
| Week 6 | 132 | 442 ± 222 | 24 | 426 ± 218 | 28 | 287 ± 165 | 31 | 256 ± 158 | 34 | 242 ± 150 |
| Week 12 | 124 | 428 ± 221 | 23 | 418 ± 207 | 25 | 292 ± 162 | 27 | 253 ± 148 | 31 | 252 ± 148 |
| Month 6 | 115 | 454 ± 241 | 22 | 444 ± 221 | 22 | 295 ± 158 | 26 | 254 ± 145 | 32 | 255 ± 146 |
| Month 12 | 105 | 410 ± 195 | 21 | 410 ± 194 | 20 | 295 ± 148 | 21 | 248 ± 130 | 24 | 254 ± 146 |
| **Sputum Eosinophil count/mm$^3$** | | | | | | | | | | |
| Baseline | 142 | 2.3 ± 0.5 | 28 | 2.4 ± 0.6 | 32 | 2.3 ± 0.5 | 35 | 2.2 ± 0.3 | 40 | 2.3 ± 0.2 |
| Week 2 | 141 | 2.4 ± 0.5 | 25 | 2.2 ± 0.8 | 30 | 2.4 ± 0.7 | 32 | 2.3 ± 0.3 | 39 | 2.2 ± 0.3 |
| Week 6 | 133 | 2.3 ± 0.6 | 26 | 2.2 ± 0.9 | 23 | 2.3 ± 0.6 | 29 | 2.1 ± 0.4 | 38 | 1.8 ± 0.2 |
| Week12 | 129 | 2.7 ± 0.9 | 24 | 2.1 ± 1.0 | 26 | 2.0 ± 0.3 | 28 | 2.0 ± 0.5 | 30 | 1.5 ± 0.1 |
| Month 6 | 119 | 2.2 ± 0.8 | 20 | 2.2 ± 0.7 | 25 | 1.5 ± 0.8 | 30 | 1.3 ± 0.5 | 35 | 1.1 ± 0.3 |
| Month 12 | 100 | 3.2 ± 1.5 | 23 | 2.0 ± 0.3 | 22 | 1.4 ± 0.6 | 32 | 1.2 ± 0.3 | 20 | 0.7 ± 0.2 |

p-value > 0.05 for placebo, p-value < 0.05 for all supplements.

asthma, supporting the idea that the omega-3 PUFA in fish oil were anti-inflammatory [31] [32]. Dietary omega-3 fatty acids straight touch arachidonic acid absorption since it displaces arachidonic acid from membranes and competes with arachidonic acid for the enzymes which catalyze the biosynthesis of thromboxanes, prostaglandins and leukotrienes. Thus, omega-3 fatty acids reduce the synthesis of these powerful arachidonic acid resulting which were mediators of inflammation [33]. By means of these anti-inflammatory effects, dietary omega-3 fatty acids improve lung functions and decrease the severity of bronchial asthma and may make asthma control easier.

It was also evident from the present study that vitamin C supplementation significantly improved pulmonary functions (both FEV1% and FEV1/FVC ratio) than placebo. It decreased the sputum eosinophil count. This finding is consistent with the work of Tecklenburg *et al.*, who found that ascorbic acid supplementation provides protective effect against exercise-induced airway narrowing in asthmatic subjects. The antioxidant effects of vitamain C counteract oxidant stress and reduce the external attacks (bacteria, virus, toxins and xenobiotics) in the lung. The antioxidant effect of vitamin C may modulate the development of asthma and the impairment of pulmonary functions.

Zn may have an important antioxidant protective role in the lung and it is important to prevent pulmonary epithelial damage. This study demonstrated improvement pulmonary functions (FEVI and FEVI/FVC ratio) in response to Zn supplement than pre-supplementation ($p < 0.05$). It also significantly decreased the sputum eosinophil as the other mediators of inflammation ($p < 0.05$).

The anti-inflammatory effect of Zn is due to different mechanisms. Of these mechanisms are the regulations of mast cell, which may play a role in the development of allergies. It also blocks the binding of leukocytes to endothelial cells via the interaction between leukocyte associated antigen I and intercellular adhesion molecule and it inhibits the release of preformed mediators from mast cells, basophils and eosinophil's. It also inhibits the activation of NF-kB, a transcription factor implicated in the expression of many pro-inflammatory genes.

The study further showed that supplementing the asthmatic subjects, diet with omega 3 fatty acid, Zinc and vitamin C in combination produced a significant improvement in symptoms (wheezing, breathlessness, cough, chest tightness), lung functions and reductions of the sputum inflammatory markers than using each of them alone ($p < 0.05$). Several factors need to be considered in the interpretation of results. The study also indicated improvement of some of the parameters with placebo treatment. However, this improvement was clinically found insignificant. This may be due to regular attendance at the clinic and closer follow up.

## 5. Conclusion

Subjects with mild and moderately persistent bronchial asthma may get benefit from their dietary supplementation with omega 3 fatty acids, Zinc and vitamin

C. The findings of the present study thus imply that omega-3 fatty acids alone or in combined supplementation significantly improved the severity of bronchial asthma.

## Ethical Approval

This research work was approved by the Institutional Animal, Medical Ethics, Biosafety, and Biosecurity Committee (IAMEBBC) on dated 26 November, 2016 for Experimentations on Animal, Human, Microbes, and Living Natural Sources, memo no: 73/321/IAMEBBC/IBSC, Institute of Biological Sciences, University of Rajshahi, Bangladesh.

## Acknowledgements

I am grateful to the Institute of Biological Sciences, University of Rajshahi and Bangladesh Medical Research Council (BMRC) for providing fund and opportunity to complete the research work successfully.

## Author Contributions

KKB, UKB, and PK were designed convicted the idea. UKB, PK, and DKG drafted the manuscript. UKB, PK, AKS, and GKP performed the experiments and analyzed the data. UKB and PK wrote the initial draft of the manuscript. KKB and PK revised the manuscript. All authors read and approved the final submitted version of the manuscript.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

## References

[1] Smolensky, M.H., Lemmer, B. and Reinberg, A.E. (2007) The Effects of Dietary Supplementation with Fish Oil Lipids on the Airways Response to Inhaled Allergen in Bronchial Asthma. *Advanced Drug Delivery Reviews*, **59**, 852-882. https://doi.org/10.1016/j.addr.2007.08.016

[2] Adams, F. (1856) The Extant Works of Arataeus the Cappadocian. The Cappadocian. Sydenham Society, London. https://archive.org/details/621510271

[3] Anderson, S.D. and Daviskas, E. (2000) The Mechanism of Exercise-Induced Asthma Is ... *Journal of Allergy and Clinical Immunology*, **106**, 453-459. https://doi.org/10.1067/mai.2000.109822

[4] Godfrey, S., *et al.* (1991) Exercise but Not Methacholine Differentiates Asthma from Chronic Lung Disease in Children. *Thorax*, **46**, 488-492. https://doi.org/10.1136/thx.46.7.488

[5] Cabral, A.L.B., Conceição, G.M., Fonseca-Guedes, C.H.F. and Martins, M.A. (1999) Exercise-Induced Bronchospasm in Children: Effects of Asthma Severity. *American Journal of Respiratory and Critical Care Medicine*, **159**, 1819-1823. https://doi.org/10.1164/ajrccm.159.6.9805093

[6] Minns, L.M., Kerling, E.H., Neely, M.R., Sullivan, D.K., *et al.* (2010) Toddler For-

mula Supplemented with Docosahexaenoic Acid (DHA) Improves DHA Status and Respiratory Health in a Randomized, Double-Blind, Controlled Trial of US Children Less than 3 Years of Age. Prostaglandins Leukot. *Essential Fatty Acids*, **82**, 287-293. https://doi.org/10.1016/j.plefa.2010.02.009

[7] Couch, J.M., Birch, E.E., Khoury, J.C., Berseth, C.L., *et al.* (2010) The Impact of Early Nutrition on Incidence of Allergic Manifestations and Common Respiratory Illnesses in Children. *The Journal of Pediatrics*, **156**, 902-906.e1. https://doi.org/10.1016/j.jpeds.2010.01.002

[8] Thienprasert, A., Samuhaseneetoo, S., Popplestone, K., West, A.L., *et al.* (2009) Fish Oil N-3 Polyunsaturated Fatty Acids Selectively Affect Plasma Cytokines and Decrease Illness in Thai Schoolchildren: A Randomized, Double-Blind, Placebo-Controlled Intervention Trial. *The Journal of Pediatrics*, **154**, 391-395. https://doi.org/10.1016/j.jpeds.2008.09.014

[9] Pastor, N., Soler, B., Mitmesser, S.H., Ferguson, P. and Lifschitz, C. (2006) Infants Fed Docosahexaenoic Acid- and Arachidonic Acid-Supplemented Formula Have Decreased Incidence of Bronchiolitis/Bronchitis the First Year of Life. *Clinical Pediatrics* (*Phila*), **45**, 850-855. https://doi.org/10.1177/1073858406289801

[10] Nagakura, T., Matsuda, S., Shichijyo, K., Sugimoto, H. and Hata, K. (2000) Dietary Supplementation with Fish Oil Rich in $\omega$-3 Polyunsaturated Fatty Acids in Children with Bronchial Asthma. *European Respiratory Journal*, **16**, 861-865. https://doi.org/10.1183/09031936.00.16586100

[11] Hodge, L., Salome, C.M., Peat, J.K., Haby, M.M., *et al.* (1996) Consumption of Oily Fish and Childhood Asthma Risk. *The Medical Journal of Australia*, **164**, 137-140. https://doi.org/10.5694/j.1326-5377.1996.tb122010.x

[12] Galli, C. and Calder, P.C. (2009) Effects of Fat and Fatty Acid Intake on Inflammatory and Immune Responses: A Critical Review. *Annals of Nutrition and Metabolism*, **55**, 123-139. https://doi.org/10.1159/000228999

[13] Reisman, J., *et al.* (2006) Treating Asthma with Omega-3 Fatty Acids: Where Is the Evidence? A Systematic Review. *BMC Complementary and Alternative Medicine*, **6**, 26. https://doi.org/10.1186/1472-6882-6-26

[14] Arm, J.P., Horton, C.E., Mencia-Heurta, J.M., House, F., *et al.* (1988) Effect of Dietary Supplementation with Fish Oil Lipids on Mild Asthma. *Thorax*, **43**, 84-92. https://doi.org/10.1136/thx.43.2.84

[15] Arm, J.P., Horton, C.E., Spur, B.W., Mencia-Huerta, J.M. and Lee, T.H. (1989) The Effects of Dietary Supplementation with Fish Oil Lipids on the Airways Response to Inhaled Allergen in Bronchial Asthma. *American Review of Respiratory Disease*, **139**, 1395-1400. https://doi.org/10.1164/ajrccm/139.6.1395

[16] Mickleborough, T.D., Murray, R.L., Ionescu, A.A. and Lindley, M.R. (2003) Fish Oil Supplementation Reduces Severity of Exercise-Induced Bronchoconstriction in Elite Athletes. *American Journal of Respiratory and Critical Care Medicine*, **168**, 1181-1189. https://doi.org/10.1164/rccm.200303-373OC

[17] Mickleborough, T.D., Lindley, M.R., Ionescu, A.A. and Fly, A.D. (2006) Protective Effect of Fish Oil Supplementation on Exercise-Induced Bronchoconstriction in Asthma. *Chest*, **129**, 39-49. https://doi.org/10.1378/chest.129.1.39

[18] Tecklenburg-Lund, S., Mickleborough, T.D., Turner, L.A., Fly, A.D., *et al.* (2010) Randomized Controlled Trial of Fish Oil and Montelukast and Their Combination on Airway Inflammation and Hyperpnea-Induced Bronchoconstriction. *PLOS ONE*, **5**, e13487. https://doi.org/10.1371/journal.pone.0013487

[19] Brannan, J.D., Koskela, H. anderson, S.D. and Chew, N. (1998) Responsiveness to

Mannitol in Asthmatic Subjects with Exercise- and Hyperventilation-Induced Asthma. *American Journal of Respiratory and Critical Care Medicine*, **158**, 1120-1126. https://doi.org/10.1164/ajrccm.158.4.9802087

[20] Brannan, J.D. anderson, S.D., Freed, R., Leuppi, J.D., *et al.* (2000) Nedocromil Sodium Inhibits Responsiveness to Inhaled Mannitol in Asthmatic Subjects. *American Journal of Respiratory and Critical Care Medicine*, **161**, 2096-2099. https://doi.org/10.1164/ajrccm.161.6.9908096

[21] Brannan, J.D. anderson, S.D., Gomes, K., King, G.G., *et al.* (2001) Fexofenadine Decreases Sensitivity to and Montelukast Improves Recovery from Inhaled Mannitol. *American Journal of Respiratory and Critical Care Medicine*, **163**, 1420-1425. https://doi.org/10.1164/ajrccm.163.6.2006019

[22] Anderson, S.D. (2004) Single-Dose Agents in the Prevention of Exercise-Induced Asthma: A Descriptive Review. *Treatments in Respiratory Medicine*, **3**, 365-379. https://doi.org/10.2165/00151829-200403060-00004

[23] Brannan, J.D., Gulliksson, M. anderson, S.D., Chew, N., *et al.* (2006) Inhibition of Mast Cell PGD2 Release Protects against Mannitol-Induced Airway Narrowing. *European Respiratory Journal*, **27**, 944-950. https://doi.org/10.1183/09031936.06.00078205

[24] Parsons, J.P. and Mastronarde, J.G. (2009) Exercise-Induced Asthma. *Current Opinion in Pulmonary Medicine*, **15**, 25-28. https://doi.org/10.1097/MCP.0b013e32831da8ab

[25] O'Sullivan, S., Roquet, A., Dahlén, B., Larsen, F., *et al.* (1998) Evidence for Mast Cell Activation during Exercise-Induced Bronchoconstriction. *European Respiratory Journal*, **12**, 345-350. https://doi.org/10.1183/09031936.98.12020345

[26] Kippelen, P., Larsson, J. anderson, S.D., Brannan, J.D., *et al.* (2010) Acute Effects of Beclomethasone on Hyperpnea-Induced Bronchoconstriction. *Medicine & Science in Sports & Exercise*, **42**, 273-280. https://doi.org/10.1249/MSS.0b013e3181b541b1

[27] Holzer, K. anderson, S.D., Chan, H.K. and Douglass, J. (2003) Mannitol as a Challenge Test to Identify Exercise-Induced Bronchoconstriction in Elite Athletes. *American Journal of Respiratory and Critical Care Medicine*, **167**, 534-537. https://doi.org/10.1164/rccm.200208-916OC

[28] Mickleborough, T.D., Lindley, M.R. and Ray, S. (2005) Dietary Salt, Airway Inflammation, and Diffusion Capacity in Exercise-Induced Asthma. *Medicine & Science in Sports & Exercise*, **37**, 904-914.

[29] Schwartz, J. (2000) Role of Polyunsaturated Fatty Acids in Lung Disease. *The American Journal of Clinical Nutrition*, **71**, 393S-396S. https://doi.org/10.1093/ajcn/71.1.393S

[30] Moreira, A., Delgado, L., Fonseca, J., Castel-Branco, G., *et al.* (2007) Pilot Study of the Effects of n-3 Polyunsaturated Fatty Acids on Exhaled Nitric Oxide in Patients with Stable Asthma. *The Journal of Investigational Allergology and Clinical Immunology*, **17**, 309-313.

[31] Calder, P.C. (2002) Dietary Modification of Inflammation with Lipids. *Proceedings of the Nutrition Society*, **61**, 345-358. https://doi.org/10.1079/PNS2002166

[32] Calder, P.C. (2006) n-3 Polyunsaturated Fatty Acids, Inflammation, and Inflammatory Diseases. *The American Journal of Clinical Nutrition*, **83**, 1505-1519. https://doi.org/10.1093/ajcn/83.6.1505S

[33] Tecklenburg, S.L., Mickleborough, T.D., Fly, A.D., Bai, Y. and Stager, J.M. (2007) Ascorbic Acid Supplementation Attenuates Exercise-Induced Bronchoconstriction in Patients with Asthma. *Respiratory Medicine*, **101**, 1770-1778. https://doi.org/10.1016/j.rmed.2007.02.014