Study the effect of supplementation of two types' of omega-3 poly unsaturated fatty acids on oxidative stress status of the asthmatic patients

Sara A. Mahdi[1], Farah A. Rasheed[1], Mustafa Nema A. Ali[2]

[1]*Department of Chemistry, College of Science, Al-Nahrain University, Baghdad, Iraq*

[2]*Department of Medicine, College of Medicine, Baghdad University, Baghdad, Iraq*

(Received: 26 / 11 / 2012---- Accepted: 8 / 4 / 2013)

Abstract

Asthma is a chronic disorder of the airways with underlying inflammation and oxidative stress. Malondialdehyde (MDA) - the lipid peroxidation product- level increases in inflammatory diseases and used as a common oxidative stress marker . Albumin and bilirubin, uric acid ; are components of antioxidant defense system. Omega-3polyunsaturated fatty acids supplementations lead to decrease the inflammatory mediators thereby decrease oxidative stress in asthmatics. Thirty seven asthmatic patients (20 females and 17 males) were involved compared with 37 healthy controls . Plasma samples analyzed for total MDA, albumin bilirubin, and uric acid before and after 3 weeks of supplementation of two types omega -3 polyunsaturated fatty acids (300mg/day) . After 3weeks of supplementation the MDA level change along supplementation period ($p< 0.05$), but it still significantly differ from control ($p<0.01$) , albumin and bilirubin return to control level with non-significant difference from control, while uric acid increase significantly. These results indicate the decrease oxidative stress situation since MDA levels decrease while endogenous antioxidant molecules (albumin , bilirubin , and uric acid) levels raised leading to conclude the valuable omega-3 fatty acids supplementation for asthmatic patients .

Introduction

Asthma is a worldwide disease. It is characterized by an influx and activation of inflammatory cells, generation of inflammatory mediators, and epithelial cell shedding [1]. It has been shown that inflammation driven by increased oxidative stress occurs in the airways of patients with asthma [2] . Inflammatory and immune cells in the airways, release increased amounts of reactive oxygen species (ROS) in asthmatic patients. The resulting reactive oxygen species (ROS) , have destructive role when produced in excessive amounts [3, 4]. The lipid peroxidation products (as part of inflammation events) easily create reactive carbon compounds. The most important one is malondialdehyde (MDA)[5]. Malondialdehyde, MDA, is a highly reactive three carbon dialdehyde, produced as a byproduct of poly unsaturated fatty acid peroxidation [6] . it is one of the most frequently used indicators of lipid peroxidation [7]. Thiobarbituric acid –reactive substances (TBARS) measure the concentration of MDA. This popular assay for MDA is based on its reaction with thiobarbituric acid (TBA) [8, 9].

Elevated MDA levels have been observed in plasma and bronchoalveolar fluid in asthmatics [10, 11]. Malondialdehyde (MDA) levels elevated also in breath condensate of the asthmatic patients [12] .

Albumin is well known for its ability to bind molecules, such as metals ions, fatty acids, drugs, and also hormones.The flexibility of the albumin structure adapts it readily to ligands, and its three domains provide a variety of binding sites that's lead to have many antioxidant activities [13]. Picado C. *et al* measure serum albumin in asthmatic patient and low plasma albumin level was reported in corticosteroid – dependent asthmatic patients [14]. The interferences of corticosteroid are eliminated in other study which stated lower plasma albumin concentration in severe asthmatic patients [15]. Another study also stated low albumin levels in asthmatic children in compare to control group [16]. Vural *et al* also stated the lower level of albumin in patients with bronchial asthma [17].

Bilirubin was reported to protect against the oxidation of lipids such as linoleic acid and vitamin A [18].R. stocker *et al* indicate that bilirubin at micromolar concentrations can scavenge the chain –carrying peroxyl radical [19]. In serum, J.Neuzil & R.Stocker demonstrate that lipoprotein-associated and albumin-bound bilirubin can efficiently protect lipid from such peroxidation [20]. Remission of severe chronic asthma was noted in a patient during an episode of hyper bilirubinemia associated with hepatitis [21].

Finally Misso*et al* reported low plasma bilirubin concentration in severe asthma [15].

Uric acid has profound beneficial effects since it scavenges potential harmful radicals [22]. Urate not only behaves as a radical scavenger but also stabilize ascorbate in biological fluids [23]. Most few studies on uric acid in asthma focus on its availability in respiratory tract lining fluid that reported availability [1, 24], and its reduction concentration than normal there [9]. While Misso *et al* found no significant differences in plasma uric acid concentrations in asthmatics [15].

The membrane of most immune cells contain large amount of arachidonic acid (AA), compared with other poly unsaturated fatty acids (PUFA) compounds, like Eicosapentanoic acid (EPA). Because that AA is usually the principal precursor for eicosanoid synthesis metabolism of AA by cycloxgynase (COX) enzyme gives rise to the 2-seriesprostaglandin (PG) and thromboxanes (TXAs) , whereas it's metabolism by 5-lipoxygenase (5-LOX) pathway gives rise 4-series leukotrienes (LTs) [25]. These series of PGs and LTs has a number of proinflammatory effects enhances generation of reactive oxygen species [26] . Among ω-3 PUFA that

possess potent immunmodulatory activities, those from fish oil (a rich source of EPA and DHA) are more biologically potent than other [25]. Ingestion of these classes of fatty acids will lead to their distribution to virtually every cell in the body with effects on membrane composition and function, eicosanoid synthesis, cellular signaling and regulation gene expression [27]. Supplementation with EPA and DHA significantly increases tissue levels of these kinds of fatty acids, and in sequence increased proportion of those fatty acids in inflammatory cell phospholipids .The incorporation of EPA and DHA into human inflammatory cells occurs in a dose-response fashion and is partly at the expense of arachidonic acid [28, 29, 30].

The ω3-PUFA (practically EPA&DHA) decreases the production of inflammatory mediators. They act in two ways; directly by replacing AA as an eicosaniod substrate and inhibiting AA metabolism and via interference with AA cascade that generate eicosanoid . EPA structurally close analogue of AA, it is not only can replace AA in phospholipid bilayers but act also as a substrate for cyclooxygenases (COX) and lipoxgynase enzymes, generating 3-series prostaglandins and thromboxane and 5-series leukotrienes [31,32,33]. SethiS. *et al* reported that ω-3 PUFAs can be oxidized non-enzymatically and that the products are both anti-inflammatory and anti-proliferative [34]. Gao, L. *et al* stated that EPA and DHA are readily oxidized under free radical conditions because they have additional carbon-carbon double bonds compared with arachidonate and other PUFAs [35].

Several studies reported this beneficial effect of ω-3PUFA supplement (i.e. EPA&DHA) . One of these studies demonstrated that dietary supplementation with ω -3 PUFAs over 6 months increased plasma levels of these fatty acids and reduced stimulated TNF-α and circulating eosinophils and reduced medication use in asthmatic children[36]. Nagakura *et al* showed that dietary supplementation with fish oil (84 mg EPA and 36 mg DHA per day) over 10 months decreased asthma scores in children with bronchial asthma [37]. Okamoto et al observed suppression of LTB_4 and LTC_4 generation by following 4 weeks of perilla seed oil (ω-3 PUFA)-rich supplementation in asthmatic subjects[38]. *Payan et al* found that high doses, compared to low doses, of EPA ethyl ester taken daily for 8 weeks increased LTB_5 generation, and reduced AA, LTB_4, and PGE_2[39].

Subjects , Materials , and Methods

Thirty seven asthmatic patients (20 females and 17 males) were evaluated in this study. Diagnosis of asthma was made by a respiratory physician . The study was carried out in Baghdad Teaching Hospital . The exclusion criteria were (i) age less than 15y (ii) vitamin supplements taken in the last 4 weeks, (iii) presence of other diseases known to be associated with elevated oxidative stress (cancer, diabetes, arthritis, etc.) . A matching group of 37 healthy volunteer subjects (21 male and 16 female) were considered as a control group . ω-3 polyunsaturated fatty acids supplements (particularly ecosapentanoic acid EPA and ecosahexanoic acid DHA) ordered to be consumed by patients (thirty one only stayed along study period) as 1 capsule per day(300mg/day:120mg DHA and 180 mg EPA) . Samples of blood collected from patients weekly for 3 weeks, in addition to base line. Total period of observation and collecting blood samples is 4 weeks for every patient .

Each plasma sample was analyzed for total malondialdehyde (MDA) , albumin, uric acid and bilirubin. Plasma albumin, uric acid and bilirubin were measured by colorimetric method using kits supplied by bioMaghrab Company.

MDA lipid peroxidation end product measured spectrophotometrically after adding thiobarbituric acid under acidic conditions [40].

Statistical analysis

Statistical package for social sciences (SPSS) version 15 was used for data entry and analysis .

Results & Discussion

Number and percentage (according to gender) of subjects who's involved in this study are given in Table (1) .

Table -1: Distribution of study participants according to their health status and gender

Gender	Study Group					
	Asthmatic		Control		Total	
	N	%	N	%	N	%
Male	17	45.9%	21	56.0%	38	51.3%
Female	20	54.1%	16	44.0%	36	48.7%
Total	37	100.0%	37	100.0%	74	100.0%

Plasma Malondialdehyde (MDA) levels (μmol/l)

The mean (±SEM) values of plasma MDA levels in control and asthmatics group before and after the course of eicosapentaenoic and docosahexaenoic acids (EPA & DHA) supplementation are listed in table (2) .

a- Before EPA and DHA supplementation

Data in table 2 showed that MDA concentration in the plasma of asthmatic group (12.6 ± 4.54 μmoll/l) was significantly higher ($p< 0.01$) than that of control group (4.50 ± 0.33μmoll/l) . Similar findings were reported by Ozaras *et al*, Jacobson *et al*, and sharma A. *et al*, who found that MDA was higher in plasma of asthmatic patients compared to controls [10, 11,41].

The increasing in the MDA concentration indicates the increased peroxidation of lipids (i.e. oxidative stress) in the asthma disease, where the oxidative stress is involved in asthma pathogenesis and symptoms [1]. High levels of MDA itself is involved in many harmful effects of inflammation [6, 42].

b- After EPA and DHA supplementation

Despite that the level of MDA in plasma of asthmatic group after4 weeks of supplementation with EPA and DHA decrease compared to that before Supplementation (mean 10.27 ± 0.86 and 12.60± 0.82 respectively) , it is still significantly higher than the control group ($p < 0.01$), as shown in table (2) .

Table (2) Plasma malnodialdehyde concentration (µmoll/l) in asthmatic patients before (week 0) and after ecosapentanoic acid and docosahexanoic acid supplementation (week 3) compared to control subjects

Study group	N	MDA* µmol/l Mean ± SEM	P	P
Control	37	4.5 ±0.33	---	N.S.
Asthmatics 0	37	12.6 ±0.82	<0.01	
Asthmatics 3	30	10.27 ±0.86	< 0.01	

***MDA= Malnodialdehyde**

During the 3weeks of EPA and DHA supplementation, plasma MDA level unchanged significantly in each week of the observation compared to the week zero (as shown in table 3) . But the decreasing of plasma MDA level with time is significant ($p< 0.05$) which indicate to the successful of EPA and DHA supplementation for extended period of time. As shown in table (3) .

Table (3) plasma Malnodialdehyde concentration (µmoll/l) in asthmatic patients during 3 weeks of ecosapentanoic acid and docosahexanoic acid supplementation

Study group	N	MDA* µmol/l Mean ± SEM	P	P
Asthmatics 0	*37*	*12.6 ±0.82*	---	<0.05
Asthmatics 1	30	11.54 ±0.87	N.S.	
Asthmatics 2	30	12.41 ±1.02	N.S.	
Asthmatics 3	30	10.27 ±0.86	N.S.	

***MDA = Malnodialdehyde**

Malondialdehyde is the result of oxidative stress due to inflammation and/or hyperresponsiveness . Inflammation and hyper responsiveness themselves are due to immune cells activation as well as some bronchial cells activation that contain AA . Arachidonic acid produces cell mediators (particularly ecosaniods) . The substitution of AA with EPA and DHA in cell membrane lead to the production 5- series leukotriene LT (with less potent inflammatory properties) compared to 4-series (LT) produced from AA, and 3-sreies prostaglandins (PG) and thromboxanes (TXAs) (with antinflammatory effects) compared to 2-series produced from AA[31,32] . These LTs, PGs and TXAs produced from EPA (in addition to reduce these compounds originated from AA) will decrease the oxidative stress that produces MDA .

Plasma albumin level (g/liter)

The mean (±SEM) values of plasma albumin level in asthmatic and control group before and after the course of eicosapentaenoic and docosahexaenoic acids (EPA & DHA) supplementation are listed in table (4) .

a- Before EPA and DHA supplementation

The mean value of albumin in plasma of asthmatic patients group (40.29±7.24 g/L) was significantly lower ($p< 0.05$) compared with control group (45.17± 1.54g/L). Albumin is known to be one of the negative acute phase proteins [42] and it is also found to have antioxidant properties [13, 20]. So the decrease in plasma albumin level obtained in the present study could be explained by either that albumin is one of the negative acute phase proteins that decreased after inflammations or due to its activity as antioxidant or both, which need more investigation in future work . The results obtained in the present study is agreed with the finding of Vural *et al* and Picado et al who reported a decrease serum albumin level in asthmatic patients [14, 17] .

b- After EPA and DHA supplementation

The level of Plasma albumin significantly increased ($p>0.05$) after3 weeks of EPA and DHA supplementation to asthmatic patients (mean 47.67 ±1.37g/L) compared to the control level (45.17±1.54 g/L). (as shown in table (4)

Table (4) plasma Albumin (g/L) in asthmatic patients before (week 0) and after ecosapentanoic acid and docosahexanoic acid supplementation (week 3) compared to control subjects

Study group	N	Albumin g/l Mean± SEM	P	P'
Control	37	45.17 ±1.54	---	
Asthmatics 0	37	40.29 ±1.24	<0.05	
Asthmatics 3	30	47.67 ±1.37	<0.01	N.S.

The supplementation of EPA and DHA leads to decrease inflammatory process in asthmatic patients which lead to decrease albumin consumption (as an antioxidant) .

In addition to that decreasing, inflammatory process also lead to decrease albumin consumption as negative acute phase protein . Both of these two processes could explain the increase in albumin level in asthmatic patients to upper normal levels three weeks after EPA and DHA supplementation . From the follow up of plasma albumin level over four weeks of EPA and DHA supplementation, it was noticed that albumin started to increase from the third week and continue to the end of the fourth week (as shown in table 5). This change in albumin level could be explained by the half-life of albumin (15 days half-life [43]) so that new albumin synthesized in this period of omega-3 compounds supplementation, is less exposed to inflammation. This idea could be applied to the action of albumin both as a negative acute phase protein and as an antioxidant .

Table (5) plasma Albumin (g/L) in asthmatic patients during 3weeks of ecosapentanoic acid and docosahexanoic acid supplementation

Study group	N	Albumin g/l Mean± SEM	P	P'
Asthmatics 0	37	40.29 ±1.24	---	
Asthmatics 1	30	45.17 ±1.84	<0.05	N.S.
Asthmatics 2	30	43.07 ±1.85	N.S.	
Asthmatics 3	30	47.67 ±1.37	<0.01	

Plasma Uric acid mg/dl

The mean (±SEM) values of plasma uric acid level in control and asthmatic group before and after the course of eicosapentaenoic and docosahexaenoic acids (EPA & DHA) supplementation are listed in table (6) .

a- Before EPA and DHA supplementation

The level of uric acid in plasma of asthmatic group show non-significant difference compare to that of the control group obtained in the present study (mean 5.40± 0.26 mg/dl and 4.66± 0.29 mg/dl respectively). although uric acid is provide as much as 60% of oxygen and free-radical scavenging in human plasma leading to make it the major antioxidant power source in the plasma, because of uric acid is ubiquitous in body fluids and tissues, this may be lead to the non-significant difference of its level in asthmatic patients found in the present study.

In addition to the relatively wide range of its physiological concentration in plasma (2.5-7.5 mg/dl) [24,44]. The result of the present study was agreed with Misso*et.al* results [15].

b- After EPA and DHA supplementation

Plasma uric acid significantly increased ($p<0.05$) after four weeks EPA and DHA supplementation to asthmatic patients (mean 5.56±0.19 mg/dl) . Supplementation of EPA and DHA leads to decrease the production of reactive molecules (free radicals in particular) which may lead to decrease consumption of uric acid as antioxidant , and hence, it may be increasing its level after 3weeks of supplementation .

Table (6) plasma uric acid concentration (mg/dl) in asthmatic before (week 0) and after ecosapentanoic acid and docosahexanoic acid supplementation (week 3) compared to control subjects

Study group	N	Uric acid mg/dl Mean ±SEM	P
Control	37	4.66 ±0.29	---
Asthmatics 0	37	5.40 ±0.26	N.S.
Asthmatics 3	30	5.56 ±0.19	<0.05

From the follow up of plasma uric acid level over 3 weeks of EPA and DHA supplementation (table 7) , it was noticed that its concentration decrease significantly in the first week and return to increase in the following weeks .

Table (7) plasma uric acid concentration (mg/dl) in asthmatic during 3 weeks of ecosapentanoic acid and docosahexanoic acid supplementation

Study group	N	Uric acid mg/dl Mean ±SEM	P	P'
Asthmatics 0	37	5.4 ±0.26	---	**<0.05**
Asthmatics 1	30	4.68 ±0.38	**<0.05**	
Asthmatics 2	30	5.15 ±0.27	N.S.	
Asthmatics 3	30	5.56 ±0.19	N.S.	

The variation of uric acid concentration over 3 weeks of supplementation course report significant difference ($p<0.05$) which mean the concentration change over time is real .

Plasma Bilirubin (mg/dl)

The mean (±SEM) values of plasma bilirubin level in control and asthmatic group before and after the course of eicosapentaenoic and docosahexaenoic acids (EPA & DHA) supplementation are listed in table (8) .

a- Before EPA and DHA supplementation

The mean of bilirubin in plasma of asthmatic patients group (0.41±0.05 mg/dl) was significantly lower ($p< 0.05$) compared with that of the control group (0.58± 0.04mg/dl) .

Bilirubin is a molecule with effective antioxidant properties due to its structure [19]; therefore it is not strangely to exhibit its antioxidant properties that leads to the consumption of this molecules and decreasing its levels in the plasma of asthmatic patients. Since asthma is an inflammatory disease produces free radicals more than normal.

The result of the present study is agreed with results obtained by Misso *et al* who found a low plasma bilirubin concentration in severe asthma [15]. And also it is emphasized with Ohrui T. *et al* who found remission of asthmatic patients who develop jaundice [21]. Neuzil & Stocker demonstrate that lipoprotein-associated and albumin-bound bilirubin can efficiently protect lipid from peroxidation [20]. Many studies stated low bilirubin levels as biomarker of many diseases' pathology. Hopkins *et al* compared familial coronary artery disease patients with control subjects.

The diseased individuals displayed substantial lower serum bilirubin levels than the control subjects [45]. Levinson S. also observed an inverse relationship between bilirubin levels and severity of ischemic heart disease [46].

In meta-analysis of 11studies,Novotny &Vitek found elevated bilirubin levels associated with diminished risk of atherosclerosis [47]. In peripheral vascular disease, bilirubin levels are lower than in the normal population [21].

b- After EPA and DHA supplementation

The plasma blilirubin levels rises after 4 weeks of EPA and DHA supplementation to asthmatic patients, reaching near normal level. No significant difference ($p> 0.05$) between asthmatics (mean 0.47± 0.07 mg/dl) and control groups noticed as shown in table -8-.

The increase in bilirubin levels after EPA and DHA supplementation may be indicate to success of replacement of AA with EPA that lead to decrease the free radicals and other reactive molecules which consume biliribin (working as antioxidant) .

Table (8) plasma bilirubin concentration (mg/dl) in asthmatic before (week 0) and after ecosapentanoic acid and docosahexanoic acid supplementation (week 3) compared to control subjects

Study group	N	Bilirubin mg/dl Mean ±SEM	P	P'
Control	37	0.58 ±0.04	---	
Asthmatics 0	37	0.41 ±0.05	<0.05	
Asthmatics 3	30	0.47 ±0.07	N.S.	N.S.

From the follow up of plasma bilirubin level over three weeks of EPA and DHA supplementation (table 9) , it was noticed that bilirubin started to increase from the second week and continue to do so to the third week. This finding is agreed with the expected action of EPA and DHA supplementation despite the increases is not significance .

Table (9) plasma bilirubin concentration (mg/dl) in asthmatic during 3 weeks of ecosapentanoic acid and docosahexanoic acid supplementation

Study group	N	Bilirubin mg/dl Mean ±SEM	P	P'
Asthmatics 0	37	0.41 ±0.05	---	N.S.
Asthmatics 1	30	0.41 ±0.044	N.S.	
Asthmatics 2	30	0.46 ±0.08	N.S.	
Asthmatics 3	30	0.47 ±0.07	N.S.	

Conclusion

1- Oxidative stress markers in this study divided into two parts; first: markers that indicate oxidative stress in asthma patients from onset time which is MDA. and in follow-up the change in oxidative stress situation. Second: markers that have beneficial in follow-up the change in oxidative stress situation like albumin, uric acid and Bilirubin .

2- omega-3 compounds used in this study (EPA&DHA) show beneficial effect in ameliorate asthma symptoms by changing levels of some oxidative stress markers at the dose used .

References

1- Kirkham P. and Rahman I. Oxidative stress in asthma and COPD: antioxidant and therapeutic strategy . Pharmcol.Ther. 111:476 (2006) .

2- Dworski R. Oxidant stress in asthma. Thorax 55(Suppl.2), S51 (2000) .

3- Suzy A.A. and Serpil C.E. Antioxidant responses to oxidant-mediated lung disease . Am. J. Physiol. Lung Cell Mol. Physiol. 283:L246 (2002) .

4- AmitKunwar and K.I. PriyadarsiniFree radicals, oxidative stress and importance of antioxidants in human health.J Me d A l l i e d S c i. 1 (2) : 53-60(2 0 1 1) .

5- Draper etala comparative evaluation of thiobarbaturic acid methods for determination of malondialdehyde in biological materials . Free radic . Boil . Med. ; 15. 353 (1993) .

6- Rio D. D. , Stewart A.J. , Pellegrini N. A review of recent studies on malondialdehyde as toxic molecule and biological marker of oxidative stress.Nutr.Metab. Cardiovasc.dis . 15:316 (2005) .

7- Nielsen F. Mikkelsen B.B. Nielsen J.B. et al. plasma malondialdehyde as biomarker for oxidative stress: reference interval and effects of life-style factor.Clin. Chem. 43:1209(1997) .

8- Shuaev V.& Oliver D.J. Metabolic and proteomic markers for oxidative stress . New tools for reactive oxygen species research.Plant. Physiol. 141:367 (2006) .

9- Wood L.G., Gibson P.G., Garg M.L. Biomarkers of lipid peroxidation, airway inflammation and asthma. Eur. Respir. J. 21:177(2003) .

10- Ozaras R., Tahan V., Turkmen S. et al. Changes in malondialdehyde levels in bronchoalveolar fluid and serum by the treatment of asthma with inhaled stroid and beta2-agonist.Respirol.5:289(2000) .

11- Jacobson , G.A. Yee, K.C. Ng, C.H. Elevated plasma glutathione peroxidase concentration in acute severe asthma: Comparison with plasma glutathione peroxidase activity, selenium and malondialdehyde. Scand. J. Clin. Lab. Invest. 67: 423(2007) .

12- Larstad M., Ljungkvist G.,Olin A.C. et al. Determination of malondialdehyde in breath condensate by high-performance liquid chromatography with fluorescence detection.J.Chromatogr .766:107(2002) .

13- Roche M., Rondeau P., Sinagh N. R. , e al. The antioxidant properties of serum albumin. FEBS Letters 582:1783(2008) .

14- Picado C.; Deulofeu R.; LleonartR.;.et alLipid and protein metabolism in asthma. Effects of diet and corticosteroid therapy.Allergy, 54:569(1999) .

15- Misso N.L.A., Wildhaber B.J., Ray S., et al. Plasma concentrations of dietary and non-dietary antioxidants are low in sever asthma. Eur. Respir. J. 26: 257(2005) .

16- Shima M.& Adachi M. Association of respiratory symptoms with serum protease inhibitors and albumin levels in Japanese children. Inter.J. Epidemiol. 25:1213(1996) .

17- Vural H&Uzun K. Serum and red blood cell antioxidant status in patients with bronchial asthma.Can Respir J. 7:476(2000) .

18- Sedlak T.W. &Synder S.H. Bilirubin Benefits: Cellular protection by a biliverdinreductase antioxidant cycle.Pediatrics 113:1776(2004) .

19- Stocker R., Yamamoto Y., McDonagh, et al. Bilirubin is an antioxidant of possible physiological importance. Science 235: 1043(1987) .

20- Neuzil J.& Stocker R. Free and albumin-bound Bilirubin are efficient Co-antioxidants for α-Tocopherol, Inhibiting Plasma and Low Density Lipoprotien Lipid Peroxidation.J.Biol.chem. 269:16712(1994) .

21- Breimer L.H., Spyropolous K.A., Winder A.F. Et al. Is bilirubin protective against coronary artery disease? Clin Chem. 40:1987(1994) .

22- Hediger M. A. Physiology and biochemistry of uric acid. Ther.Umsch. 61:541(2004)[Abstract] .

23- Savanian A., Davies K.J.A., Hochstein P. Serum urate as an antioxidant for ascorbic acid.Am.J. Clin. Nutr.54:1129S(1991) .

24- Rautiainen S., SerafiniM. , Morgenstern R. , et al. The validity and reproducibility of food -frequency questionnaire– based total antioxidant capacity estimates in Swedish women .Am . J. Clin. Nutr.87:1247(2008) .

25- Calder P.C.Polyunsaturated fatty acids , inflammation , and immunity. Lipids 36:1007(2001) .

26- Mandal A.K., Jones P.B., Biar A.M.,et al. The nuclear membrane organization of leukotriene synthesis.PNAS 105:20439(2008) .

27- Benatti P., Peluso G., Nicolai R. et al. Polyunsaturated fatty acids : Biochemical , nutritional and epigenetic properties . J. Am. College Nutr .23:281(2004) .

28- Jump D.B. The biochemistry of n-3 polyunsaturated fatty acids.J.Biol. Chem. 277:8755(2002) .

29- Calder P.C. n-3 Polyunsaturated fatty acids, inflammation, and inflammatory diseases. Am. J. Clin. Nutr.83:S1505 (2006) .

30- Calder P.C. Immunoregulatory and anti - inflammatory effects of n-3 polyunsaturated fatty acids . Braz . J. Med. Biol . Res. 31:467(1998) .

31- Calder P.C. n-3 Polyunsaturated fatty acids and inflammation: from molecular biology to clinic. Lipids 38:343(2003) .

32- Yin H., Brooks J.D., Gao L., et al. Identification of novel antioxidation products of the ω-3 fatty acid eicosapentaenoic acid in vitro and in vivo. J. Biol. Chem. 282:29890 (2007) .

33- Mas, Emilie ; Woodman , Richard J.; Burke , Valerie et al The omega-3 fatty acids EPA and DHA decrease plasma F (2) –isoprostanes : Results from two placebo-controlled interventions . Free Radic . Res. Sep ; 44 (9) :983-90(2010) .

34- Sethi S., Ziouzenkova, O., Ni, H., Wagner, D. et al. Oxidized omega-3 fatty acids in fish oil inhibit leukocyte-endothelial interactions through activation of PPARα Blood 100:1340(2002) .

35- Gao, L., Yin H., Milne G. L., Porter N. A., et al. Formation of F-ring Isoprostane-like Compounds (F3-Isoprostanes) in Vivo from Eicosapentaenoic Acid J. Biol. Chem. 281, 14092(2006) .

36- Hodge L., Salome C.M., Hughes J.M ., et al. Effect of dietary intake of omega-3 and omega-6 fatty acids on severity of asthma in children. Eur. Respir. J. 11:361(1998) .

37- Nagakura T., Matsuda S., Shichijyo K., et al. Dietary supplementation with fish oil rich in omega-3 polyunsaturated fatty acids in children with bronchial asthma. Eur. Respir. J. 16:861(2000) .

38- Okamoto M., Mitsunobu F., Ashida K., et al. Effects of dietary supplementation with n-3 fatty acids compared with n-6 fatty acids on bronchial asthma.Intern.Med. 39:107(2000) .

39- Payan D.G., Wong M.Y., Chernov-Rogan T., et al. Alterations in human leukocyte function induced by ingestion of eicosapentaenoic acid. J. Clin. Immunol.6: 402 (1986).

40- Shah S.V. &Walker P.D.Evidence suggesting a role for hydroxyl radical in glycerol-induced acute renal failure. Am. J. Physiol. 255: F438 (1988) .

41- Sharma A. ,Bansal S., Nagpal R. K. Lipid peroxidation in bronchial asthma. Indian J. of Pediatrics 70:715(2003) .

42- Karaman U. Çelik T. Kiran T.R.et al. Malondialdehyde, Glutathione, and Nitric Oxide Levels in Toxoplasma gondii Seropositive Patients. Korean J. Parasitol . 46:4: 293(2008) [Abstract] .

43- Quinlan G. J. , Martin G.S., Evans T.W.Albumin : Biochemical Properties and Therapeutic Potential .Hepatology . 41:1211(2005) .

44- Becker B.F., Reinholz N., Leipert B., et al. Role of uric acid as an endogenous radical scavenger and antioxidant. Chest 100:176S(1991) .

45- Hopkins P.N., Wu L.L., Hunt S.C. , et al . Higher serum bilirubin is associated with decreased risk for early familial coronary artery disease. Arterioscler ThrombVascBiol .16:250(1996)[abstract].

46- Levinson S.S. Relationship between bilirubin , apolipoprotein B, and coronary artery disease . Ann Clin Lab Sci. 27:185(1997) .

47- NovotnyL. & Vitek L. Inverse relationship between serum bilirubin and atherosclerosis in men : a meta-analysis of published studies. ExpBiol Med. 228: 568(2003) .

دراسة تأثير اضافة نوعين من الأحماض الدهنية غير المشبعة نوع أوميغا 3 على مرضى الربو باستخدام مؤشرات الاكسدة

سارة عبد القادر مهدي[1] ، فرح عقيل رشيد[1] ، مصطفى نعمة عبد علي2

[1] قسم الكيمياء ، كلية العلوم ، جامعة النهرين ، بغداد ، العراق

[1] قسم الكيمياء ، كلية العلوم ، جامعة النهرين ، بغداد ، العراق

[2] قسم الباطنية ، كلية الطب ، جامعة بغداد ، بغداد ، العراق

(تاريخ الاستلام: 26 / 11 / 2012 ---- تاريخ القبول: 8 / 4 / 2013)

الملخص

يعد الربو من الامراض ذات الصفة الالتهابية والاستجابة المفرطة . كلا هاتين الصفتين تؤدي الى حالة من الجهد التأكسدي والتي يعتقد بتأثيرها على الحالة الفسلجية-المرضية للربو . تزداد مستويات المالون داي الديهايد Malondialdehyde (MDA) - ناتج تفاعل فوق اكسدة الدهون- في الأمراض الالتهابية ويستخدم كعلامة شائعة لقياس الجهد التاكسدي . الألبومين والبيليروبين ، وحمض اليوريك ، هي مكون النظام الدفاعي المضادة للأكسدة ، استعمال الاحماض الدهنية متعددة عدم التشبع نوع اوميجا3 ، يؤدي إلى تقليل المركبات الوسيطة في الالتهابات وبالتالي يقلل الجهد التاكسدي في مرضى الربو.

شارك في هذه الدراسة سبعة وثلاثون (20 إناث – 17 ذكور) من مرضى الربو مقارنة مع 37 الاصحاء كمجموعة سيطرة . تم قياس MDA ، البيليروبين ، الالبومين ، وحمض اليوريك في بلازما المشاركين قبل وبعد 4 أسابيع من استعمال نوعين أحماض أوميغا 3 الدهنية المتعددة غيرالمشبعة (300mg/day) . بعد3 أسابيع من استعمال هذه المركبات كالمستوى MDA لايزال يختلف اختلافا كبيرا عن مستواه في مجموعة السيطرة ($P < 0.05$) ، بينما البيليروبين والالبومين عادا لمستويات مجموعة السيطرة بدون اي فرق معنوي ، في حين مستويات حمض اليوريك قد ازدادت بشكل ملحوظ . هذه النتائج تشير إلى انخفاض مستويات الجهد التأكسدي نظرا لانخفاض مستويات MDA بينما الجزيئات المضادة للأكسدة الذاتية (الألبومين ، البيليروبين ، وحمض اليوريك) قد ارتفعت مما يؤدي الى الاستنتاج اهمية استعمال ألاحماض الدهنية غير المشبعة نوع أوميغا 3 لمرضى الربو .