

Original Research Article

Effect of Omega 3 Polyunsaturated Fatty Acids Supplementation on Osteoarthritic Knees among Females

Nesrin Kamal Abd El-Fatah¹, Safa Mounir Mohammed Kheder², Nawal Abd EL-Rehim El-Sayed³,
Abd- El Moniem Hussein Helal⁴

¹Lecturer, Nutrition Department High Institute of Public Health, Alexandria University.

²Resident Dermatologist

³Professor, Nutrition Department High Institute of Public Health, Alexandria University.

⁴Professor, Physical Medicine Department, Faculty of Medicine, Alexandria University.

Corresponding Author: Nesrin Kamal Abd El-Fatah

Received: 09/12/2015

Revised: 12/03/2016

Accepted: 29/03/2016

ABSTRACT

Background: Applying advances in nutritional science to musculoskeletal medicine remains challenging, although in vivo data are lacking, the inhibitory effects of omega-3 on inflammatory factors implicated in the pathogenesis of osteoarthritis provide ample rationale for further investigation in humans with osteoarthritis.

Aim: was to determine the effect of omega-3 fatty acids supplementation for ameliorating clinical signs of osteoarthritis.

Materials & Methods: An intervention randomized pretest-posttest study was carried out on 47 females aged 40- 65 years with osteoarthritis. Patients were interviewed about knee complaints, progression of the disease, medical and physical treatment. Body weight and height were measured, and knee was examined. Functional assessment was done using Lequesne's functional index. Patients received a daily dose of 2000 mg fish oil for 3 months. Clinical and functional reassessment of the were done after three month from starting supplementation.

Results: The majority of females had osteoarthritis in both knees and all of them complained of knee pain, swelling and joint disability. About three quarter (78.7%) of cases took NSAID and a lower percentage (6.4%) used topical treatment only and 14.9% used both. After omega 3 supplementations for 3 months many improvements have occurred in patients' symptoms, signs and drug intake. The percent of cases that still have knee swelling and tenderness dropped from 100% to reach 27.6% and 36.1% respectively.

Conclusions: Findings from this study are strongly suggestive that a daily dose of 2000 mg omega 3 PUFAs significantly inhibits inflammation and reduces arthritic symptoms within a treatment period of 3 months.

Keywords: Omega-3 PUFAs, Sea foods, Fish oil, Anti-inflammatory diet, osteoarthritis.

INTRODUCTION

Nutritional interventions and nutraceutical applications for medical conditions, including OA, are currently riding the crest of public enthusiasm. The medical community must be familiar with the current state of the science to evaluate the potential benefits of nutritional methods

for preventing and treating OA. The integration of complementary and/or nutraceutical a method expands treatment options for patients with established OA beyond the traditional rehabilitation, bracing, medication, interventional, and surgical strategies. ⁽¹⁾

Osteoarthritis (OA) is a group of mechanical abnormalities involving degradation of joints. ⁽²⁾ It is associated with ageing and affect the joints that have been continually stressed. Studies confirm that low-grade inflammation plays a pathophysiological role in OA. There is a strong association between obesity; it is more prevalent among Egyptian females; and OA. ^(3,4) Obesity is typified by nutrient excess and insulin resistance, closely related to excessive proinflammatory cytokine production seen in chronic inflammation. Nutrient excess produces reactive oxygen species, resulting in oxidative stress that damages cells and triggers an inflammatory response. As insulin resistance progresses, inflammation increases, initiating a vicious cycle of excessive nutrient intake, insulin resistance and inflammation. ⁽⁵⁾

Targeting the cause of inflammation in the body is an important factor in the management of OA. Aggressive lifestyle intervention helps reduce inflammatory responses. Non-loading activities such as swimming and weight-bearing exercises have been shown to reduce symptoms, increase mobility and reduce continuing damage from OA. Weight loss reduces risk factors for symptomatic knee OA and reduces pro-inflammatory cytokines and adipokines believed to play a role in cartilage degradation, thus reducing OA-associated pain and improving physical activity. ⁽⁶⁾

A diet high in n-3 FA has been proven to reduce inflammation. The ratio of omega-6 to n-3 PUFAs in most common western diets favours omega-6 PUFAs. As a result, the anti-inflammatory effects of n-3 PUFAs are counteracted by the proinflammatory effects of omega-6. It is therefore recommended that a diet rich in n-3 fatty acids be consumed, by including the best dietary sources of n-3 FAs, which are fatty fish (e.g. herring, trout, salmon, pilchards) at least twice a week, to improve the omega-6/omega-3 ratio and help reduce inflammation. ⁽⁷⁾

Although in vivo data are lacking, the inhibitory effects of n-3 on inflammatory factors implicated in the pathogenesis of OA provide ample rationale for further investigation in humans with OA or at risk for developing OA. Also, when considering the emerging basis for broad recommendations to increase dietary n-3 PUFA intakes for cardiovascular benefit, the possible positive effects of fish oil on OA need to be defined. The aim of the present work to study the effectiveness of n-3 fatty acid supplementation in alleviation of symptoms of osteoarthritis, to assess the change in physical function of affected knee, and to evaluate its possible effect on ameliorating exacerbation of acute attacks.

MATERIALS AND METHODS

Study design and setting

An intervention approach, one group pre-post test design was conducted in the outpatient physical medicine department of hospitals affiliated to Alexandria University ***Study population, sample size and method of sampling***

Using the computer programme Epi-info version "6.0" based on previous study on n-3 fatty acids on osteoarthritis. Assuming % of using NSAID for pain relief to be 50% and to lower by 59% after usage of n-3, ⁽⁸⁾ with an alpha of 0.05 and power 80%. Forty seven female patients with confirmed diagnosis of OA, accepting to participate, were included in our study. Diagnosis was done based on criteria of the American College of Rheumatology for osteoarthritis of the knee with exclusion of pregnant women or patients with acute traumatic injury, Any concurrent diseases involving the liver, kidney, systemic diseases, Surgical procedure on either lower extremity in the past 6 months, Morbid obesity or patients received cortisone injection to the knee within the previous 30 days. All eligible patients within a period of nine months were included in the study until the required sample size was fulfilled.

Data collection

All females were interviewed to answer a pre-designed questionnaire which included sociodemographic characteristics, medical history (knee complaint; as pain, swelling, morning stiffness; progression and duration), drug history and physical therapy data.

Anthropometric assessment:

All measurements were carried out according to criteria described by Gibson (2005).⁽⁹⁾ Body weight and height were measured and body mass index was calculated.

Clinical examination:

General examination of gait and alignment and complete knee examination

were done. A gait in which a phase of gait is shortened on injured side to alleviate the pain experienced when bearing weight on that side is called antalgic gait. When standing, if there was evidence of bowing (varus) or knock-kneed (valgus) deformity, this was categorized to; normal, varum deformity and valgum deformity.

Local knees examination include discover tenderness, swelling or effusion, estimations of quadriceps muscle atrophy in girth measurements with a tape, testing Quadriceps and Hamstrings muscle power (Test extension and flexion), crepitus identification and Patellar tap test.⁽¹⁰⁾

Table (1): Grading for muscle wasting:⁽¹⁰⁾

0	No muscle contraction is detected
1	A trace contraction is noted in the muscle by palpating the muscle while the patient attempts to contract it.
2	The patient is able to actively move the muscle when gravity is eliminated.
3	The patient may move the muscle against gravity but not against resistance from the examiner.
4	The patient may move the muscle group against some resistance from the examiner.
5	The patient moves the muscle group and overcomes the resistance of the examiner. This is normal muscle strength.

Functional assessment of OA severity:

Functional assessment was done using Lequesne's functional index⁽¹¹⁾ to rate the overall condition in the patient's point of view, and a score was given.

Intervention

Daily supplementation with n-3 PUFAs in the form fish oil capsule providing 1000 mg n3 twice daily for 3 months. Dosage is considered safe according to the US FDA.⁽¹²⁾ Supplements used in the present study also contained wheat germ oil added to prevent oxidation of fatty acids in the capsule. Reassessment of the osteoarthritic knee patients was done after three months from starting supplementation with fish oil supplements. Both clinical and functional assessments were done.

Statistical analysis

Data analysis was performed using the SPSS software version 20. For descriptive statistics mean and standard deviation were used. For analysis of numeric data one sample Kolmogorov-Smirnov test was used. To test the

association between 2 categorical variables, Pearson's chi square test, Mont Carlo exact test, Fishers exact test and Test of marginal homogeneity (Mc-Nemar) were used. Finally, Paired t-test is a parametric statistical test that used to compare means of quantitative data measured two times (repeated measures) for two related sample which follow a normal distribution. The P-value less than 0.05 were considered to be statistically significant.

Ethical considerations:

The study was approved by Ethics Committee of High Institute of Public Health. Every patient was informed about the purpose of the study and written consent to participate in the study was obtained and confidentiality was assured.

RESULT

The study included forty seven women diagnosed as having knee osteoarthritis and fulfilling the inclusion criteria. Almost half of the female patients were 45 to 50 years, with mean age of 47.3± 3.9 year. Above three quarter (85.1%) of the

studied sample were married and concerning educational level, the higher percentage (53.2%) of them were above middle. Overweight is prevalent (78.7%) among studied females, while 21.3% had normal BMI. The mean BMI of studied sample was $26.5 \pm 1.5 \text{ kg/m}^2$. Table (2)

Table (2): Socio-demographic Characteristics and BMI of Osteoarthritic Females

Sociodemographic data	No (n=47)	%
Age (years)		
■ 40-	11	23.4
■ 45-	24	51.1
■ 50+	12	25.5
Mean \pm SD	47.3 \pm 3.9	
Marital status		
■ Married	40	85.1
■ Divorced /widow	7	14.9
Education		
■ Illiterate / Read & write	3	6.4
■ Preparatory	6	12.8
■ Secondary	10	21.3
■ Above middle	25	53.2
■ University	3	6.4
Working status		
■ Not working	2	4.3
■ Employee	34	72.3
■ Professional	7	14.9
BMI		
■ Normal weight	10	21.3
■ Overweight	37	78.7
■ Mean BMI	26.5 \pm 1.5	

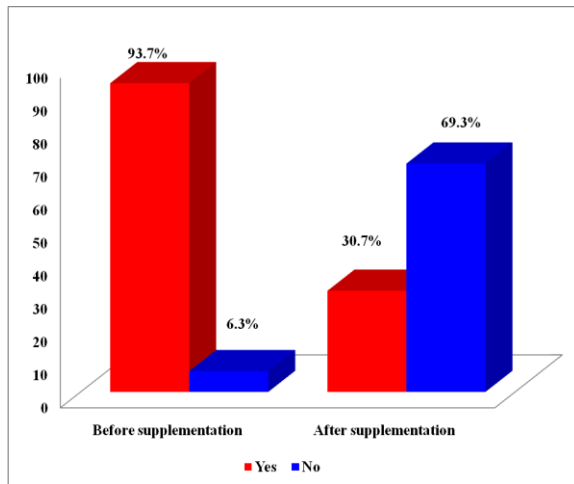


Figure (1): Effect of Omega 3 PUFA supplementation on NSAIDs intake

Seventy percent of studied females had osteoarthritis in both knees and all of them complained of knee pain, knee swelling, joint disability and frozen leg sensation. Most of the studied sample (91.5%) their complaint was for years. About three quarter (78.7%) of cases took NSAID and a lower percentage (6.4%) used topical treatment only and 14.9% used both.

Regarding, Local examination of the knee, about two third of cases (72.3%) had bilateral knee swelling, 14.9% of cases with left knee swelling and 12.8% with right knee swelling. Crepitus was felt in 91.5% of cases and 8.5% had no crepitus on knee examination. All of cases had knee tenderness; most of them had crepitus at the joint line (91.5%). The mean of Lequesne's functional index total pretest was 18.2 ± 0.8 of studied sample, with a range of 16 - 20. Figure (1 & 2) and Table (3)

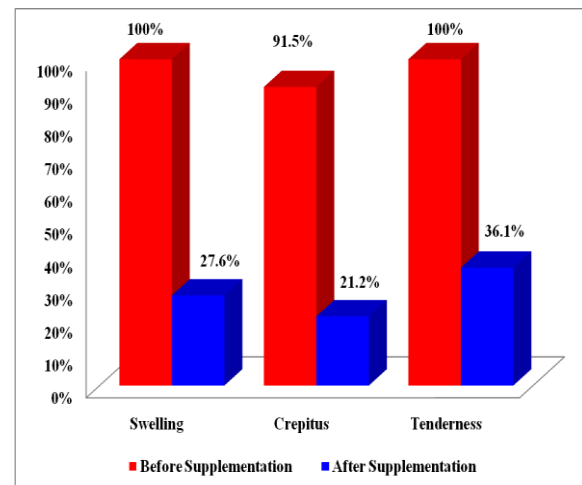


Figure (2): Effect of omega 3 supplementation on clinical knee examination

Results after n-3 PUFAs supplementations:

After n- 3 PUFAs supplementations for 3 months many improvements have occurred in patients' symptoms, signs and drug intake. Regarding drug intake, number of patients who took NSAIDs decreased significantly (30.7%) after the period of the intervention program.

On clinical knee examination, there was highly significant improvement. The percent of cases that still have knee swelling dropped from 100% to reach 27.6%. Concerning crepitus of knee joint, there was obvious significant improvement, the percent dropped from 91.5% to 21.2%. Finally, there was a highly significant improvement in knee tenderness where 100% of patients had tenderness before intervention and this was decreased significantly to 36.1% after 3 months of supplementations. Figure (1 & 2)

There is a highly significant difference in the mean total of Lequesne's functional index before and after n- 3

PUFAs supplementation which was 18.2 ± 0.8 and dropped to 10.2 ± 1.3 after 3 months. Table (3)

Table (3): Effect of omega3 PUFA supplementation on the functional assessment of knee joint

Item	Before intervention		After intervention		P value
	No	%	No	%	
Nocturnal pain					0.001*
■ No	0	0.0	26	55.3	
■ On moving	43	91.5	21	44.7	
■ When immobile	4	8.5	0	0	
Morning stretching					<0.001*
■ No	0	0.0	10	21.3	
■ 1 min	8	17.0	37	78.7	
■ 1-15 min	39	83.0	0	0.0	
Pain on standing upright					<0.001*
■ No	0	0.0	47	100.0	
■ Yes	47	100.0	0	0.0	
Pain on walking					0.587
■ No	0	0.0	2	4.3	
■ Only after walking a certain distance	46	97.9	45	95.7	
■ Very rapid	1	2.1	0	0.0	
Pain on rising from a seat					0.674
■ No	0	0.0	1	2.1	
■ Yes	47	100.0	46	97.9	
Maximum walking perimeter					0.007*
■ Grade 1	0	0.0	1	2.1	
■ Grade 2	1	2.1	2	4.3	
■ Grade 3	2	4.3	29	61.7	
■ Grade 4	29	61.7	15	31.9	
■ Grade 5	15	31.9	0	0.0	
Daily difficulties affecting upstairs					<0.001*
■ Grade 0	0	0.0	3	6.4	
■ Grade 1	0	0.0	44	93.6	
■ Grade 2	47	100.0	0	0.0	
Daily difficulties affecting downstairs					<0.001*
■ Grade 1	0	0.0	47	100.0	
■ Grade 2	47	100.0	0	0.0	
Daily difficulties affecting adopt crouching position					0.002*
■ Grade 1	0	0.0	16	34.0	
■ Grade 2	47	100.0	31	66.0	
Daily difficulties affecting walk over uneven surface					<0.001*
■ Grade1	0	0.0	47	100.0	
■ Grade 2	47	100.0	0	0.0	
Lequensens functional index total					<0.001*#
■ Mean \pm SD	18.2 ± 0.8		10.2 ± 1.3		

* P < 0.05 (significant)

DISCUSSION

Given our current understanding of the pathobiology of OA, the potential influence of dietary n-3 on the occurrence and progression of OA is obvious and must be explored further. In vitro and preclinical data on n-3 PUFAs have been extensively studied in various cell types, but only few studies have assessed their anti-OA effects in joint cell models. Three in vitro studies have been identified which demonstrated the potency of n-3 PUFAs at reducing inflammatory mediators. (13) On the other hand, in vivo data are lacking and the possible positive effects of fish oil on OA

need to be defined. In adding to the credence of using n-3 in OA in vivo, Knott et al and Roush JK et al (14,15) have recently published data derived from a spontaneous OA guinea pig model and dogs respectively to characterize the effects of an n-3 rich diet on biomarkers of OA. The results are in favor of the beneficial effect of n-3 PUFAs on OA animals. Finally, Clinical data on n-3 are limited; two studies that investigated the effect of n-3 on OA symptoms were identified. One study of showed that a daily intake of 10 ml of cod liver as an adjunct to NSAID medication was not effective to improve pain and ability. The use of olive

oil as placebo control may have introduced a bias in the result of this study. On the contrary, the second study showed that the consumption of n-3 improved OA symptoms, including pain and joint function. ^(16,17)

Findings of the present study revealed a great and mostly significant improvement in symptoms, signs and drug treatment of OA after 3 months 2000 mg n-3 daily supplementation. Concerning NSAIDs use, there was a quite decrease in the percent of cases still using them; this is due to the relieving effect on swelling and pain. Pain in knee OA could be multifactorial, and might arise from a number of different structures related to the joint or might be secondary to abnormal forces and possible damages as articular cartilage has been lost. ⁽¹⁸⁾ In the present study, all cases felt pain in knee joint, this was in agreement with the finding of the study done by Afifi et al in 2010. ⁽¹⁹⁾ Inflammation is the predominant cause of pain which is the most debilitating component of arthritis. Omega-3 PUFAs inhibits cyclo-oxygenase (cox) enzyme which oxygenates arachidonic acid leading to the formation of prostaglandins which are pro inflammatory. Many of the drugs used in treating arthritic diseases diminish prostaglandins synthesis. PUFAs are essential fatty acids and precursors to a number of important factors called eicosanoids, such as prostaglandins, thromboxanes, leukotrienes and resolvins. These mediate various processes including inflammation and bone metabolism. Conversion of PUFAs to eicosanoids is achieved by the action of cyclo-oxygenases (COX) and lipoxygenases (LOX). N-3 and omega-6 generate different series of eicosanoids, those from omega-6 are generally highly pro-inflammatory and those from n-3 have the potential clinical benefits of n-3 fatty acids controlling inflammation and reducing the expression and activity of cartilage proteoglycan degrading enzymes. ⁽²⁰⁾

On Evaluation Lequesne's functional index in our trial, the administration of daily doses of n-3 decreased the severity of OA after three months. Such improvement affected the condition of the studied females and they were very satisfied and expressed their relief, and were happy with improvement of the quality of life. Mao-Hsiung Haung et al (2005) ⁽²¹⁾ found that there was a significant relationship between Lequesne's functional index and duration of symptoms in knee OA as this there may be a significant correlation between functional status and cartilage thickness.

Finally, clinical examination of the Osteoarthritic knee, patients had antalgic gait, swelling, crepitus and tenderness in one or both knee joints. After supplementation with n-3 PUFAs all are improved. This may be attributed to the alleviating properties of n-3 by suppressing the immune system that causes joint inflammation that lead to tender and swollen joints and reducing the activity of cartilage proteoglycan degrading enzymes. ⁽²⁰⁾ Omega-3 fatty acids act by replacing arachidonic acid inhibiting its metabolism by altering the expression of inflammatory genes through effects on transcription factor activation and leading to anti-inflammatory mediators termed resolvins. ⁽²²⁾

Osteoarthritis rarely develops before the age of forty, but it affects everyone after the age of sixty. In our study the age of OA diagnosis ranged from 39 - 51 years with a mean of 43.9 ± 2.7 years. This was inconsistent with other study where the mean age of their patients was 53.24 ± 9.64 years. ⁽¹⁹⁾ This revealed that OA is the disease of old age group and may indicate that by time it is starting to afflict persons in younger age.

Overweight was prevalent in our study Osteoarthritic females, over weight causes strain on joints and should be managed early by health professionals to protect the joints. The combination of modest weight loss plus moderate exercise

provides better overall improvements in function and pain of knee OA. (23,24)

CONCLUSION

Findings from this study are strongly suggestive that a daily dose of 2000 mg n-3 PUFAs within a treatment period of 3 months significantly inhibits inflammation and helping to provide relief from arthritis when it occurs.

It is recommended that all patients with knee osteoarthritis should be encouraged to eat more than 2 meals of seafood per week coupled with n-3 supplementation capsules

REFERENCES

1. Roddy E, Doherty M. Guidelines for management of osteoarthritis published by the American College of Rheumatology and the European League Against Rheumatism: Why are they so different? *Rheum Dis Clin North Am* 2003; 29:717-31.
2. Rayman M, Callaghan A. Nutrition and Arthritis. 4th ed. Oxford: Blackwell; 2006. p.282.
3. Centers for Disease Control and Prevention. Prevalence of disabilities and associated health conditions among adults, United States. *MMWR Morb Mortal Wkly Rep.* 2005; 50 (7): 120.
4. Ministry of Health and Population [Egypt], El-Zanaty and Associates [Egypt], and ICF International. 2015. Egypt Demographic and Health Survey 2014. <http://dhsprogram.com/what-we-do/survey/survey-display-397.cfm>
5. Hurst S, Rees SG, Randerson BF. Contrasting effects of n-3 and n-6 fatty acids on cyclooxygenase-2 in model systems for arthritis. *Lipids* 2009; 44:889-96.
6. Bank RA, Verzijl N, Lafeber FP, Tekoppele JM. Putative role of lysyl hydroxylation and pyridinoline cross-linking during adolescence in the occurrence of osteoarthritis at old age. *Osteoarthritis Cartilage* 2002; 10:127.
7. Curtis CL, Rees SG, Cramp J, Flannery CR, Hughes CE, Little CB, et al. Effects of n-3 fatty acids on cartilage metabolism. *Proc Nutr Soc.* 2002 Aug; 61(3):381-9.
8. Enderlein G, Danie WI, Wayne W. *Biostatistics - A Foundations for Analysis in the Health Sciences.* Wiley & Sons, New York-Chichester-Brisbane-Toronto-Singapore, 6th ed. *Biom. J* 1995; 37: 744. doi: 10.1002/bimj.4710370610.
9. Gibson RS: Principles of nutrition assessment. Second edition. Oxford: Oxford University press 2005.
10. Rutjes AW, Nuesch E, Sterchi R, Kalichman L, Hendriks E, Osiri M, et al. Transcutaneous electro stimulation for osteoarthritis of the knee. *Cochrane Database of Systematic Reviews* 2009, Issue 4. Art. No.: CD 002823. DOI: 10.1002/14651858. CD002823. pub2.
11. Lequesne M.G., Mery C., and Samson M., Gerard P. Indexes of severity for osteoarthritis of the hip and knee: Validation-value in comparison with other assessment tests. *Scandinavian Journal of Rheumatology* 1987; 16, 85-9.
12. US Food and Drug Administration, Center for Food Safety and Applied Nutrition, Office of Nutritional Products, Labeling, and Dietary Supplements. Letter responding to a request to reconsider the qualified claim for a dietary supplement health claim for omega-3 fatty acids and coronary heart disease. FDA Website. Available at: <http://www.cfsan.fda.gov/~dms/ds-ltr28.html>.
13. Henrotin y, Lambert y, Couchourel z, Ripoll x, Chiotelli z. Nutraceuticals: do they represent a new era in the management of osteoarthritis? a narrative review from the lessons taken with five products. *Osteoarthritis and Cartilage* 2011; 19:1-21.
14. Knott L, Avery NC, Hollander AP, Tarlton JF. Regulation of osteoarthritis by omega-3 (n-3) polyunsaturated fatty acids in a naturally occurring model of disease. *Osteoarthritis Cartilage* 2011; 19:1150-7.
15. Roush JK, Dodd CE, Fritsch DA, Allen TA, Jewell DE, Schoenherr WD, et al. Multicenter veterinary practice assessment of the effects of omega-3

- fatty acids on osteoarthritis in dogs. *J Am Vet Med Assoc* 2010; 236:59.
16. Stammers T, Sibbald B, Freeling P. Efficacy of cod liver oil as an adjunct to non-steroidal anti-inflammatory drug treatment in the management of osteoarthritis in general practice. *Ann Rheum Dis* 1992; 51:128.
 17. Cho SH, Jung YB, Seong SC, Park HB, Byun KY, Lee DC, et al. Clinical efficacy and safety of Lyprinol, a patented extract from New Zealand green-lipped mussel (*Perna Canaliculus*) in patients with osteoarthritis of the hip and knee: a multicenter 2-month clinical trial. *Eur Ann Allergy Clin Immunol* 2003; 35:212.
 18. Huk A, Xul M, Coal L. pathogenesis of osteoarthritis- like changes in the joints in type IX collagen. *Arthritis Rheum* 2006; 54:2891-900.
 19. Afifi AH. Relation between cartilage thickness, degree of synovitis, pain and functional performance in knee osteoarthritis [dissertation]. Alexandria: Alexandria University; 2010.
 20. Curtis C.L. Pathologic indicators of degradation and inflammation in human osteoarthritic cartilage are abrogated by exposure to n-3 fatty acids. *Arthritis Rheum.* 2002; 46 (6):1544-1553.; 2002.
 21. Mao HH, Rei CY. Preliminary Results of Integrated Therapy for Patients with Knee Osteoarthritis. *Arthritis and Rheumatism (Arthritis Care and Research)* 2005; 53: 812-20.
 22. Philip C Calder. N-3 Polyunsaturated fatty acids, inflammation, and inflammatory diseases *Am J Clin Nutr* June 2006; 83(6):1505-19.
 23. Bennell K, Hinman R. A review of the clinical evidence for exercise in osteoarthritis of the hip and knee. *Journal of Science and Medicine in Sport* 2011; 14:4-9.
 24. Messier S, Loeser F., Miller D, Morgan M, Rejeski J, Sevick A, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: The arthritis, diet, and activity promotion trial. *Arthritis & Rheumatism.* 2004; 50: 1501-10.

How to cite this article: Abd El-Fatah NK, Kheder SMM, EL-Rehim El-Sayed NA et al. Effect of omega 3 polyunsaturated fatty acids supplementation on osteoarthritic knees among females. *Int J Health Sci Res.* 2016; 6(4):362-369.
