

THE EFFECT OF EICOSAPENTANOIC ACID ADMINISTRATION ON CLINICAL OUTCOME OF PATIENTS WITH MAJOR DEPRESSION: A PILOT STUDY

BY

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ABSTRACT

Background.

Major depressive disorder (MDD) is a common brain disorder that affects approximately 10% of the world population and leads to significant disability. The current study aimed to evaluate the impact of Omega3 PUFAs administration on the clinical outcome of patients with depression.

Patients and Methods.

A prospective, randomized controlled study conducted at the outpatient clinics of a University Hospital, Cairo, Egypt on patients diagnosed with depression according to a strict inclusion and exclusion criteria. Forty two patients were randomly assigned to either; **Group1**; (intervention n=21); received the prescribed antidepressant + omega3 (2100mg) for 8 weeks, or **Group 2**; (control, n=21); received the prescribed antidepressant only for 8 weeks. Baseline evaluation and 8-week assessment included; patient demographic-data collection, history taking and clinical assessment of DSM-5 criteria & HAM-D score. Laboratory assessment included; complete blood picture (CBC), prothrombin time (PT), activated partial thromboplastin time (aPTT). Patients were followed up regularly every 2 weeks for 8 weeks for the occurrence of side effects due to antidepressants/ Omega 3 and compliance with medications.

Results. The 2 groups were comparable at baseline. The test group showed a significant improvement in the HAMD score from baseline values and versus the control. There was no significant difference in the reported side effects between the 2 groups.

Conclusion. Omega -3 PUFAs administration at a dose of 2100 (EPA1350 mg/ , DHA 600 mg/ 150 mg other omega 3 FA) for 8 weeks, improved depression symptoms and was well tolerated.

Keywords; Omega-3 PUFAs, depression, HAMD, EPA/DHA.

Introduction

Major depressive disorder (MDD) is a common brain disorder that affects approximately 10% of the world population. According to the Diagnostic and Statistical Manual of Mental Disorder, Fifth Edition (DSM-5, 2013), MDD is characterized by the loss of interest in pleasure, low self-esteem, disturbed sleep or appetite, fatigue, and

diminished ability to think or concentrate. These problems often become chronic and recurrent, and at the worst, can lead to suicide (**Song et al., 2016**).

Major depression is a commonly occurring, serious, recurrent disorder linked to diminished role functioning and quality of life, medical morbidity, and mortality. The World Health Organization (WHO) has ranked depression as the fourth leading cause of disability worldwide and projects that, by 2020, it will be the second leading cause (**Kessler and Bromet, 2013**).

The lifetime prevalence of depression in urban and rural Egyptian populations found to be 11.4 and 19.7% (**Beshai et al., 2016**).

New-generation antidepressants appear more effective than older drugs in treatment of major depression, with response rates of up to 50%, but they do not effectively treat all depressed patients. In addition, many drugs have side effects that can affect compliance and morbidity. So patients are increasingly using complementary and alternative medicine (CAM) therapies to treat depression (**Qureshi and Al-Bedah, 2013**). One such possibility is the use of n-3 omega polyunsaturated fatty acids (PUFAs) for the treatment of depression. A link between omega-3 fatty acids and mood disorders has been suggested by some studies showing a lower incidence of depression among populations with a diet rich in omega-3 fatty acids (**Gertsik et al., 2012a**).

Omega-3 PUFA have been proposed, for treatment of Major depressive disorder. The positive effects of omega-3 PUFA on depression may depend on their physiological abundant content in the human nervous system and their involvement in neurogenesis and neuroplasticity (**Grosso et al., 2014**). Moreover, their anti-inflammatory capacity may counteract inflammatory processes occurring in depression (**Hennebelle et al., 2012**). Also lower concentrations of omega 3 PUFA in plasma or red blood cells may contribute to depression. Administration of omega 3 PUFAs significantly improved depressive symptoms in patients with major depression (**Lesperance et al., 2011**).

Several studies used omega-3 polyunsaturated fatty acids (PUFA) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in similar doses with varying results.

It has been previously documented that EPA at ratios > 60% can positively affect depression outcome. EPA and DHA are structurally similar and might be expected to compete in approximately a 1:1 ratio for binding sites. Thus the amount of EPA unopposed by DHA may be critical for effective PUFA supplementation in treatment of depressive episodes (**Sublette et al., 2011**).

Hence the aim of the current study was to evaluate the impact of Omega-3 PUFAs administration (using an EPA in a dose more than twice the concentration of DHA), on the clinical outcome of patients with depression.

Patients and Methods

The current study was a prospective, randomized controlled study conducted at the outpatient clinics of a University Hospital (Al Zahraa), in Cairo, Egypt. All patients presenting to the outpatient clinic of the Department of Psychiatry at Al Zahraa University Hospital, were assessed for eligibility according to the following inclusion and exclusion criteria. Inclusion criteria included; an age range of (18-65 years); a diagnosis of depression according to the Diagnostic statistical manual for mental

disorders 5th Edition DSM-5; and a Hamilton Depression Rating Scale (HAM-D) score of greater than or equal to 17. Exclusion criteria included having any of the following, a psychotic or seizure disorder; a current drug/ alcohol abuse or dependence; or history of drug or alcohol abuse or dependence within the previous six months; an unstable medical or neurological condition that is likely to interfere with the treatment of depression; pregnancy; history of allergy to omega-3 fatty acids, or shellfish; concomitant therapy with psychotropic medications; active suicidal ideation or other safety concerns; exposed to treatment with fluoxetine or monoamine oxidase inhibitors (MAOIs) in the previous two months; on anticoagulant therapy; receiving dietary intake of omega-3 at baseline; or refusal to participate in the study

A signed informed consent was obtained from all participants and the study design was approved by the Ethical Research Committee of Faculty of Pharmacy, Ain Shams University, and registration number (61). All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional and/or National Research Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The current study recruited 42 patients with a 1:1 randomization; the small sample size is justified by the fact that we are just piloting the idea to test its feasibility.

Forty eligible patients were randomly assigned to either:

Group 1;

(intervention n=21); received the prescribed antidepressant + Ocean blue professional omega3 2100 (Eicosapentanoic acid 1350 mg, Decosahexanoic acid 600 mg and 150 mg other omega 3 fatty acids) for 8 weeks.

Group 2;

(control, n=21); received the prescribed antidepressant only for 8 weeks.

At Baseline patients in both groups were all subjected to the following;

-Patient demographic-data collection, history taking and clinical assessment including, assessment of DSM-5 criteria by psychiatric interview & clinical pharmacist assessment of HAM-D score to assess the severity of depression.

- Laboratory assessment including; complete blood picture (CBC), prothrombin time (PT), and activated partial thromboplastin time (aPTT).

- Patients were followed up regularly every 2 weeks for 8 weeks for assessment of the following: HAM-D score, occurrence of side effects due to antidepressants/ Omega 3 and compliance with medications.

- At the end of the study (after 8 weeks), both groups were reassessed for the following; CBC, PT, aPTT, and depression outcome using HAM-D score.

- The occurrence of side effects to medications was assessed using patient side effect-reporting cards that patients had to fill daily in between visits.

- HAM-D score was interpreted using the following scores; 0-7 indicated no depression; 8- 16, mild depression; 17 – 23, moderate depression, and > 23, indicated severe depression (Zimmerman et al., 2013).

A response to treatment was defined as at least a 50% reduction in the HAM-D score, while “Remission” is a return to a normal state or a HAM-D of 7 or less.

The primary end point was comparing the differences in HAMD score from baseline to 8 weeks between groups. Other end points were comparing the difference in side effect occurrence between groups.

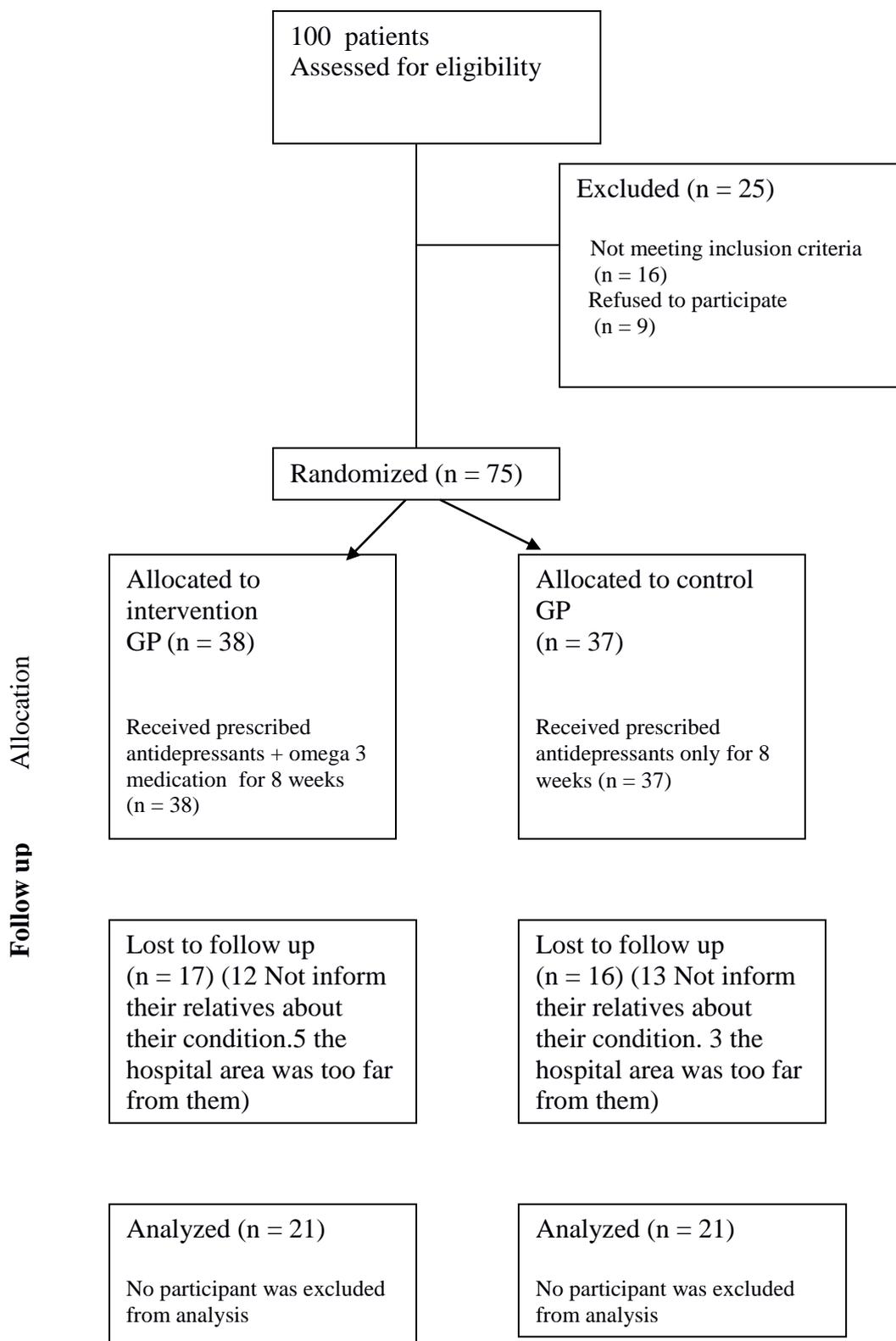
Statistical Analysis

Data management and analysis was performed using Statistical Package for Social Sciences (SPSS) vs. 23. Numerical data was summarized using means and standard deviations or medians and ranges, as appropriate. Categorical data was summarized as numbers and percentages. Numerical data was explored for normality using Kolmogorov-Smirnov test and Shapiro-Wilk test. Exploration of data revealed that the collected values were not normally distributed. Comparisons between both groups was done by Mann-Whitney test. Change between baseline and end of study was tested using the Wilcoxon Rank Signed. All p-values were two-sided. P-values < 0.05 were considered significant.

Results

From February 2015 till August 2016, out of a total of 75 depression patients screened, only 42 fulfilled the inclusion criteria & were included in the study.

Figure 1, shows study flow chart.



Baseline laboratory evaluation and patients' demographics were comparable between 2 groups as showed by table 1.

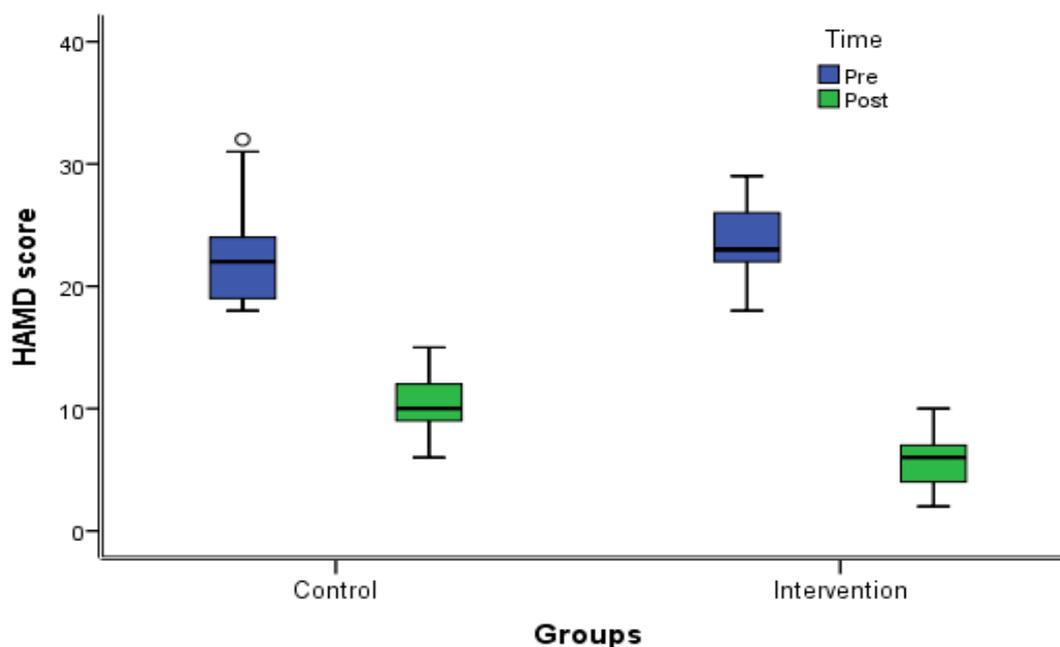
Table 1: Comparison between control and intervention groups in demographics, laboratory and clinical parameters

Table 1	Group		P-values		
	Control; n (21)	Intervention; n (21)	P1	P2	P3
Baseline Evaluation					
Age (yrs); mean \pm S.D	36.8 \pm 12.2	40.8 \pm 13	0.311		
Sex; male (M); n (%)	7 (33.3 %)	5 (23.8%)	0.495		
Female (F); n (%)	14 (66.7%)	16 (76.2%)			
Over time- Evaluation					
HAMD score: median (range)					
Pre	22 (18-32)	23 (18- 29)	\$ 0.583		
Post	10 (6-15)	6 (2-10)	\$ <0.001		
P4	# 1.000	# < 0.001			
% change	53 (40-70)	78 (55-91)	\$ <0.001		
aPTT/ sec; mean \pmS.D					
pre	32.4 \pm 3.2	31.3 \pm 3.2	\$ 0.59		
post	32.3 \pm 3.1	33.6 \pm 3.7	\$ 0.73		
P4	# 1.000	# 0.001			
% change	0.13 \pm 5.26	-7.32 \pm 5.09	\$ <0.001		
INR					
pre	1.07 \pm 0.06	1.04 \pm 0.06	\$ 0.125		
post	1.09 \pm 0.08	1.09 \pm 0.1	\$ 1.000		
P4	# 1.000	# 0.005			
% change	-2.46 \pm 7.59	-4.86 \pm 5.18	\$ 0.55		
*Hemoglobin gm/dl; mean \pmS.D					
pre	12.4 \pm 1.0	12.3 \pm 1.6			
post	12.2 \pm 1.1	12.3 \pm 1.5	0.919	0.406	0.335
% change	1.5 \pm 4.6	-0.5 \pm 6.3	0.248		
*Platelets countx1000/ul; mean \pmS.D					
pre	260.2 \pm 67.4	283.6 \pm 84.9	0.253	0.415	0.438

post	260.3± 65.9	289.5± 77.6			
% change	-0.3± 3.9	-3.2± 10.3	0.239		
*WBCx1000/ul; mean ±S.D					
pre	5.9± 1.7	6.9± 2.0			
post	6.0± 1.7	6.7± 1.8	0.112	0.208	0.019
% change	-1.7± 4.9	2.8± 8.5	0.043		
*, Repeated measure ANOVA #, Wilcoxon signed rank test \$, Mann Whitney test P1= p-value for the difference between groups P2= p-value for the difference between pre/post P3= p-value for the interaction between groups and time P4= non parametric change between pre and post values					

After 8 weeks, the intervention group showed a significant decline in the overall HAMD score and the percentage change over time versus the control as showed by Figure 2.

Figure 2: Box plot of HAMD score over time between control and intervention groups



Over the study period, there was no significant difference between the 2 groups in WBCs, Hemoglobin or platelets counts. The intervention group showed a significant difference in the percentage change over time of the aPTT versus the control.

There was no significant difference between in the 2 groups in the occurrence of side effects, namely; sexual dysfunction, dizziness, GIT upset or sleep abnormalities.

The side effects reported in the intervention group were non-remakable except for; fishy- after taste was reported in 8 patients (38.1%) , itching was reported in 4 patients (19%) and GIT upset was reported in 4 patients (19%). All of these side effects were mild and self-limited and did not require drug discontinuation.

Discussion

Major depressive disorder (MDD) is the most prevalent Axis I disorder and one of the leading causes of disability in the United States and worldwide. In the global burden of disease (GBD) 2000, depressive disorders were ranked the third leading cause of burden (equivalent to 4.3% of all disability adjusted life years (DALYs)) after lower respiratory infections and diarrheal diseases (**Ferrari et al., 2013**).

The lifetime prevalence of depression in urban and rural Egyptian populations was reported to be 11.4 and 19.7% (**Beshai, Dobson et al. 2016**).

Pharmacotherapy is the mainstay of treatment for depression, yet an adequate response to a single antidepressant medication, measured as an attenuation of 50% or more in the severity of depressive symptoms, only occurs in about 50%-75% of patients. Moreover, remission rates are even less and do not usually exceed 30% with any single agent. Hence, the search for a naturally occurring, inexpensive, safe, and effective agent continues. The use of n-3 omega polyunsaturated fatty acids (PUFAs) for treatment of depression is a potential option (**Gertsik, Poland et al. 2012**).

The results of the current study showed that the addition of omega 3 fatty acids to the standard antidepressant treatment was associated with improvement of both HAM-D score and depression symptoms.

The current study used 2100 mg omega 3 fatty acids, which is comprised of 1350 mg eicosapentanoic acid, 600 mg docosahexanoic acid and 150 mg decosapentanoic acid in addition to the traditional selective serotonin reuptake inhibitors used for depression. The rationale for this high concentration of EPA is the previous evidence reporting that EPA at doses more than twice the dose of DHA can positively affect depression outcome (**Sublette, Ellis et al. 2011**).

Moreover it has been shown that EPA and DHA are structurally similar and might be expected to compete in approximately a 1:1 ratio for binding sites. This explanation implies a functional competition not only between omega-3 and omega-6 PUFAs but also within omega-3 species, with regard to depression. Thus EPA in excess of DHA may be considered mechanistically to be unopposed EPA and so will be considered as the active component of PUFAs which will exhibit a therapeutic outcome with regard to depression treatment (**Sublette, Ellis et al. 2011**).

The Hamilton Rating Scale for Depression (HAM-D) used in this study, is a clinician rating scale, which is used to assess the severity of major depression and to assess the response to treatment. It includes 21 items that the clinician has to ask the patient about. To assess disease severity, a score from; 17-19 is moderate depression,

20- 22 is severe depression, > 22 is very severe depression (**Zimmerman, Martinez et al. 2013**).

In the current study, baseline HAM-D score was comparable in both groups. The omega 3 fatty acids group showed a significant improvement in HAM-D score levels as compared to baseline values and to the control.

Similarly several studies have supported this finding. M H Rapaport et al, evaluated whether inflammatory biomarkers act as moderators of clinical response to omega-3 (n-3) fatty acids in subjects with major depressive disorder (MDD). One hundred fifty-five subjects with (DSM-IV) MDD, with a baseline (HAM-D-17) score of 15 and baseline biomarker data (interleukin (IL)-1ra, IL-6, high-sensitivity C-reactive protein (hs-CRP), leptin and adiponectin) were randomized for about 8 weeks to double-blind treatment with eicosapentaenoic acid (EPA) 1060 mg, docosahexaenoic acid (DHA) 900 mg or placebo. Outcomes were determined using mixed model repeated measures analysis for 'high' and 'low' inflammation groups based on individual and combined biomarkers. Results showed significant changes in HAM-D-17 from baseline to treatment week 8 between intervention and placebo group (**Rapaport et al., 2016**).

Gertsik, L et al evaluated 42 subjects with MDD in a nine week randomized, masked, placebo-controlled study of combination therapy (2 grams containing a blend of 900mg EPA, 200mg DHA, and 100mg other omega-3 fatty acids twice daily + citalopram) versus monotherapy (2 grams olive oil per day plus citalopram) treatment of MDD. The combination therapy demonstrated significantly greater improvement in HAMD scores beginning at week 4 and was more effective than monotherapy in decreasing signs and symptoms of MDD during the 8 weeks of active treatment (**Gertsik et al., 2012b**).

Su et al, conducted an 8-week, double-blind, placebo-controlled trial, comparing omega-3 PUFAs (6.6 g/day) with placebo, on the top of the usual treatment, in 28 patients with major depressive disorder. Patients in the omega-3 PUFA group had a significantly lower score on the HAMD score than those in the placebo group (**Su et al., 2003**).

In another study by Su et al on Perinatal depression, an 8-week, double-blind, placebo-controlled trial comparing omega-3 PUFAs (3.4 g/d) with placebo in pregnant women with (DSM-IV criteria) was conducted. No psychotropic agent was given 1 month prior to or during the study period. The results showed that subjects in the omega-3 group had significantly lower HAM-D scores at weeks 6 and 8, a significantly higher response rate (62% vs. 27%, $p = .03$), and a higher remission rate. At the study end point, subjects in the omega-3 group also had significantly lower depressive symptoms ratings on the used scores and no adverse effects on the subjects and newborns were reported from Omega 3 administration (**Su et al., 2008**).

Frangou and colleagues randomized 75 depressed subjects in a double-blind trial to receive 1 g/d ethyl-EPA, 2g/d ethyl-EPA, or placebo for 12 weeks. EPA outperformed placebo significantly at both ethyl-EPA doses, based on HAM-D scores; the higher dose of ethyl-EPA seemed to confer no added benefit in comparison with 1 g/d (**Frangou et al., 2006**).

Peet and Horrobin conducted a randomized, placebo-controlled, dose-finding study of ethyl-eicosapentaenoate (ethyl-EPA) as adjunctive therapy for 70 adults with unipolar major depressive disorder (MDD) who were not responsive to standard antidepressants. A dose of 1 g/d ethyl-EPA for 12 weeks yielded significantly higher response rates (53%) than placebo (29%), with notable improvement of depressed mood, anxiety, sleep disturbance, libido, and suicidality. The 2 g/d group showed no significant difference between drug and placebo, and the 4 g/d group showed a non-significant trend toward improvement. These results suggested a therapeutic window for n-3FA required for maximum benefit, and it is possible that an “overcorrection” of the n-6FA:n-3FA ratio with higher n-3FA doses may limit the antidepressant effect of ethyl-EPA (Peet and Horrobin, 2002).

In contrast, Careny et al, evaluated 122 patients with major depression and CHD who were randomized in double-blind fashion to receive 50 mg/d of sertraline and 2 g/d of omega-3 acid ethyl esters (930 mg of EPA and 750 mg of DHA) or to corn oil placebo capsules for 10 weeks. The results of this study showed omega-3 fatty acids did not result in superior depression symptoms reduction (by BDI-II and HAM-D) at 10 weeks, compared with sertraline and placebo. The discrepancy in these results with others could be attributed to the presence of CHD with depression and the smaller ratio between EPA/ EPA which was not twice the DHA (Carney et al., 2009).

Moreover in a study by Silvers et al, 77 participants were randomly assigned to receive 8 g of fish or olive oil per day in addition to their existing therapy. Fish oil was no more effective than the control as an add-on therapy for depression in this setting (Silvers et al., 2005). These results could be attributed to the higher omega3 dose of 8g/day, as doses \geq 4g were proven to be non-effective and attained a non-linear dose effect. “Overcorrection” of the n-6FA:n-3FA ratio with higher n-3FA doses may limit the antidepressant effect of omega 3 fatty acids (Silvers et al., 2005).

The omega-3 fatty acids have been shown to be very safe and well tolerated. The most reported side effects, such as gastrointestinal upset and fishy aftertaste, tend to occur with higher doses (greater than 5 g/d) and with less pure preparations. At the more typical doses of 1 g/d with highly purified omega-3 preparations, these adverse effects are less common. There has been some concern about the possibility of bleeding with doses greater than 3 g/d, although this risk seems to be minimal, except in patients who are taking other agents that also affect platelet function (Mischoulon and Freeman, 2013).

The current study did not report any significant side effects with Omega -3 that required intervention or therapy discontinuation.

Similarly, Kiecolt-Glaser and colleagues reported non-serious adverse events with omega 3 fatty acids administration including, sore throat, nasal symptoms, stomach pain, tachycardia, and Diarrhea with non significant differences between intervention and control group (Kiecolt-Glaser et al., 2011).

In a review by Kris-Etherton et al, it was reported that the FDA has ruled that intakes of up to 3 g/d of marine omega-3 fatty acids are GRAS (Generally Recognized As Safe) for inclusion in the diet. Perhaps the most common side effect was a fishy aftertaste.

In a 6-month trial providing 275 patients with 6.9 g of EPA+DHA in 10 capsules daily, there was no difference between the fish oil and corn oil control groups for any adverse event. GIT upset was reported by 8% of the latter and 7% of the former. Omega 3 preparations appear to be well tolerated with non serious adverse events (**Kris-Etherton et al., 2002**).

Conclusion

Omega 3 PUFAs administration resulted in improvement of major depressive symptoms indicated by a HAMD score reduction. Omega 3 PUFA was well tolerated and patients who experienced side effects did not require any drug-intervention, dose reduction or dose discontinuation. Omega-3 PUFAs at a dose of 2100 (Eicosapentanoic acid 1350 mg, Docosahexanoic acid 600 mg and 150 mg other omega 3 fatty acids) for 8 weeks is a well tolerated supplement that improves depressive symptoms.

REFERENCES:

- BESHAI, S., DOBSON, K. S., ADEL, A. & HANNA, N. 2016.** A cross-cultural study of the cognitive model of depression: cognitive experiences converge between Egypt and Canada. *PloS one*, 11, e0150699.
- CARNEY, R. M., FREEDLAND, K. E., RUBIN, E. H., RICH, M. W., STEINMEYER, B. C. & HARRIS, W. S. 2009.** Omega-3 augmentation of sertraline in treatment of depression in patients with coronary heart disease: a randomized controlled trial. *JAMA*, 302, 1651-7.
- FERRARI, A. J., CHARLSON, F. J., NORMAN, R. E., PATTEN, S. B., FREEDMAN, G., MURRAY, C. J., VOS, T. & WHITEFORD, H. A. 2013.** Burden of depressive disorders by country, sex, age, and year: findings from the global burden of disease study 2010. *PLoS Med*, 10, e1001547.
- FRANGOU, S., LEWIS, M. & MCCRONE, P. 2006.** Efficacy of ethyl-eicosapentaenoic acid in bipolar depression: randomised double-blind placebo-controlled study. *Br J Psychiatry*, 188, 46-50.
- GERTSIK, L., POLAND, R. E., BRESEE, C. & RAPAPORT, M. H. 2012a.** Omega-3 fatty acid augmentation of citalopram treatment for patients with major depressive disorder. *Journal of clinical psychopharmacology*, 32, 61.
- GERTSIK, L., POLAND, R. E., BRESEE, C. & RAPAPORT, M. H. 2012b.** Omega-3 fatty acid augmentation of citalopram treatment for patients with major depressive disorder. *J Clin Psychopharmacol*, 32, 61-4.
- GROSSO, G., GALVANO, F., MARVENTANO, S., MALAGUARNERA, M., BUCOLO, C., DRAGO, F. & CARACI, F. 2014.** Omega-3 fatty acids and depression: scientific evidence and biological mechanisms. *Oxidative medicine and cellular longevity*, 2014.
- HENNEBELLE, M., BALASSE, L., LATOUR, A., CHAMPEIL-POTOKAR, G., DENIS, S., LAVIALLE, M., GISQUET-VERRIER, P., DENIS, I. & VANCASSEL, S. 2012.** Influence of omega-3 fatty acid status on the way rats adapt to chronic restraint stress. *PLoS One*, 7, e42142.
- KESSLER, R. C. & BROMET, E. J. 2013.** The epidemiology of depression across cultures. *Annu Rev Public Health*, 34, 119-38.

- KIECOLT-GLASER, J. K., BELURY, M. A., ANDRIDGE, R., MALARKEY, W. B. & GLASER, R. 2011.** Omega-3 supplementation lowers inflammation and anxiety in medical students: a randomized controlled trial. *Brain Behav Immun*, 25, 1725-34.
- KRIS-ETHERTON, P. M., HARRIS, W. S., APPEL, L. J. & AMERICAN HEART ASSOCIATION. NUTRITION, C. 2002.** Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation*, 106, 2747-57.
- LESPERANCE, F., FRASURE-SMITH, N., ST-ANDRE, E., TURECKI, G., LESPERANCE, P. & WISNIEWSKI, S. R. 2011.** The efficacy of omega-3 supplementation for major depression: a randomized controlled trial. *J Clin Psychiatry*, 72, 1054-62.
- MISCHOULON, D. & FREEMAN, M. P. 2013.** Omega-3 fatty acids in psychiatry. *Psychiatr Clin North Am*, 36, 15-23.
- PEET, M. & HORROBIN, D. F. 2002.** A dose-ranging study of the effects of ethyl-eicosapentaenoate in patients with ongoing depression despite apparently adequate treatment with standard drugs. *Arch Gen Psychiatry*, 59, 913-9.
- QURESHI, N. A. & AL-BEDAH, A. M. 2013.** Mood disorders and complementary and alternative medicine: a literature review. *Neuropsychiatr Dis Treat*, 9, 58.
- RAPAPORT, M. H., NIERENBERG, A. A., SCHETTLER, P. J., KINKEAD, B., CARDOOS, A., WALKER, R. & MISCHOULON, D. 2016.** Inflammation as a predictive biomarker for response to omega-3 fatty acids in major depressive disorder: a proof-of-concept study. *Molecular psychiatry*, 21, 71-79.
- SILVERS, K. M., WOOLLEY, C. C., HAMILTON, F. C., WATTS, P. M. & WATSON, R. A. 2005.** Randomised double-blind placebo-controlled trial of fish oil in the treatment of depression. *Prostaglandins Leukot Essent Fatty Acids*, 72, 211-8.
- SONG, C., SHIEH, C. H., WU, Y. S., KALUEFF, A., GAIKWAD, S. & SU, K. P. 2016.** The role of omega-3 polyunsaturated fatty acids eicosapentaenoic and docosahexaenoic acids in the treatment of major depression and Alzheimer's disease: Acting separately or synergistically? *Prog Lipid Res*, 62, 41-54.
- SU, K. P., HUANG, S. Y., CHIU, C. C. & SHEN, W. W. 2003.** Omega-3 fatty acids in major depressive disorder. A preliminary double-blind, placebo-controlled trial. *Eur Neuropsychopharmacol*, 13, 267-71.
- SU, K. P., HUANG, S. Y., CHIU, T. H., HUANG, K. C., HUANG, C. L., CHANG, H. C. & PARIANTE, C. M. 2008.** Omega-3 fatty acids for major depressive disorder during pregnancy: results from a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry*, 69, 644-51.
- SUBLETTE, M. E., ELLIS, S. P., GEANT, A. L. & MANN, J. J. 2011.** Meta-analysis: effects of eicosapentaenoic acid in clinical trials in depression. *The Journal of clinical psychiatry*, 72, 1577.
- ZIMMERMAN, M., MARTINEZ, J. H., YOUNG, D., CHELMINSKI, I. & DALRYMPLE, K. 2013.** Severity classification on the Hamilton Depression Rating Scale. *J Affect Disord*, 150, 384-8.

تأثير تناول حمض الإيكوزابنتانويك على النتائج الإكلينيكية للمرضى الذين يعانون من الاكتئاب الشديد

للسادة الدكتورة

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الملخص العربى

مرض الاكتئاب الشديد هو اضطراب دماغي شائع يؤثر على حوالي ١٠٪ من سكان العالم ويؤدي إلى إعاقة على النتائج الإكلينيكية للمرضى الذين يعانون من كبيرة. ولذلك تهدف الدراسة الحالية لتقييم تأثير الأوميغا ٣ الاكتئاب الشديد.

فالدراسة الحالية هي دراسة مستقبلية عشوائية أجريت في العيادات الخارجية بمستشفى الزهراء الجامعى على المرضى الذين تم تشخيصهم بالاكتئاب وفقاً لمعايير اشتغال وإقصاء صارمة. تم توزيع اثنين و أربعين مريضاً بشكل عشوائي على إحدى المجموعتين:

مجموعة (١) (٢١ مريض) وهى مجموعة الإختبار وسيتم إعطاءها العلاج الموصوف + أوميغا ٣ ٢١٠٠ مج لمدة ٨ اسابيع

مجموعة (٢) (٢٠ مريض) وهى مجموعة التحكم التى سيتم إعطاءها العلاج الموصوف لمدة ٨ أسابيع

وقد خضع المرضى عند بدء الدراسة للتقييم الديموغرافى وأيضاً لتقييم التاريخ الأسرى وتاريخ الأدوية المستخدمة استخدام HAMD. وقد خضعوا أيضاً لتقييم خطوره أعراض الاكتئاب عن طريق وقد توبعوا بانتظام كل أسبوعين لمدة ٨ أسابيع وذلك لتحديد:

خطورة الإكتئاب ومعدل وخطورة الأعراض الجانبية الناتجة عن استخدام مضادات الإكتئاب وكذلك معدل وخطورة الأعراض الجانبية الناتجة عن استخدام الأوميغا ٣ وكذلك قد توبع الإمتثال مع الأدوية نسبة إلى المرضى.

وقد قيمت نتائج الإكتئاب عند نهاية الدراسة بعد ٨ أسابيع باستخدام ال

HAMD.

النتائج

ولم يكن هناك اختلاف كبير قد كانت المجموعتين قابلين للمقارنة وقد أظهرت مجموعة الإختبار تحسناً كبيراً في ال HAMD. في الآثار الجانبية المبلغ عنها بين المجموعتين.

الإستنتاج:

إعطاء الأوميغا لمدة ٨ أسابيع بجرعة ٢١٠٠ مج (١٣٥٠ مج حمض الإيكوزابنتانويك و ٦٠٠ مج حمض الديكوزا هيكسانويك و ١٥٠ مج احماض اوميغا ٣ أخرى) قدحسن أعراض الاكتئاب وكان جيد التحمل.