Global Advanced Research Journal of Pharmacy and Pharmacology (GARJPP) Vol. 2(2) pp. 021-032, November 2013
Available online http://garj.org/garjpp/index.htm

Full Length Research Paper

Effects of metformin, or metformin with omega 3 combination on serum leptin in Iraqi obese subjects

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Accepted October 28, 2013

Obesity is an excessive development of fat throughout the body in which a body mass index (BMI) is over 30.According to the world health organization (WHO) reports, obesity is a global epidemic throughout the world. Iraq is in the seventh rank of the prevalence of obesity in the world. In this research we aim to study the effects of metformin and omega 3 drugs alone or their combination on BMI, fasting blood glucose, lipid profile, liver enzymes (ALT, AST), Malondiadehyde (MDA), and leptin. In this research we have thirty six obese subjects and divided into three groupsthese subjects were selected from the Al-Kindi Medical College, obesity research and therapeutic unit where they were visiting the unit for treatment.The first group used metformin 1500 mg/day for two months, and the second group used placebo drug once daily for two months. The third group used metformin 1500 mg/day plus omega 3 for the same period. The finding of the research imply that the comparison between the second treated group and the third treated group showed a significant change in this study parameters ($p<0.05$). However, in comparison between the second group with the first treated group showed a significant change in the study parameters ($p<0.05$). Comparison the first treated group with thethird treated group showed no significant change ($p>0.05$) except with triglyceride, MDA parameters ($p<0.05$). In general, it can be concluded that metformin plus omega 3 by far is the best choice for obese subjects in this study.

Keywords: obesity, metformin, omega 3, BMI, leptin

INTRODUCTION

In the simplest terms, obesity results from an imbalance in energy intake and expenditure. However, it has shown that modulating these factors alone does not help in weight loss (WL) (Chugh and Sharma 2012). A number of chemical mediators and neurochemical pathways, including negative feedback regulation, are involved in controlling food intake, satiety, and energy expenditure and, hence, weight, The etiology of obesity is multifactorial. An understanding of the contributions of various causal factors is essential for the proper management of obesity (Mitra and Clarke 2010). Although it is primarily thought of as a condition brought on by lifestyle choices, recent evidence shows there is a link between obesity and viral infections. Numerous animal models have documented an increased body weight and a number of physiologic changes, including increased insulin sensitivity, increased glucose uptake and decreased leptin secretion that contribute to an increase in body fat in viral infection (Farooqi and O'Rahilly 2007). Genetic predisposition can influence the amount and rate at which weight is gained and lost.

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Important parameter that can measure the level of obesity isBody mass index (BMI) which is used to define severityof overweight and obesity across populations.

Leptin, a protein hormoneencoded by the ob gene, is produced and secreted by the white adipose tissue (WAT) (Gautron and Elmquist 2011). This hormone reflects fat deposits andits levels are modulated by feeding behaviors (Gautron and Elmquist 2011). The primary role of leptin is to provide the centralnervous system with a signal of energy (adipose) stores inthe body to enable the brain to make the adjustments necessaryto balance energy intake and expenditure (Spiegelman and Flier 2001). In common obesity, leptin loses the ability to inhibit energy intake and increase energy expenditure; this is termed leptin resistance (Commins et al., 1999).

Other parameter could be related to leptin resistance which is oxidative stress which was measured in this study by the MDA,In an animal study, it was reported that leptin increases formation of reactive oxygen species (ROS) in a process coupled with increased fatty acid oxidation and activation of protein kinase A in endothelial cells. They postulated that fat soluble antioxidant vitamins may furthermore play a role in the preservation of insulin action through the maintenance of endothelial function. Endothelial dysfunction has recently been linked to abnormal glucose homeostasis (Beydoun et al., 2011).

The general goals for weight management are to reduce body weight (BW), maintain a lower weight over long term and toprevent further weight gain first by life style modification then by pharmacological treatment, which we used in this study metformin drug is anti-diabetic, and also can be used for losing weight, It limits the amount of glucose that is produced by the liver as well as increases muscle consumption of glucose (Collier et al., 2006).

Omega3, also known as polyunsaturated fatty acids (PUFAs), omega 3 fatty acids play a crucial role in brain function as well as normal growth and development.it also sometimes can help reducing weight Omega 3 PUFA intake can be related to the appetite suppressive properties as well as an increase in fat oxidation and energy expenditure. Findings related to the decrease in body fat also include a reduction in adipocyte diameter in subcutaneous fat and possessing a synergistic decrease in adipose tissue when coupled with exercise. Thoughthere are only a relatively few number of studies with humans, the data suggests an increase of omega 3 PUFA intake aides in reducing body fat and improving body composition (Kabir et al., 2007).

Aim of this study

The aim of this study is to assess the potential anti-obesity effects of metformin and metformin plus omega 3 on serum leptin Iraqi obese subjects.

MATERIALS AND METHODS

A randomized controlled trial was conducted to compare the effect of metformin on BMI, lipid profile, FBG, ALT, AST, MDA, leptin, compare it with placebo group, and metformin plus omega 3 combination group, each of these parameters were measured pretreatment, after one month, and then after two months which was the end of the treatment between January 2013 and April 2013.These subjects were selected from the Al-Kindi Medical College, obesity research and therapeutic unit where they were visiting the unit for treatment.

In total, 36 obese subjects (the range of age was 18-40 years) who have visited our clinic because of their obesity, most of the obese female were tried to lose BMI because of the PCOS that they might have or already have.

The exclusion criteria were included all other diseases that might mainly effect the obese subjects, such as heart problems, diabetes, etc.

BMI was measured and recorded in all patients before and after one and two months of treatment. The sample of fasting peripheral drug was taken in order to measure FBG, cholesterol, triglyceride, HDL, LDL, MDA, and finally leptin. Then patients were randomly divided into three groups, metformin, metformin plus omega 3 groups each was prescribed for case group (n=12) and placebo for control group (n=12).

The dose of metformin was three tablets mg/ day, while the other group been treated with 1500 mg metformin/ day plus omega 3 twice a day gel capsules. Placebo was prescribed for control group. After one and two months, the sample of blood peripheral was taken again In order to check the mentioned parameters. Then the data was compared between these months and with these amounts before treatment.

The results are expressed as means and standard deviation, and the data were analyzed by using the student's t-test and analysis of variance (ANOVA). The significance level for all tests was taken as P value < than 0.05.

RESULTS

In this study, 36 obese subjects were recruited during 2 months. 12 obese participants were in the metformin group, other 12 with metformin plus omega 3 combination group, and 12 in the placebo group. Their ages range (18-40 years),

Results showed that metformin group have a significant decrease in BMI after one month and after two months of treatment with an 8% decrease in there BMI, it showed a significant difference compared with placebo group($p<0.05$), for FBG, there was also a significant reduction compared with placebo group also after one month compared to baseline and two months compared

Table 1: Effect of treatment with placebo, metformin, metformin plus omega treated groups on BMI.

BMI (kg/m²)			
Groups n=12	**pretreatment**	**After 1 month**	**After 2 months**
Placebo	35.25 ± 1.22	35.00 ± 1.25	34.75 ± 1.23
Metformin	35.08 ± 1.66	33.64 ± 1.84[a]	32.20 ± 1.31[b,c]
Metformin+ omega 3	35.83 ± 1.62	33.92 ± 1.40[a]	32.25 ± 1.15[b,c]
Placebo compared with			
Metformin	NS	S	S
Metformin+ omega 3	NS	S	S
Metformin compared with			
Metformin+ omega 3	NS	NS	NS

Data were expressed as mean± SD; n=number of patients; values with non-identical superscripts (a,b,c) within the same group were considered significantly different (p<0.05), (a=pretreatment vs one month, b=pretreatment vs two months, c=one month vs two months), (S); represents significant difference between groups. (NS); represents non-significant difference between groups.

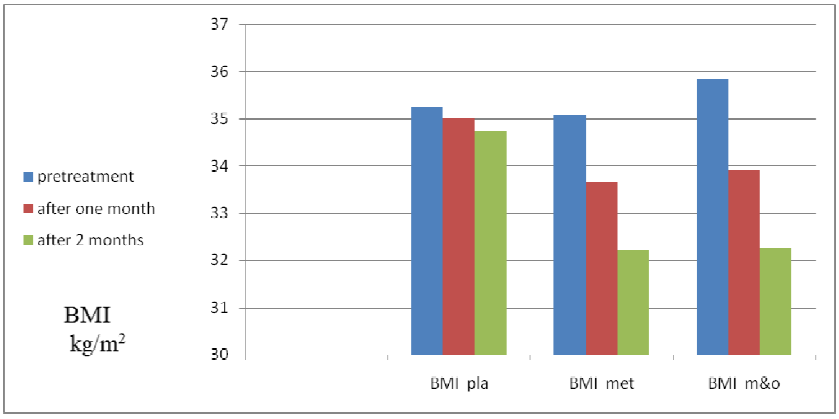

Figure 1: Mean changes in body mass index levels in obese subjectspretreatment, after one, and two months in different treatment groups: BMIP=placebo group,BMIM=metformin group, BMIMO=metformin plus omega 3 group.

with one month of treatment (p<0.05) with great percent of reduction up to 24%, for lipid profile parameters as a start cholesterol, metformin group showed a significant difference compared to placebo and after the first and second month of treatment(p<0.05), TGs have been significant after one and in the end of the treatment and compared with placebo group(p<0.05), but it wasn't significant between the first and second months of treatment, for HDL parameter it showed a non-significant elevation after baseline to the first month of the treatment and first month to two months of the treatment, but from the baseline until the end of treatment it showed a significant elevation, and significant compared with placebo group(p<0.05), on the other hand LDL showed a significant reduction between first month and the second month and from the baseline until the end of the treatment and compared with placebo group (p<0.05), for both of the liver enzymes (ALT,AST) it showed a non-significant reduction(p>0.05), MDA parameter was significant after one month and after two months and between the baseline to the end of the treatment with metformin drug compared with placebo group (p<0.05) with 45% reduction in its level, finally for leptin, it showed only a significant reduction between the first and the second month of using metformin, and between the baseline and the end of the treatment, and compared with placebo group(p<0.05) with 12% percent of reduction of lepton level.

BMI was significant after one month and between the first and second month and between baseline until two

Table 2: Effect of treatment with placebo, metformin, metformin plus omega on FBG levels in serum

FBG(mg/dl)			
Groups n=12	**pretreatment**	**After 1 month**	**After 2 months**
Placebo	96.17 ± 3.69	94.08 ± 3.83	93.33 ± 3.38
Metformin	97.50 ± 3.82	88.42 ± 2.94[a]	73.60 ± 2.96[b,c]
Metformin+ omega 3	96.92 ± 3.52	87.42 ± 2.56[a]	71.83 ± 2.55[b,c]
Placebo compared with			
Metformin	NS	S	S
Metformin+ omega 3	NS	S	S
Metformin compared with			
Metformin+ omega 3	NS	NS	NS

Data were expressed as mean± SD; n=number of patients; values with non-identical superscripts (a,b,c) within the same group were considered significantly different ($p<0.05$), (a=pretreatment vs one month, b=pretreatment vs two months, c=one month vs two months), (S); represents significant difference between groups. (NS); represents non-significant difference between groups.

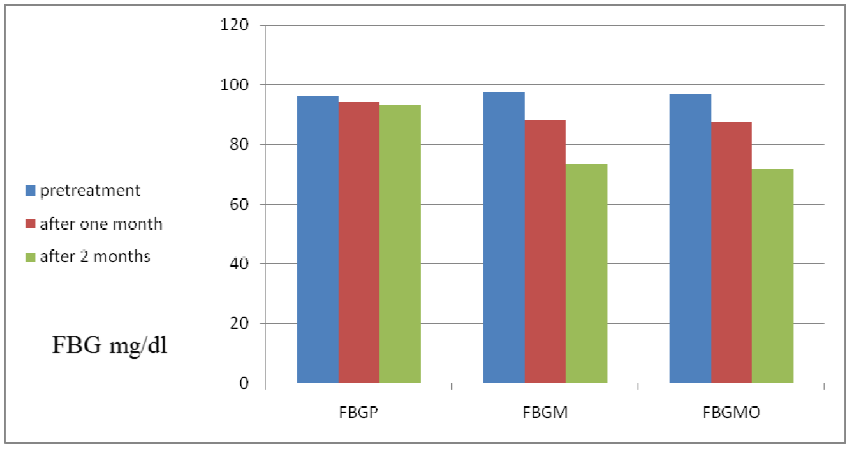

Figure 2: Mean changes in fasting blood glucose levels in obese subjectspretreatment, after one, and two months in different treatment groups: FBGP=placebo group,FBG M=metformin group, FBGMO=metformin plus omega 3 group.

months ($p<0.05$), and showed great percent of reduction up to 9%, but it wasn't significant compared with metformin group ($p>0.05$), for FBG it showed a significant reduction ($p<0.05$) also a non-significant compared to metformin group, cholesterol showed significant reduction in its level for both months of treatment ($p<0.05$), compared with metformin group it showed a n0n-significant difference ($p>0.05$), TGs showed a significant reduction in its level ($p<0.05$)during the period of the treatment, but compared with metformin group it showed a non-significant difference ($p>0.05$), HDL been only significant elevation between the first and second month of treatment ($p<0.05$) and between baseline and the end of the treatment ($p<0.05$), also showed a non-significant difference compared with metformin group ($p>0.05$), LDL level was significantly decreased($p<0.05$) in this group up to 31% ,but also showed a non-significant difference with metformin group ($p<0.05$), ALT enzyme showed significant reduction between first and second months of the treatment, and from the baseline until the end of the second month ($p<0.05$), AST enzyme showed a significant reduction at the end of the treatment ($p<0.05$), both of these enzymes showed a non-significant difference compared with metformin group ($p>0.05$), on the other hand MDA level was significantly reduced after the first and the second months of using this combination of the drugs ($p<0.05$) and significantly different from metformin group ($p<0.05$), and it was percent of reduction

Table 3: Effect of treatment with placebo, metformin, metformin plus omega 3 on serum cholesterol levels

Cholesterol (mg/dl)			
Groups n=12	**pretreatment**	**After 1 month**	**After 2 months**
Placebo	184.18 ± 11.20	181.92 ± 10.24	180.25 ± 10.01
Metformin	184.75 ± 11.89	169.75 ± 13.93[a]	151.42 ± 9.74[b,c]
Metformin+ omega 3	184.92 ± 17.20	165.00 ± 12.98[a]	147.92 ± 11.20[b,c]
Placebo compared with			
Metformin	NS	S	S
Metformin+ omega 3	NS	S	S
Metformin compared with			
Metformin+ omega 3	NS	NS	NS

Data were expressed as mean± SD; n=number of patients; values with non-identical superscripts (a,b,c) within the same group were considered significantly different ($p<0.05$), (a=pretreatment vs one month, b=pretreatment vs two months, c=one month vs two months), (S); represents significant difference between groups. (NS); represents non-significant difference between groups.

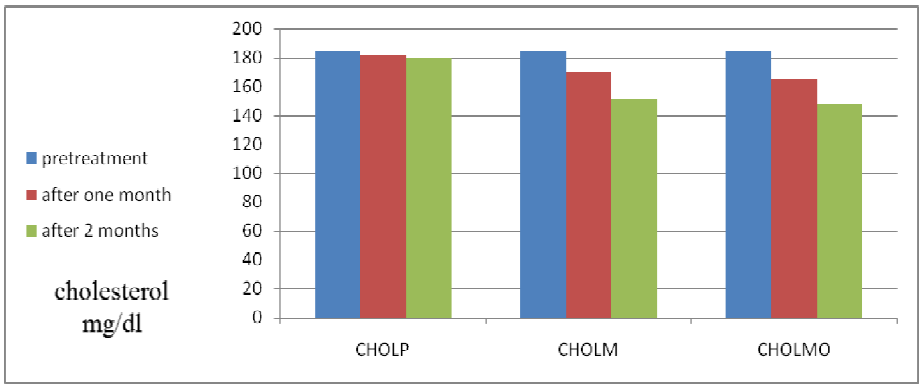

Figure 3: Mean changes in serum cholesterol levels in obese subjectspretreatment, after one, and two months in different treatment groups: CHOLP=placebo group,CHOLM= metformin group, CHOLMO=metformin plus omega 3 group.

Table 4: Effect of treatment with placebo, metformin, metformin plus omega 3 on serum triglyceride levels

TGs (mg/dl)			
Groups n=12	**pretreatment**	**After 1 month**	**After 2 months**
Placebo	176.25 ± 14.34	174.00 ± 10.04	173.08 ± 14.81
Metformin	175.17 ± 13.30	160.25 ± 11.96[a]	150.67 ± 10.94[b,c]
Metformin+ omega 3	176.08 ± 11.94	155.50 ± 10.68[a]	141.25 ± 10.42[b,c]
Placebo compared with			
Metformin	NS	S	S
Metformin+ omega 3	NS	S	S
Metformin compared with			
Omega 3	NS	NS	NS
Metformin+ omega 3	NS	NS	S

Data were expressed as mean± SD; n=number of patients; values with non-identical superscripts (a,b,c) within the same group were considered significantly different ($p<0.05$), (a=pretreatment vs one month, b=pretreatment vs two months, c=one month vs two months), (S); represents significant difference between groups. (NS); represents non-significant difference between groups.

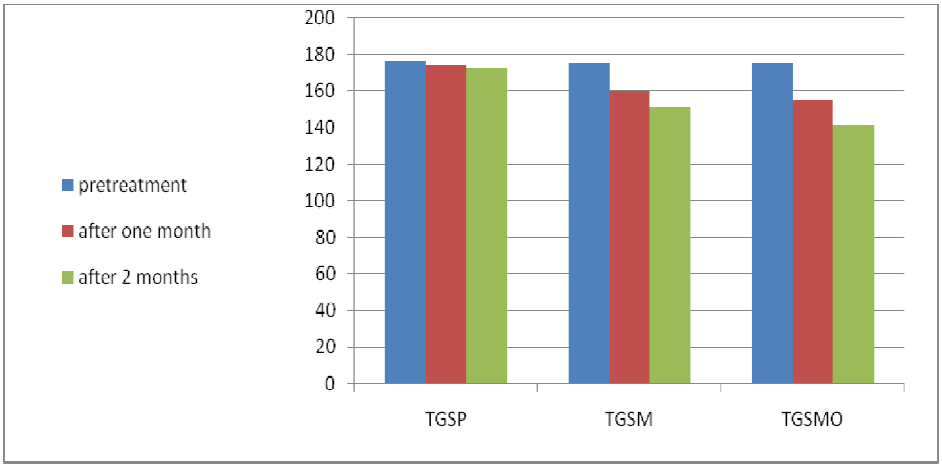

Figure 4: Mean changes in TG serum levels in obese subjectspretreatment, after one, and two months in different treatment groups: TGSP=placebo group, TGSM=metformin group, TGSMO=metformin plus omega 3 group.

Table 5: Effect of treatment with placebo, metformin, metformin plus omega 3 on serum HDL levels

HDL (mg/dl)			
Groups n=12	**pretreatment**	**After 1 month**	**After 2 months**
Placebo	39.08 ± 3.58	40.25 ± 2.43	40.83 ± 2.61
Metformin	41.50 ± 3.53	43.33 ± 3.26	45.42 ± 2.65[b]
Metformin+ omega 3	39.67 ± 2.60	42.81 ± 3.29[a]	44.84 ± 1.02[b,c]
Placebo compared with			
Metformin	NS	S	S
Metformin+ omega 3	NS	S	S
Metformin compared with			
Metformin+ omega 3	NS	NS	NS

Data were expressed as mean± SD; n=number of patients; values with non-identical superscripts (a,b,c) within the same group were considered significantly different ($p<0.05$), (a=pretreatment vs one month, b=pretreatment vs two months, c=one month vs two months), (S); represents significant difference between groups. (NS); represents non-significant difference between groups.

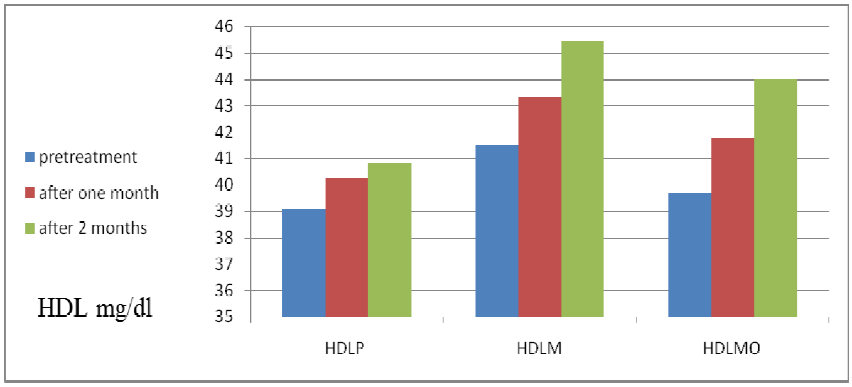

Figure 5: Mean changes in serum HDL-C levels in obese subjectspretreatment, after one, and two months in different treatment groups: HDLP=placebo group, HDLM=metformin group, HDLMO=metformin plus omega 3 group.

Table 6: Effect of treatment with placebo, metformin, metformin plus omega 3 on serum LDL levels

LDL (mg/dl)			
Groups n=12	**pretreatment**	**After 1 month**	**After 2 months**
Placebo	110.00 ± 11.58	106.67 ± 10.13	105.17 ± 10.77
Metformin	108.58 ± 16.63	94.67 ± 17.80	80.25 ± 16.22[b,c]
Metformin+ omega 3	110.33 ± 11.80	92.92 ± 8.78[a]	76.08 ± 9.63[b,c]
Placebo compared with			
Metformin	NS	S	S
Metformin+ omega 3	NS	S	S
Metformin compared with			
Metformin+ omega 3	NS	NS	NS

Data were expressed as mean± SD; n=number of patients; values with non-identical superscripts (a,b,c) within the same group were considered significantly different ($p<0.05$), (a=pretreatment vs one month, b=pretreatment vs two months, c=one month vs two months), (S); represents significant difference between groups. (NS); represents non-significant difference between groups.

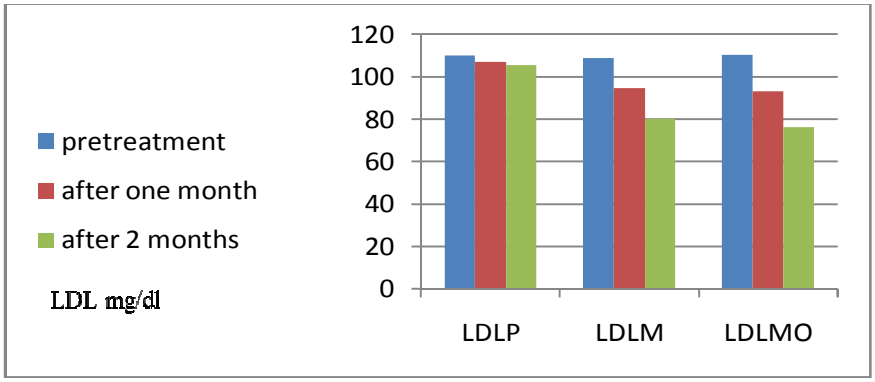

Figure 6: Mean changes in serum LDL-C levels in obese subjectspretreatment, after one, and two months in different treatment groups: LDLP=placebo group, LDLM=metformin group, LDLMO=metformin plus omega 3 group.

Table 7: Effect of treatment with placebo, metformin, metformin plus omega 3 on serum ALT levels

ALT (U/L)			
Groups n=12	**pretreatment**	**After 1 month**	**After 2 months**
Placebo	24.67 ± 2.63	23.75 ± 2.36	23.50 ± 1.90
Metformin	22.67 ± 3.27	21.50 ± 2.99	20.33 ± 2.77
Metformin+ omega 3	24.08 ± 2.96	22.50 ± 2.28	20.66 ± 1.80[b,c]
Placebo compared with			
Metformin	NS	S	S
Metformin+ omega 3	NS	NS	S
Metformin compared with			
Metformin+ omega 3	NS	NS	NS

Data were expressed as mean± SD; n=number of patients; values with non-identical superscripts (a,b,c) within the same group were considered significantly different ($p<0.05$), (a=pretreatment vs one month, b=pretreatment vs two months, c=one month vs two months), (S); represents significant difference between groups. (NS); represents non-significant difference between groups.

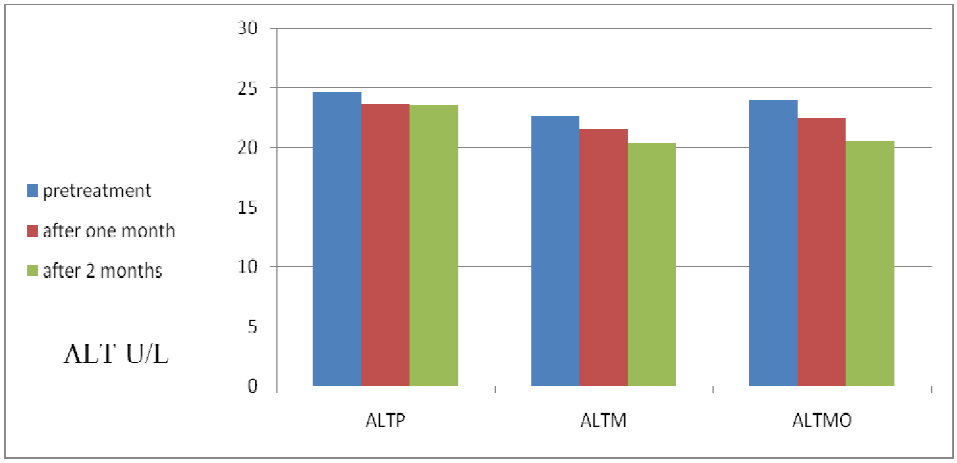

Figure 7: Mean changes in serum ALT levels in obese subjectspretreatment, after one, and two months in different treatment groups: ALTP=placebo group, ALTM=metformin group, ALTMO=metformin plus omega 3 group.

Table 8: Effect of treatment withplacebo, metformin, metformin plus omega 3 on serum AST levels

AST (U/L)			
Groups n=12	**pretreatment**	**After 1 month**	**After 2 months**
Placebo	26.08 ± 2.96	25.25 ± 2.76	24.33 ± 1.70
Metformin	24.42 ± 2.89	23.25 ± 2.50	22.58 ± 1.50
Metformin+ omega 3	24.25 ± 2.63	23.08 ± 2.52	21.42 ± 1.48[b]
Placebo compared with			
Metformin	NS	NS	S
Metformin+ omega 3	NS	S	S
Metformin compared with			
Metformin+ omega 3	NS	NS	NS

Data were expressed as mean± SD; n=number of patients; values with non-identical superscripts (a,b,c) within the same group were considered significantly different ($p<0.05$), (a=pretreatment vs one month, b=pretreatment vs two months, c=one month vs two months), (S); represents significant difference between groups. (NS); represents non-significant difference between groups.

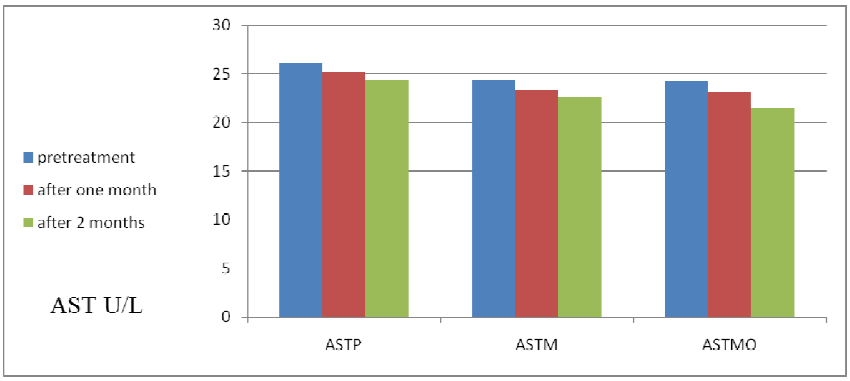

Figure 8: Mean changes in serum AST levels in obese subjectspretreatment, after one, and two months in different treatment groups: ASTP= placebo group, ASTM=metformin group, ASTMO=metformin plus omega 3 group.

Table 9: Effect of treatment with placebo, metformin, metformin plus omega 3 on serum MDA levels

MDA (µmol / L)			
Groups n=12	**pretreatment**	**After 1 month**	**After 2 months**
Placebo	3.35 ± 0.47	3.21 ± 0.50	3.10 ± 0.53
Metformin	3.50 ± 0.64	2.42 ± 0.59[a]	1.91 ± 0.53[b,c]
Metformin+ omega 3	3.64 ± 0.48	2.29 ± 0.48[a]	1.29 ± 0.22[b,c]
Placebo compared with			
Metformin	NS	S	S
Metformin+ omega 3	NS	S	S
Metformin compared with			
Metformin+ omega 3	NS	NS	S

Data were expressed as mean± SD; n=number of patients; values with non-identical superscripts (a,b,c) within the same group were considered significantly different ($p<0.05$), (a=pretreatment vs one month, b=pretreatment vs two months, c=one month vs two months), (S); represents significant difference between groups. (NS); represents non-significant difference between groups.

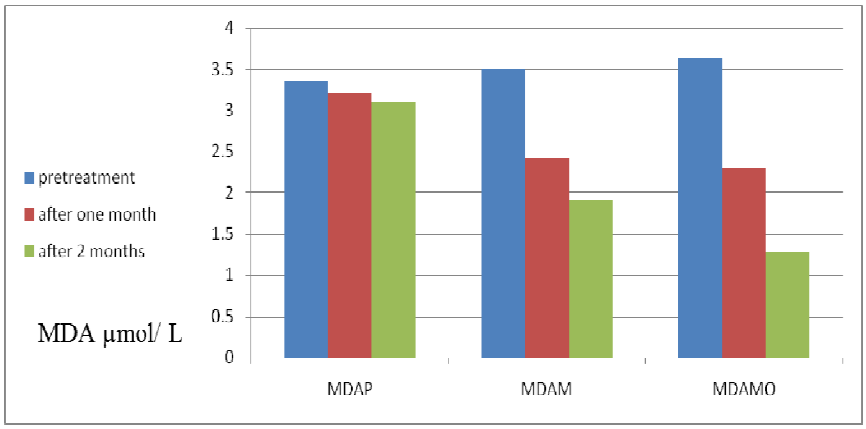

Figure 9: Mean changes in serum MDA levels in obese subjectspretreatment, after one, and two months in different treatment groups: MDAP=placebo group, , MDAM=metformin group, MDAMO=metformin plus omega 3 group.

Table 10: Effect of treatment with placebo, metformin, plus omega 3 on serum leptin levels

leptin (ng /ml)			
Groups n=12	**pretreatment**	**After 1 month**	**After 2 months**
Placebo	15.35 ± 1.37	15.06 ± 1.31	14.85 ± 0.37
Metformin	14.35 ± 1.04	13.85 ± 1.12	12.61 ± 1.08[b,c]
Metformin+ omega 3	14.65 ± 1.14	13.04 ± 1.75[a]	11.79 ± 1.23[b,c]
Placebo compared with			
Metformin	NS	S	S
Metformin+ omega 3	NS	S	S
Metformin compared with			
Metformin+ omega 3	NS	NS	NS

Data were expressed as mean± SD; n=number of patients; values with non-identical superscripts (a,b,c) within the same group were considered significantly different ($p<0.05$), (a=pretreatment vs one month, b=pretreatment vs two months, c=one month vs two months), (S); represents significant difference between groups. (NS); represents non-significant difference between groups.

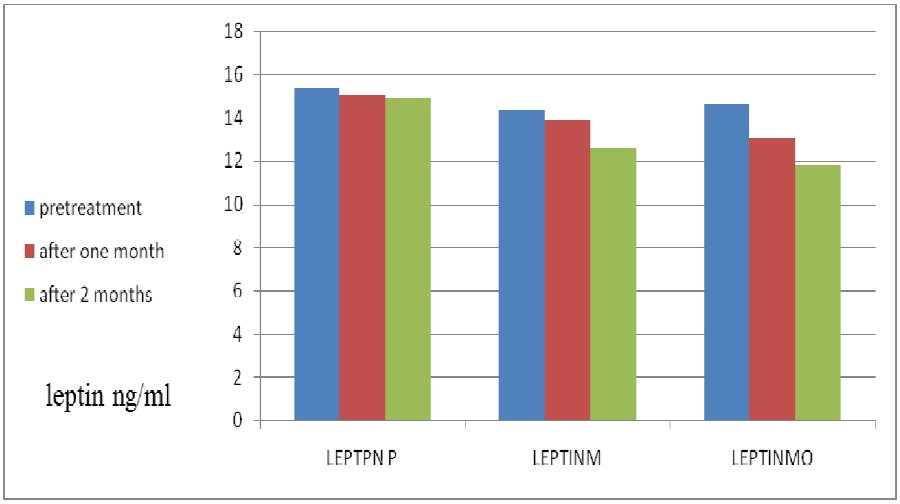

Figure 10: Mean changes in serum leptinlevels in obese subjectspretreatment, after one, and two months in different treatment groups: leptinP=placebo group, leptinM=metformin group, leleptinMO=metformin plus omega 3 group.

up to 64% , leptin was significantly reduced ($p<0.05$), and it was significant compared with metformin group ($p>0.05$), all the parameters that have been measured in this group showed a significant difference compared with placebo group ($p<0.05$).

DISCUSSION

In the present study, metformin drug was given on a daily bases 1500 mg divided three times a day for two months for non-diabetic obese subjects. its effect on body mass index after one month and later after two months revealed significant decrease for both months ($p<0.05$).

Compared with all other groups, metformin caused a significant reduction on BMI ($p<0.05$), except with metformin plus omega 3 treated group which showed a non-significant difference ($p>0.05$).

The mechanisms by which metformin contributes to weight loss may be explained through a reduction in gastrointestinal absorption of carbohydrates, insulin resistance, and reduction of leptin, and ghrelin levels after glucose overload , and by induction of a lipolytic and anoretic effects by acting on glucagon–like peptide 1 (Zheng et al., 2012).

By comparingthe present study with the other reports, which revealed that metformin produced modest differences in BMI *that*, as found for adolescents, butlargely persisted during 1 year of treatment (Desilets et al., 2008). Metforminimproved several other measures of body fatness, although consistent with some (Fantus and Brosseau 2002) but not all studies (Eleftheriadou et al., 2008).

Metformin combined with omega 3, caused a significant reduction in BMI after one and two months ($p<0.05$), compared with placebo treated group except metformin. This group caused a more percent of reduction in BMI than any other group, which make it the best choice for reducing BMI in present study.

Metformin group has a significant decline in FBG after one month, and two months of treatment ($p<0.05$), and as compared with placebo treated group it showed a significant difference ($p<0.05$), except with metformin plus omega 3 treated group metformin group showed a non-significant difference ($p>0.05$), which agrees with other studies (Lamanna et al., 2011).

On the other hand metformin plus omega 3 treated group has a significant effect on FBG after one month and after two months ($p<0.05$) when compared with placebo treated group except with metformin ($p>0.05$).

Serum cholesterol, triglyceride, and LDL parameters have a significant decline in their levels for the obese subjects after one and two months of regular use of metformin ($p<0.05$), and for serum HDL showed a significant elevation ($p<0.05$).

Other studiesshow discrepant results about the influence of metformin on lipid profile (The effects of medications used for the management of diabetes and obesity on postprandial lipid metabolism 2008), Investigations showed an association of metformin with an improvement in the lipid profile especially with triglyceride (Wulffele et al., 2004), these studies, in agreement with ours, reported reduction in lipid profile levels (Ghaeli et al., 2002; Grant PJ 1996),while other studies disagreed (Roessner et al., 2004; Abbink et al., 2002), other studies of obese patients, however, found no independent effects of metformin on serum lipidsand had inconsistent effects on serum triglyceride (Nobili et al., 2008).

Metformin plus omega 3 treated group has a significant effect ($p<0.05$) after one month and two months of

treatment on lipid profile parameters, and it showed a significant difference compared with all treated groups except with metformin treated group ($p<0.05$) for serum cholesterol, HDL, and LDL parameters. And showed a significant difference compared with all treated groups for serum triglyceride ($p<0.05$).

Metformin treated group has a non-significant reduction ($p>0.05$) on serum ALT and AST enzymes, which is compatible with other studies which reported that metformin was not more effective than lifestyle intervention in reducing aminotransferaseslevels (Lima et al., 2009).

While in metformin plus omega 3 treated group, serum ALT enzyme showed a non-significant effect after the first month ($p>0.05$), but at the end of the second month, significant reduction have been showed ($p<0.05$). This group showed significant reduction for AST levels pretreatment until two months ($p<0.05$), in comparison with other treated groups.

Metformin drug has a significant effect after one and two months of treatmenton serum MDA level ($p<0.05$).Metformin has antioxidant properties which are not fully characterized. It reduces reactive oxygen species (ROS) by inhibiting mitochondrial respiration, and decreases advanced glycosylation end product (AGE) indirectly through reduction of hyperglycemia and directly through an insulin-dependent mechanism (Skrha et al., 2007). Data presented were compatible with other studies which revealed a significant decrease in serum MDA levels in patients after therapy with metformin (Gupta et al., 2010), on the contrast, other study observed no change in serum MDA levels at the end of the treatment with metformin (Glueck et al., 2001).

Metformin plus omega 3 treated group showed a significant reduction on serum MDA levels ($p<0.05$). compared with other treated groups, it showed a significant reduction compared with placebo treated group after first month of treatment, and after the second month it was significantly different compared with the other treated groups ($p<0.05$).

Metformin showed a non-significant reduction on serum leptin levels after one month of treatment ($p>0.05$), but significantly reduced it in the second month of treatment ($p<0.05$),since a significant decrease in BMI was observed after treatment with metformin, it is most likely that this factor is responsible for decreased leptin levels after treatment with metformin. Which confirm with other studies reported that serum leptin levels declined significantly (Komori et al., 2004), but disagreed with other studies that reported the effect of metformin on serum leptin was transient, disappearing after 2 to 4 months of treatment (Patel et al., 2007).

Metformin plus Omega 3 combination showed a significant reduction on the serum leptin level ($p<0.05$). Comparison this treated group with others after first and second month of treatment showed a significant reduction with placebo treated group ($p<0.05$).

CONCLUSION

From the previous data, it can be concluded that metformin plus omega 3 showed a most significant effect on all the parameters whether after one month or at the end of the two months of using these drugs as combination to reduce BMI primarily, and leptin level.

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