Drugs used for Weight Reduction among Iraqi Population Sample, a Comparative Study

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Abstract

Obesity is a complex disease characterized by fat accumulation in the body which led to increased risk of other disease such as diabetic, cancer and others. Body mass index (BMI), is the main criteria to define overweight and obesity. In addition to the change in diet, exercise and life style, pharmacological options were used for complicated cases.

This study is a retrospective one where the data collected were from 117 obese patients in obesity research and therapy unit in AL-Kindy medical college in Iraq and were divided into four groups according to the drugs that were taken (metformin group, metformin and orlistat group, metformin and fluoxetine group, metformin, orlistat and fluoxetine group)

It has been found that each group showed a significant difference in BMI after 2 and four months and by comparison among the four group, metformin group was given a significant difference in BMI after 2 months while no significant difference in BMI among groups after 4 months.

In conclusion metformin alone gave the best change in BMI in short period with less side effect while for long time, the administration of these three drugs together may lead to more desirable results

Keywords: *obesity, body mass index, metformin, fluoxetine, orlistat.*

Introduction

Obesity is a complex disease characterized by excessive abnormal accumulation of body fat accumulation resulting from of high intake of high-calorie diet and reduced physical performance [1].

It is a rapidly growing public health issue affecting the developed and the developing countries as well [2]. The prevalence of obesity is generally high [3]. Over the last decades, the prevalence rate of obesity has substantially increased [4]. In 2016, it has been reported around 1.9 billion adults were overweight, and 650 million adults, among them, have obesity [5]. It has been estimated that by 2030, if secular trends continue, 38% of the world's adults will be overweight and 20% will have obesity [6].

Obesity increases morbidity and mortality rates [7]. Obesity has been linked to the increased risk of cancers, stroke, type 2 diabetes mellitus (T2DM), heart failure, and other cardiovascular diseases]4, 8[**.** Obesity generally occurs when energy consumption, dietary intake, exceeds the energy lost through physical and metabolic activity [9]. Many factors may contribute to obesity, including genetic, behavioral, socioeconomic, and environmental factors [10]. Food is the main environmental factor for obesity, while the reduction in physical activity is the second factor to be blamed [11].

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Body mass index (BMI), weight in kg/height in m^2, is the most widely used criteria to define overweight and obesity [12]. A BMI of 25 kg/m^2 or higher is considered overweight, while obesity is defined as a BMI equal to or greater than 30 kg/m^2 [13].

Diet, exercise and changes in lifestyle are the key elements for obesity treatment, but pharmacotherapy and surgery are becoming important [14].

Drugs used to treat obesity include sympathomimetic appetite suppressant drugs, antidiabetic agents, pancreatic lipase inhibitors, serotonin 5-HT2C agonists, anticonvulsant drugs, atypical antidepressants, selective β3 adrenoceptor agonists, and various combination therapies [15].

Among medications, orlistat and metformin are the most studied drugs] 16, 17[. Orlistat, available since 1999 in many countries, is an inhibitor of gastric and pancreatic lipase [12]. It decreases the intestinal absorption of fat, and as a result reducing the calorie intake [18]. It prevents the digestion of about 30% the dietary fat, with considerable decrease in body weight, BMI, total cholesterol, and low density lipoprotein (LDL) cholesterol (9). It is the only approved anti-obesity drug that does not act primarily through appetite suppression, and has a relatively good safety profile on long-term use [19].

Metformin is an oral hypoglycemic agent used for treatment of T2DM [20]. Metformin is frequently used for obesity treatment in adult patients [21]. In general metformin is well-tolerated, and it produces small but significant decrease in body weight] 22, 23[.It has been suggested that metformin induces weight loss through its effect on the regulatory pathways of appetite in the brain, and also through its effects on adipose and gut-mediated signals [20].

Fluoxetine is an oral antidepressant agent and considered to be the prototype of the selective serotonin reuptake inhibitors (SSRIs) [24].

The effects of fluoxetine on reducing caloric intake through altering appetite have been reported in both lean and obese people [25].

The aim of this study is to evaluate different pharmacological options that have been used as an anti-obesity therapy among Iraqi populations and to investigate the therapy with the best outcomes.

Methods

Treated group

This retrospective clinical trial was collected between 2014 and 2017 records from the obesity research and therapy unit in AL-Kindy medical college in Iraq.

117 obese patients (95 women and 22 male) were included in this study and were classified into 4 groups as follows:

Group 1. Metformin (500mg three time a day) (n=35).

Group 2. Metformin and Orlistat (Metformin 500mg three time a day and Orlistat 120mg twice daily) (n=40).

Group 3. Metformin and Fluoxetine (Metformin 500mg three time a day and Fluoxetine 20mg per day) (n=30).

Group 4. Metformin, Orlistat and Fluoxetine (Metformin 500mg three time a day+ Orlistat 120mg twice daily + Fluoxetine 20mg per day) (n=12).

Weight, BMI were assessed at baseline, after 2 months and after 4 months for each group.

The intake of nutrients, total calories, and caffeine was maintained at constant level during the study. Each patient received a personalized food plant from her dietician and do exercises. During the trial, the consumption of dietary supplements was not recommended except some patients who received omega 3 with treatment.

Statistical Analysis

In this study, least significant difference –LSD test (ANOVA analysis) was used to significant compare between BMI means of the different groups after 2 and 4 months while *t* test was used to significant compare between BMI means of the same group after 2 and 4 months.

Data were expressed as mean ± SEM, where P value < 0.05 was considered to be significant and P value < 0.01 was considered to be highly significant.

RESULT

Effect of metformin on body mass index after 2 months and 4 months.

Metformin was tested for its ability to affect BMI after 2 and 4 months, BMI at baseline is (39.02±8), highly significant difference in BMI result was found after 2 months(36.99±7.46) (p= 7.29 E-10) and highly significant difference in BMI result was found after 4 months (35.62±7.40) (p= 4.09 E-10) as figure 1.

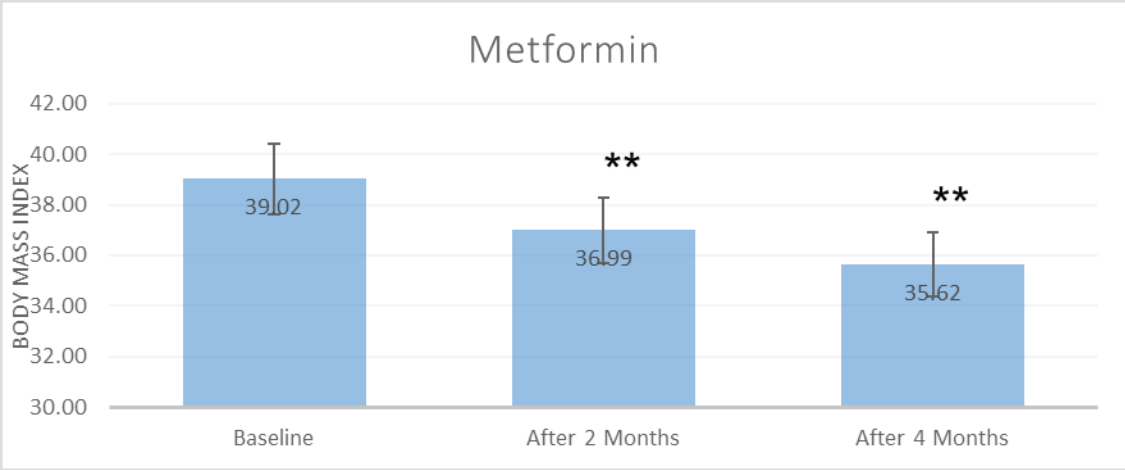

Figure 1: the effect of metformin on BMI value in obese patients after 2 months and after 4 months

Effect of metformin and fluoxetine on body mass index after months and 4 months

Metformin and Fluoxetine were tested for their abilities to affect BMI after 2 and 4 months, BMI at baseline is (41.86±1.99), highly significant difference in BMI result was found after 2 months(40.48±1.90) (p= 2.49 E-22) and highly significant difference in BMI result was found after 4 months (38.50±1.77) (p= 1.58 E-22) as shown in figure 2.

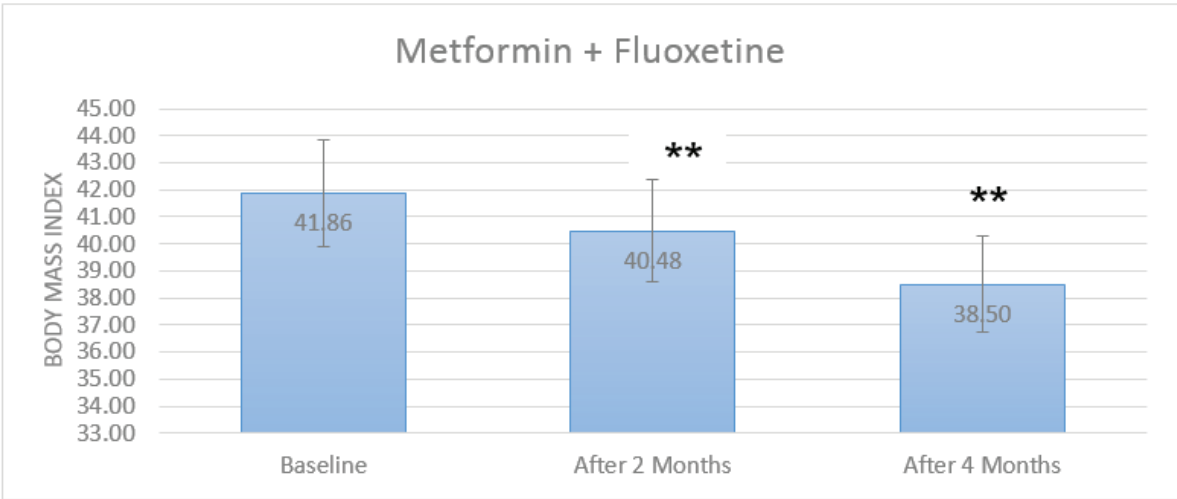

Figure 2: the effect of metformin and fluoxetine on BMI value in obese patients after 2 months and after 4 months

Effect of metformin and orlistat on body mass index after 2 months and 4 months.

Metformin and orlistat were tested for their abilities to affect BMI after 2 and 4 months, BMI at baseline is (39.87±1.84), highly significant difference in BMI result was found after 2 months (38.09±1.78) (p= 4.87 E-11) and

highly significant difference in BMI was found after 4 months (36.75±1.95) (p= 7.99 E-14) as shown in figure 3.

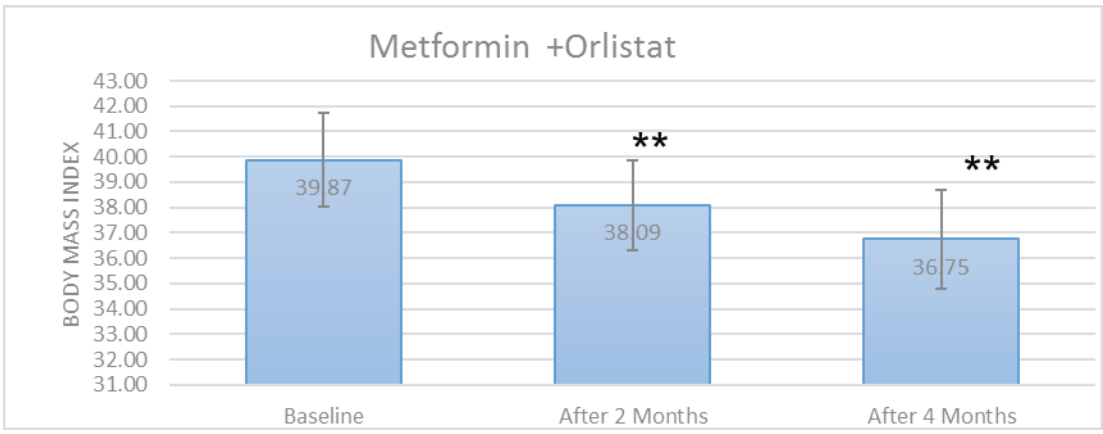

Figure 3: the effect of metformin and orlistat on BMI value in obese patients after 2 months and after 4 months.

Effect of metformin with fluoxetine and orlistat on body mass index after 2 months and 4 months.

Metformin, fluoxetine and orlistat were tested for their abilities to affect BMI after 2 months and after 4 months, BMI at baseline is (36.90±1.35), highly significant difference in BMI result was found after 2 months (35.65 ±1.42) (p= 0.000356), highly significant difference in BMI result was found after 4 months (33.50±1.45) (p= 0.00000569) as shown in figure 4.

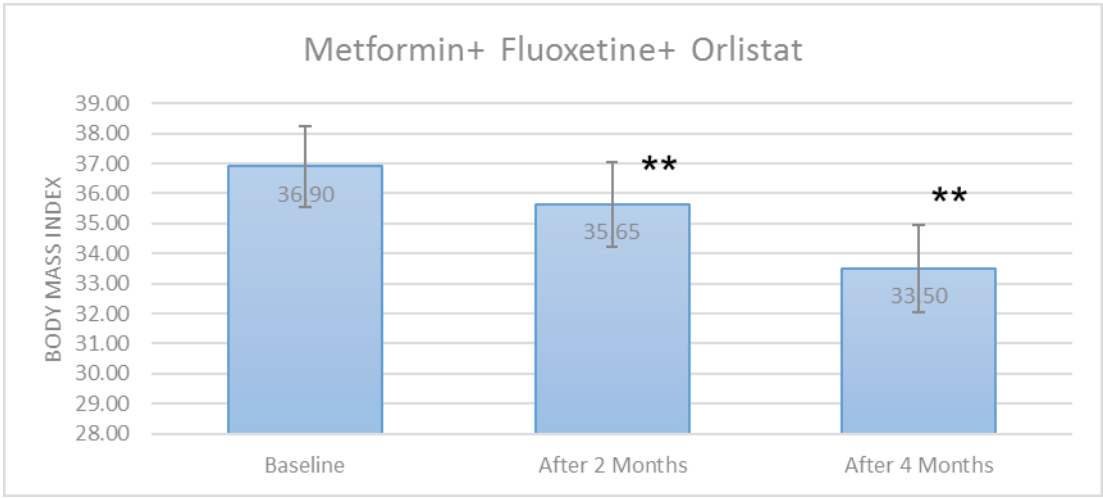

Figure 4: the effect of metformin, fluoxetine and orlistat on BMI value in obese patients after 2 months and after 4 month.

A Comparison among the effect of treated groups on the body mass index after 2 and 4 months

Using ANOVA test, group treated with metformin was showed the most significant percentage change in BMI result after 2 months (5.50±0.67) (p = 0.036) than the other treated groups while after4 months, non-significant difference in BMI among treated groups were found as shown in table 1.

Table 1: The effect of treated groups on the percentage change in body mass index after 2 and 4 months

Group	Metformin	Metformin +Fluoxetine	Metformin + Orlistat	Metformin +Fluoxetine+ Orlistat
% change in BMI (kg/m2) after 2 months (Mean±SED)	5.50 ± 0.67 *	3.28 ± 0.38	4.31 ± 0.60	3.49±0.69
% change in BMI (kg/m2) after 4 months (Mean±SED)	7.94 ± 0.79	6.83 ± 0.93	6.89 ± 0.88	9.34 ± 1.14

*significant change of BMI percentage in metformin group after 2 months.

Discussion

In this study we compared the effect of different drugs on weight of Iraqi obese patient's sample in the obesity research and therapy unit in AL-Kindy medical college.

The pharmacological options that were studied include metformin group alone and three combinations, (metformin and fluoxetine) group, (metformin and orlistat) group, and (metformin, orlistat and fluoxetine) group.

The results of BMI in this study for the metformin (500mg twice daily) group showed highly significant difference after 2 months and after 4 months of using metformin alone.

Seifarth et al [26] found a highly significant difference in BMI after use of metformin and this agree with our study results.

Jarskog et al[27], enrolled 148 overweight patients with chronic schizophrenia or schizoaffective were randomly assigned to receive 16 weeks of metformin(1,000 mg) or placebo, group treated with metformin also presented a significant difference in BMI value as in this study.

Significant reduction in BMI were showed in obese women after treatment with metformin which was agree with the results in this study [28].

Other study used [29] the combination metformin (500mg three times daily) and fluoxetine (20 mg once daily) on 203 patients in 6.6 months, their outcome results also revealed a significant difference in BMI and agree with our study results.

The second combination metformin and orlistat results showed that the BMI highly significant decrease after 2 and 4 months of using metformin and orlistat.

Halpern et al [30] used the combination of (orlistat and metformin) for weight reduction in obese women patients, their results revealed that there are no benefit in association in non-insulin resistant women, so their results disagree with this research results, in other hand, Sari et al expected the beneficial effect of the addition of metformin to orlistat therapy on body weight reduction with highly significant value after treatment within 1 and 4 months in obese women. [31]

Our results revealed that after 2 months of study the metformin gave a best level in reducing BMI in comparison with other combinations groups.

After 4 months of study all the options were approximately equal in effectiveness of changing the BMI.

When we studied the side effect profile of the combinations that we used the outcomes revealed that the using of metformin alone had a minimal or no side effect, as most patients that used the combinations that contain fluoxetine suffered from insomnia after 2 months of therapy and all the patients that used combinations contain orlistat suffered from GIT side effects so the Metformin gave better outcomes with less side effect profile than other drugs.

Conclusion

In this study we used different pharmacological options which led to weight reduction in obese patients. All the drugs that we used gave a good therapeutics outcome in weight reduction but the Metformin gave a better outcome than the other combinations after two months of the study. After 4 months all combinations were almost equal in effectiveness but the combination of three drugs (metformin, orlistat and fluoxetine) was the nearest to the significant value. Hence use the metformin alone in a short time management is the best to get better outcomes, minimal side effects and lower charge on the patients and to use the combination of three drugs for longer period of time.

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Conflict of Interest: Nil

Refrences

1. Narayanaswami V, Dwoskin LP. Obesity: Current and Potential Pharmacotherapeutics and Targets. Pharmacol Ther. 2017; 170: 116–147.
2. Bhurosy T, Jeewon R. Overweight and obesity epidemic in developing countries: a problem with diet, physical activity, or socioeconomic status?. ***The Scientific World Journal.2014***; 964236 (2014).
3. Seidell, JC, Halberstadt J. The global burden of obesity and the challenges of prevention. Annals of Nutrition and Metabolism. 2015; 66(2):7-12.
4. Ghoorah K, Campbell P, Kent A, Maznyczka A, Kunadian, V. Obesity and cardiovascular outcomes: a review. European Heart Journal: Acute Cardiovascular Care. 2016; 5(1): 77-85.
5. Schlesinger S, Neuenschwander M, Schwedhelm C, Hoffmann G, Bechthold A, Boeing H, Schwingshackl L. Food groups and risk of overweight, obesity, and weight gain: a systematic review and dose-response meta-analysis of prospective studies. Advances in Nutrition. 2019; 10(2): 205-218.
6. Hruby A, Hu FB. The epidemiology of obesity: a big picture. Pharmacoeconomics. 2015; 33(7): 673-689.
7. Al-Ghamdi S, Shubair MM, Aldiab A, Al-Zahrani JM, Aldossari KK, Househ M, El-Metwally A. Prevalence of overweight and obesity based on the body mass index; a cross-sectional study in Alkharj, Saudi Arabia. Lipids in health and disease. 2018; 17(1):134.
8. de Heredia FP, Gómez-Martínez S, Marcos A. Obesity, inflammation and the immune system. Proc Nutr Soc. 2012; 71(2):332-338.
9. Ghouse MS, Barwal S, Wattamwar A. A Review on Obesity. Health Science Journal. 2016; 10(4):13.
10. Hruby A, Hu FB. The epidemiology of obesity: a big picture. Pharmacoeconomics. 2015; 33(7): 673-689.
11. Bray GA, Kim KK, Wilding JPH, & World Obesity Federation. Obesity: a chronic relapsing progressive disease process. A position statement of the World Obesity Federation. Obesity Reviews. 2017; 18(7):715-723.
12. Gadde KM, Martin CK, Berthoud HR, Heymsfield SB. Obesity: pathophysiology and management. Journal of the American College of cardiology. 2018; 71(1) ;69-84.
13. Fruh SM. Obesity: Risk factors, complications, and strategies for sustainable long□term weight management. Journal of the American Association of Nurse Practitioners. 2017; 29(S1): S3-S14.
14. Gonzalez-Muniesa P, Martinez-Gonzalez MA, Hu FB, Despres JP, Matsuzawa Y, Loos RJF, et al. Obesity. Nature Reviews Disease Primers. 2017; 3.
15. Fasipe OJ. Recent advances and current trend in the pharmacotherapy of obesity. Archives of Medicine and Health Sciences. 2018; 6(1):99.
16. Kumar S, KellyAS. Review of childhood obesity: from epidemiology, etiology, and comorbidities to clinical assessment and treatment. Mayo Clinic Proc. (2017); 92: 251–265.

17. Kelly AS, Fox CK. Pharmacotherapy in the management of pediatric obesity. Curr. Diab. Rep. (2017); 17:55

18. Bonamichi BDSF, Parente EB, dos Santos RB, Beltzhoover R, Lee J, et al. The challenge of obesity treatment: a review of approved drugs and new therapeutic targets. J Obes Eat Disord. 2018; 4:2.

19. Lee PC, Dixon J.Pharmacotherapy for obesity. Aust Fam Physician. 2017; 46(7):472–77.

20. Malin SK, Kashyap SR .Effects of metformin on weight loss: potential mechanisms. Current Opinion in Endocrinology, Diabetes and Obesity. 2014; 21(5): 323-329.

21. Lentferink YE, van der AaMP, van Mill EGAH, Knibbe CAJ, van der Vorst MMJ. Long-term metformin treatment in adolescents with obesity and insulin resistance, results of an open label extension study. Nutrition & diabetes. 2018; 8(1):47.

22. Burgert TS. et al. Short-term metabolic and cardiovascular effects of metformin in markedly obese adolescents with normal glucose tolerance. Pediatr. Diabetes. 2008; 9: 567–576

23. Marques P, Limbert C, Oliveira L , et al. Metformin effectiveness and safety in the management of overweight/obese nondiabetic children and adolescents: metabolic benefits of the continuous exposure to metformin at 12 and 24 months. International journal of adolescent medicine and health. 2016; 29:5.

24. Afkhami-Ardekani M, Sedghi H. Effect of fluoxetine on weight reduction in obese patients. Indian J. Clin. Biochem. 2005; 20(1): 135–138.

25. Melendez G, Serralde-Zúñiga AE, Garay AGG, et al. Fluoxetine for adult overweight or obese people. Cochrane Database of Systematic Reviews.2015; 5.

26. Seifarth C, Schehler B, Schneider HJ. Effectiveness of metformin on weight loss in non-diabetic individuals with obesity. Exp Clin Endocrinol Diabetes. 2013; 121(1):27-31.

27. Jarskog LF, Hamer RM, Catellier DJ, Stewart DD, LaVange L, Ray N, Golden LH, Lieberman JA, Stroup TS, METS Investigators. Metformin for weight loss and metabolic control in overweight outpatients with schizophrenia and schizoaffective disorder. American Journal of Psychiatry. 2013; 170(9):1032-1040.

28. Ghandi S, Aflatoonian A, Tabibnejad N, Moghaddam MH. The effects of metformin or orlistat on obese women with polycystic ovary syndrome: a prospective randomized open-label study. J Assist Reprod Genet. 2011; 28(7):591-6.

29. Dastjerdi MS, Kazemi F, Najafian A, Mohammady M, Aminorroaya A, Amini M. An open-label pilot study of the combination therapy of metformin and fluoxetine for weight reduction. International journal of obesity. 2007; 31(4):713.

30. Halpern B, Oliveira ES, Faria AM, Halpern A, Melo ME, Cercato C, Mancini MC. Combinations of drugs in the treatment of obesity. Pharmaceuticals. 2010; 3(8):2398-2415.

31. Sari R, Balci MK, Coban E, Yazicioglu G. Comparison of the effect of orlistat vs orlistat plus metformin on weight loss and insulin resistance in obese women. International Journal of Obesity. 2004; 28(8):1059.