Impact of Orlistat on Body Weight and Lipid Profile of Adult Population

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Abstract: Orlistat is currently the best available form of prescribed obesity medication which acts on the gastrointestinal system and works by reducing fat absorption in the gut which is eliminated in bowel movements. **The aim of this study** was to determine the impact of Orlistat on weight reduction, body mass index (BMI) and lipid profile of the Egyptian peoples. **Methodology** We recruit 55 healthy obese persons (BMI more than 30) and the same number of normal weight act as a control; both groups completed a questionnaire for demographic data and risk factors of obesity and the obese group takes Orlistat for 2 months while the control group take placebo tablet containing vitamins and both groups adheres to 1200 Calories diet. Weight and lipid profile (Total cholesterol, Triglycerides, LDL and HDL) were measured before and after Orlistat administration in both groups. By the end of two months only 35 obese and 38 none obese complete the study and the remaining were drouped out from the study. **Results:** The results showed that there is a statistical significant difference in BMI before and after Orlistat ($P < 0.001$) as it decreased from 37.08 ± 4.67 before to 35.40 ± 4.60 after, the same occurred in weight reduction as it decreased from 95.3 ± 12.6 kg before orilstat to 91.1 ± 12.9 after, Waist circumference decreased from 113.0 ± 11.2 to 109.6 ± 11.7 and this difference was statistically significant also. there is a statistical significant difference in all parameters of lipid profile before and after Orlistat traetement as total cholesterol decreased from 199.9 ± 29.5 to 173.7 ± 27 and . Triglycerides from 199.4 ± 54.6 to 174.3 ± 50.7, LDL cholesterols decreased from 120.7 ± 24.8 to 102.4 ± 25.1, while HDL cholesterols increased from 38.3 ± 4.6 to 42.5 ± 5.5 and p value was <0.001. **We conclude** that Orlistat is one of the best prescribed obesity medications available for obese patients. Although research indicates that it can promote weight loss, there remain problems with adherence and much variability in patient outcomes.

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Keywords: obesity, Orlistat, body weight, Lipid profile.

1. Introduction

Orlistat (marketed under the trade name Xenical® by Roche; or as alli [1] by GlaxoSmithKline also known as (tetrahydrolipstatin) is a drug designed to treat obesity[2]. Its primary function is preventing the absorption of fats from the human diet, thereby reducing caloric intake. It is intended for use in conjunction with a physician-supervised reduced-calorie diet. Orlistat is the saturated derivative of lipstatin a potent natural inhibitor of pancreatic lipases isolated from the bacterium *Streptomyces toxytricini* [3]. However, due to simplicity and stability, Orlistat rather than lipstatin was developed into an anti-obesity drug [4].

Orlistat works by inhibiting pancreatic lipase, an enzyme that breaks down triglycerides in the intestine. Without this enzyme, triglycerides from the diet are prevented from being hydrolyzed into absorbable free fatty acids and are excreted undigested. Only trace amounts of Orlistat are absorbed systemically; the primary effect is local lipase inhibition within the GI tract after an oral dose. The primary route of elimination is through the feces. It also blocks the availability of fat-soluble vitamins (vitamins A, D, E, and K), so patients may need to take a vitamin supplement [5]. At the standard prescription dose of 120 mg three times daily before meals, Orlistat prevents approximately 30% of dietary fat from being absorbed and about 25% at the standard over-the-counter dose of 60 mg and Higher doses do not produce more potent effects[6].

Current recommendations suggest that it is used for patients who have a history of failed weight-loss attempts using behavioral methods and who can demonstrate at least 2.5kg weight loss by diet and exercise in the month prior to their first prescription. It is suggested that patients reduce their daily calorie intake by 500 to 1000 calories to promote weight loss, and the Dietary Guidelines for Americans recommend that dietary fat is limited to about 30% of daily calories. As a result of its impact upon fat absorption, Orlistat has unpleasant side effects including liquid stools, an urgency to go to the toilet, and anal leakage which are particularly apparent following a high-fat meal as the drug causes the fat consumed to be removed from the body. Between

1998 and 2005, Orlistat prescriptions rose 36-fold from 17,880 to 646,700 and the total cost increased by over 35-fold [7].

Research has explored the effectiveness of Orlistat in treatment of obesity improved weight loss, weight-loss maintenance, (BMI) and reduces cholesterol blood levels. Research indicates that Orlistat can improve weight loss if used alongside behavioral and lifestyle interventions. There remain, however, two main problems with Orlistat as a treatment for obesity. First, although evidence indicates that it can improve weight-loss outcomes, these improvements are not always substantial and there is much variability with many patients showing no improvements at all. Second, research also indicates high attrition rates with patients not adhering to their medication due to the unpleasant side effects and many stopping taking the drug entirely or using it selectively according to the content of their diet. In summary, although Orlistat is currently the most commonly prescribed medication for the obese, there remains much variability in its effectiveness with only a minority of patients showing weight loss (8).

Research has therefore explored the possible reasons for the effectiveness of Orlistat and whereas some studies have emphasized baseline characteristics, others have highlighted changes in beliefs and behavior brought about by the mechanisms of the drug itself. To date, however, such studies have focused either on drugs other than Orlistat or have used small qualitative designs. The present study, therefore, aimed to explore weight loss following a two months course of Orlistat (9). The amount of weight loss achieved with Orlistat varies. In one-year clinical trials, between 35.5% and 54.8% of subjects achieved a 5% or greater decrease in body mass, although not all of this mass was necessarily fat. Between 16.4% and 24.8% achieved at least a 10% decrease in body mass.[9] After Orlistat was stopped, a significant number of subjects regained weight—up to 35% of the weight they had lost [10]. Despite this relatively small body mass effect, there was a 37% reduction in the incidence of type 2 diabetes, a significant difference. This study (XENDOS) proved that the side effect profile of Orlistat remained the same up to 4 years. Respondents who lost 5% of their initial body weight in the first three months plus 2.5 gm in the first 4 weeks prior to the study, lost 16.4% of their weight at the end of one year [11].

2. Subjects and Methods

Design:

The study was composed of two parts: the first part was case control and the second part was controlled clinical trail one.

Study site:

The study was conducted in a private clinic concerned with obesity management in Mallawi city in El Minia Governorate, where all anthropometric measures and data collection was done.

Data collection techniques and tools

Data was collected by two well-designed structural questionnaires which filled by the investigator himself. Each subject was informed about the aim and the details of the study and give initial verbal consent to participate in the study. Questionnaire (1) asks about risk factors and co-morbidities of obesity. It includes data such as Personal data including age, sex, residence and occupation, Family history of obesity. Socio-economic status of the participants using suitable socioeconomic score. While Questionnaire (2) includes the Anthropometric measurements including weight, height, BMI and waist circumference,

Lipid profile (total cholesterol, triglyceride, LDL and HDL) was determined in blood samples from participants post 12 hours fasting. Analysis of the samples was done by the following techniques:

1- Triglycerides: Caymans Triglycerides assay method [12, 13]

2- Cholesterol: Caymans Cholesterol assay method [14, 15]

3- High density lipoprotein (HDL) and Low density lipoproteins (LDL) measured by using phosphotuncstic acid method [16-17].

Then the same anthropometric measures and blood analysis was done after 2 months of Orlistat.

Sample size

We start the study by 55 obese persons as cases and the same numbers as control and at the end of the 2 months of intervention only 35 obese subjects complete the study and 38 non obese subjects as control, we chose the obese subjects with BMI 30 kg/m2 or more for both sexes. Waist circumference 94 cm or more for men and 80 cm or more for women, cases and control were 18 years old or older and with in 5 years age group regarding study and control were matched as regards sex.

Data analysis

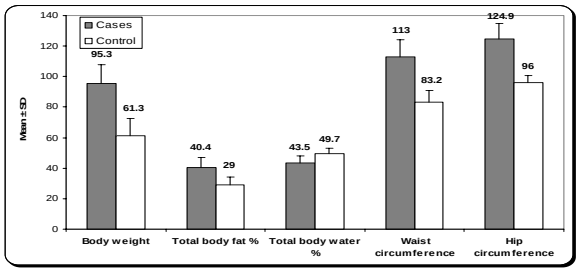
Data was entered and cleaned in Excel sheet, and then analyzed using SPSS software package version 16 that was used for data processing. Descriptive statistics was done in the form of mean and SD. paired t-test was used to compare numerical parametric data before and after Orlistat administration. Values were considered significant when P values were equal or less than 0.05.

3. Results

Figure 1 shows the anthropometric measures of cases and control and demonstrated that the mean body weight of cases was 96.3 kg while that of the control was 61.3 kg, it also shows marked differences of all body parameters between cases and control in the form of total body fat %, total body water, waist and hip circumferences.

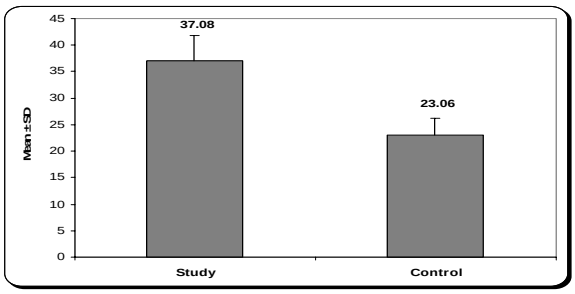
Figure 2 shows the difference of BMI between cases and control and shows that mean BMI of cases was 37.08 while that of control was 23.06 with statistical significant difference of BMI between cases and control.

Figure (1): Differences in anthropometric measures between cases and control



. Independant sample t test was used.

Figure (2): BMI before treatment in cases and control.



Independant sample t test was used P = 0.001*

Table (1): lipid profile of cases and contol in the studied sample

Variable	Cases (n= 55)	Control (n= 55)	P-value
Total cholesterol Mean ± SD	199.89 ± 29.54	176.63 ± 21.42	0.163
Range	150 – 277	146 – 232	
Triglycerides Mean ± SD	199.43 ± 54.55	106.23 ± 42.79	0.001*
Range	105 – 315	45 – 250	
LDL cholesterols Mean ± SD	120.66 ± 24.83	113.34 ± 17.97	0.001*
Range	77 – 180	79 – 160	
HDL cholesterols Mean ± SD	41.83 ± 6.09	42.86 ± 5.45	0.459
Range	32 – 65	33 – 54	

Independant sample t-test was used

Table (1) shows Lipid profile of cases and control and shows that there was a statistical significant difference between the 2 groups in Triglycerides and LDL cholesterol while shows no statistical significant differences in Total cholesterol and HDL cholesterol .

Table (2): Anthropometric measures of obese persons before and after Orlistat

Type of anthropometric measures	Before (n= 55)	After (n= 35)	P-value
Body weight: Mean ± SD	95.3 ± 12.6	91.1 ± 12.9	<0.001*
Range	65.0 – 126.8	60.0 – 120.8	
Waist circumference: Mean ± SD	113.0 ± 11.2	109.6 ± 11.7	<0.001*
Range	86 – 133	82 – 129	
Hip circumference: Mean ± SD	124.9 ± 9.8	120.0 ± 10.1	<0.001*
Range	106 – 144	100 – 139	
Body fat %: Mean ± SD	40.4 ± 6.7	38.9 ± 6.9	0.034*
Range	24.9 – 50.8	21.0 – 47.0	
Body water %			0.827
Mean ± SD	43.5 ± 4.6	43.6 ± 4.3	
Range	36.0 – 53.2	37.0 – 54.0	

Paired t test was used

Table (2) shows the mean ± SD of anthropometric measures before and after Orlistat treatment and demonstrate a statistical significant difference in weight reduction (P = 0.001) as it decreased from 95.3 ± 12.6 kg before Orlistat to 91.1 ± 12.9 after, Waist circumference decreased from 113.0 ± 11.2 to 109.6 ± 11.7 and this difference was statistically significant also, the same finding was observed in hip circumference and in total body fat %, while there was no statistical significant difference in total body water percentage .

Table (3) shows lipid profile of the studied sample before and after Orlistat treatment and shows that there is a statistical significant difference in all parameters of lipid profile before and after Orlistat treatment as total cholesterol decreased from 199.9 ± 29.5 to 173.7 ± 27 and p value was <0.001. Triglycerides decreased from 199.4 ± 54.6 to 174.3 ± 50.7 and p value was <0.001, LDL cholesterols decreased from 120.7 ± 24.8 to 102.4 ± 25.1 and p value was <0.001, while HDL cholesterols increased from 38.3 ± 4.6 to 42.5 ± 5.5 and p value was <0.001.

Table (3): lipid profile of obese persons before and after Orlistat.

Variable	Before (n= 55)	After (n= 35)	P-value
Total cholesterol:			<0.001*
Mean ± SD	199.9 ± 29.5	173.7 ± 27	
Range	155 – 277	120 – 243	
Triglycerides:			<0.001*
Mean ± SD	199.4 ± 54.6	174.3 ± 50.7	
Range	105 – 315	95 – 295	
LDL cholesterols:			<0.001*
Mean ± SD	120.7 ± 24.8	102.4 ± 25.1	
Range	77 – 180	65 – 163	
HDL cholesterols:			<0.001*
Mean ± SD	38.3 ± 4.6	42.5 ± 5.5	
Range	29-49	33-54	

Paired t test was used

Table (4): BMI in obese persons before and after Orilstat.

	Before	After	P-value
Mean ± SD	37.08 ± 4.67	35.40 ± 4.60	0.001*
Range	27.41 – 49.47	25.30 – 46.22	

Paired t test was used

Table (4) shows the BMI of cases before and after Orlistat treatment and shows that there is a statistical significant difference in BMI before and after Orlistat ($P < 0.001$) as it decreased from 37.08 ± 4.67 before to 35.40 ± 4.60 after Orlistat.

4. Discussions

The present study aimed to explore the predictors of weight loss and lipid profile following 2 months of Orlistat therapy. The results showed that by the end of 2 months patients reported both weight loss and reduction in their BMI and lipid profile (except HDL) that falling within the expected range with previous outcome studies (18, 19). Furthermore, just about 10% reported flexibly in response to their dietary choices, habits and behaviors. Also the attrition rate was 20% which is consistent with attrition rates found in previous studies and the use of Orlistat as a lifestyle drug [19, 20].

Research has explored the effectiveness of Orlistat compared to other drug treatments, placebo, or behavior-focused interventions. For example Padwal *et al.* [19] reported that patients taking Orlistat lost 2.7kg more than patients taking placebo, and Avenell *et al.* [20] carried out systematic review of trials involving a combination of diets, drug therapy, exercise, and behavior therapy and concluded that adding Orlistat to a dietary intervention improved weight loss by 3.26 kg up to 24 months. Research also indicated that Orlistat reduces cholesterol and blood pressure levels and improves glycemic control when compared to placebo [19]. Basal cholesterol absorption from the test meal (without Orlistat) was 59±6%.Cholesterol absorption from the test meal given concomitantly with Orlistat was 44±5%.Therefore; Orlistat decreased the absolute amount of cholesterol absorbed from the test meal by 23±5%(from 43 to 32 mg; $p < 0.01$) [20].

In other study a total of 448 patients with elevated cholesterol according to cardiovascular risk factors entered a 2 week single-blind run-in period on a hypocaloric diet. Of 384 patients was subsequently assigned double-blind treatment with Orlistat (3 x 120 mg/day) or placebo for 6 months in conjunction with the hypo caloric diet. The result weight loss in the Orlistat group was 7.4 kg vs. 4.9 kg with placebo. Total and low-density lipoprotein cholesterol decreased by 25-30 mg/dl vs. 10-15 mg/dL with placebo. Reduction of cholesterol with Orlistat was significantly greater than anticipated from weight loss alone. In patients with cardiovascular risk factors entering the study with lower cholesterol values Orlistat was also superior to placebo. On the contrary, reduction of cholesterol concentrations never exceeded 20% [21].

Similarly, Phelan and Wadden [22] concluded from their review that adding Orlistat to lifestyle modification interventions improves both weight loss and weight-loss maintenance Furthermore, in a recent updated meta-analysis, Rucker *et al.* (23) synthesized the results of randomized placebo controlled trials of approved anti-obesity drugs in adults aged 18 and over for one to four years They concluded that with the active drug treatments patients were more likely to reach 5% and 10% weight-loss thresholds and that weight losses for three key drugs were as follows Sibutramine: 4.2kg rimonabant: 4.7kg, and Orlistat: 2.9kg. Research therefore indicates that Orlistat can improve weight loss if used alongside behavioral and lifestyle interventions.

There remain however, two main problems with Orlistat as a treatment for obesity First, although evidence indicates that it can improve weight-loss outcomes, these improvements are not always substantial and there is much variability with many patients showing no improvements at all Second, research also indicates high attrition rates with patients not adhering to their medication due to the unpleasant side effects and many stopping taking the

drug entirely or using it selectively according to the content of their diet. For example, Padwal *et al.* [19] concluded from their review of randomized control trials that the mean attrition rate for Orlistat was 33% and Vray *et al.* [24] suggested that in clinical practice attrition rates are even higher at 64%–77%. In our study the attrition rate for Orlistat was 20% Research has therefore addressed how the effectiveness of Orlistat can be improved However other researchers exploring alternative forms of medical management has explored a range of clinical, psychological, and behavioral variables as predictors of outcomes (e.g., [25–26],research focusing on Orlistat has mainly emphasized laboratory and clinical variables [27].

In general, however such studies conclude that the best predictor of outcome following medical management is initial weight loss, but to date few studies have explored psychological and behavioral predictors of outcome following Orlistat. An alternative approach has addressed the mechanisms of how Orlistat works, by reducing fat absorption in the gut However due to the unpleasant side effects, Finer has labeled it the anti-abuse effect" as it deters the intake of high-fat foods [28].

Further, Ogden and Sidhu [29] carried out a qualitative study with patients who had taken Orlistat to explore their beliefs about why it either did or did not facilitate weight loss. The results showed that inline with previous research some patients stopped taking their medication due to the unpleasant symptoms such as anal leakage or oily stools. Many obese people focus on medical causes of their problem such as hormones and genetics [30, 31] the results from this qualitative study of Orlistat users indicated that Orlistat make them taking a healthier diet. Leventhal *et al.* [32] described the notion of coherence between beliefs about causes and solutions to any particular medical problem. Inline with this, Ogden and Sidhu [29] argued that Orlistat functions by educating patients and creating coherence between behavioral causes and therefore behavioral solutions for obesity. To date, however, this process remains untested in a larger quantitative study.

In Somchai *et al.,* study they take study sample as Participants were females aged 18-45 years with BMI of more than 25 kg/m^2 and were medical examined to receive either Orlistat or Sibutramine. Participants could read and write Thailand (Thia) language and could completely join the project (i.e. visiting a physician every two weeks for 6 weeks).The instrument tool was a 6-page questionnaire. It was divided into 4 parts: part 1 is demographic data i.e. age, occupation, education, salary, marital status, weight, height, waist circumference and hip circumference; part 2 is question about exercise (e.g. type of exercise, duration, frequency per week) and the calories burnt by exercise were calculated from the data; part 3 is question about eating behavior which could classify participants into 4 types: heavy eating, over eating, moderate eating, and on diet, and part 4 is question about satisfaction of drug used, side effect and drug adverse reaction. Then Data were collected for a period of six months from March 2004 to August 2004. Data were 100% collected (n = 160). From Table 1, average ages of participants were 36.20 ±4.10 years old for Orlistat group and 37.11 ± 6.01 years old for Sibutramine group. Most of the participants were married and housewives. The largest subgroup at a particular level of educational attainment had completed high school after 6 weeks of drug treatment, the means of BMI of Orlistat and Sibutramine groups are significantly decreased (p = 0.03 and 0.02 respectively) during the treatment period[33].

Conclusion:

Orlistat is the best prescribed obesity medication available for obese patients which acts on the gastrointestinal system and works by reducing fat absorption in the gut. Although it can promote weight loss, decrease lipid profile and increase HDL, there remain problems with adherence and much variability in patient outcomes.

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