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WEIGHT REDUCTION;

TO EVALUATE IN OBESE PATIENTS WITH ORLISTAT AS COMPARED TO PLACEBO USING BODY MASS INDEX IN AN OPD SETTINGS

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ABSTRACT… Objective: Obesity is a serious disease and a precursor to other morbidities such as CVD and type 2 DM. Lifestyle modifications are recommended to control obesity along with pharmacological and surgical interventions. In this study, we evaluate the beneficial effects of orlistat in BMI reduction of obese patients in an OPD setup of Azad Jammu Kashmir. **Study Design:** It is a quasi-experimental placebo controlled trial. **Setting:** Divisional Headquarters Hospital Mirpur Azad Kashmir. **Period:** October 2013 to March 2014. **Methods:** 75 patients were enrolled having BMI of more than 27 using BMI machine model 2012. 38 Patients were randomly selected to receive orlistat 120 mg B.D for two months. 32 patients were given placebo and the reduction in BMI between the two arms was analyzed using SPSS 20. **Results:** After two months of study, significant reduction of 2.78 kg +/-1.718 kg in weight was observed in the study group. The reduction in average BMI in study group was 1.867 with -5.21 % reduction in BMI vs control group which had an average BMI reduction of 0.46 with -1.411% reduction in BMI. The p value is 0.001. 37.71% of patients taking orlistat reported side effects such as flatulence, fatty stools and myalgia which were 8%, 18.91% and 10.8% respectively. **Conclusions:** Orlistat along with life style modification is effective in BMI reduction of patients significantly as compared to placebo and may be helpful in reducing the morbidity and mortality in the long term. However, caution should be administered with orlistat because of high incidence of associated side effects.

Key words: BMI, CVD, ORLISTAT, Weight Reduction.

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INTRODUCTION

The American Medical Association regarded obesity as a disease in 2013. Obesity denotes the presence of excess body fat and is also a precursor to a number of other diseases as well such as cardiovascular disease (CVD), Type 2 diabetes mellitus.[1] Further, increasing bias, prejudice and discrimination has also been reported and associated with overweight and obese in the society.[2] Obesity has a multiplicative effect In the presence of other risk factors such as smoking, hypertension and elevated blood cholesterol.[3] Obesity is associated with sedentary life style, inadequate physical activity and high calorie intake, however a number of other complex mechanisms are also involved. Genetic predisposition is also an important factor in obesity. About 200 different genes or loci have been linked to obesity in human beings.[4] South Asian population has higher tendency for abdominal fat deposition as compared to Europeans.[5] While men having higher tendency to acquire abdominal fat as compared to women experiencing post menopausal symptoms. Obesity is emerging in Pakistan as a public health problem and is a leading contributing factor in prevalence other diseases as well such as CVD, type 2 DM, stroke, HTN and arthritis. In 1997 the World Health Organization (WHO) recommended the use of Body Mass Index, a tool for measurement of obesity in adults owing to its: validity in relation to morbidity and mortality outcomes, simplicity, widespread acceptability, and robust nature.[6] The use of BMI has also been reinforced by ACC-AHA November 2013 guidelines. The BMI classifies overweight as BMI >25 and obesity as BMI >30. The popularity of BMI is due to its convenience, safety, minimal

cost, and its wide spread use.[7] BMI provides us with an accurate estimate of the percent body fat.[8] BMI is calculated by dividing the body mass in Kg by height in meters or dividing the body mass in pounds by height in inches square and multiplying by 703.

Once the obesity has been established, the patient should be appropriately treated. Treatment of the overweight and obese patient is a two-step process: assessment and management. Assessment requires determination of the degree of obesity and absolute risk status. Management includes both, weight control or reducing excess body weight and maintaining that weight loss as well as instituting other measures to control associated risk factors.[9] To treat obesity as a disease, life style modifications are recommended along with pharmacological and surgical interventions. Due to low socio economic status of patients in Pakistan, patients cannot afford Bariatric surgery both due to lack of availability and increased cost. Thus, pharmacological treatment remains a viable option for such patients. Since drugs like Phentermine and Sibutramine have been withdrawn from the market due to serious adverse cardiovascular effects we are left with the choice of Orlistat, the only anti-obesity drug available in Pakistan. Orlistat is a lipase inhibitor that reversibly inhibits human gastrointestinal lipases and is FDA-approved for the long-term treatment of obesity. Orlistat effectively blocks 30% of fat absorption and has low bio availability thus does not have any significant systemic side effects, although the gastrointestinal side effects may be substantial. Thus, we intend to evaluate the weight reduction in obese patients with orlistat.

METHODOLOGY

This is a quasi-experimental, prospective, open label, non randomized placebo controlled, intent to treat study. The study was conducted in Divisional Headquarters Hospital Mirpur Azad Kashmir from October 2013 to March 2014. The patients having BMI of more than 27 and with atleast one risk factor such as hypertension or smoking were randomly selected and assigned to use orlistat or placebo after an informed consent. A total of 75 patients were recruited in the study. 52 were female and 23 were male. 37 patients were given orlistat 120 mg B.D for two months and 38 patients were given placebo. 6 patients in placebo group were lost in followup although no adverse events reported. BMI of the patients was taken using BMI machine model 2012. The adverse events were recorded in an Adverse Drug Reaction Reporting form available with the chief investigator. The patients had to visit the investigator for follow up visits on 20th, 40th and 60th day during the course of study. Patients were advised to use orlistat during meal. Light exercise was also advised to be done on daily basis to encourage weight loss and healthy lifestyle. The data was analyzed using SPSS version 20. The patients fulfilled the following inclusion and exclusion criteria. Use of multivitamin was also advised at night time so that vitamin deficiency could be avoided in patients as orlistat may lead to inadequate vitamin absorption. Figure-1.

Ethics

Approval was taken from the ethical committee of the hospital and with the Helsinki Declaration of 1975, as revised in 1983.

Statistics

Paired sample t test was used after generating null hypothesis that there was no difference between 2 groups. Assumptions for parametric tests met Sample Size Estimation was calculated based upon a previous study done at Karachi in which almost similar number of patients was used.

Average BMI of patients of control group was 32.610 with minimum BMI of 28 and maximum BMI of 40, while the average BMI of study group was 35.837 with minimum BMI of 31 and maximum BMI of 44. The average age of patients in control group was 51.42 years with maximum age of 84 years and minimum age of 35 years, whereas, the average age of study group was 50 years, with minimum age of 28 and maximum age of 70 years. All the patients satisfied the inclusion and exclusion criteria and had at least one major risk factor. The statistical analysis was done using SPSS version 20. 37.71% of patients reported of experiencing side effects with the orlistat however

no patient had to withdraw from therapy.

RESULT

After two months of study, significant reduction of 2.78 kg +/-1.718 kg in weight was observed in the study group of patients that were taking orlistat. The average reduction in BMI was 1.867 as compared to control group which had an average BMI reduction of 0.46 with the p value of 0.001. Therefore null hypothesis was rejected and alternative hypothesis accepted 37.71% of patients reported of experiencing side effects with the use of orlistat. 8% of the patients reported flatulence, 18.91% of patients reported frequent episodes of fatty stools whereas 10.8% of patients were observed with clinically significant myalgia while using orlistat in the study group.

Inclusion Criteria	Exclusion Criteria
Patients of either sex of age between above 18 years	Malabsorption syndrome OR obesity of endocrine origin.
Patients with BMI >27 with at least one risk factor.	Pregnancy and Lactation.
Patients who did not opt for bariatric surgery	Patients using other medications that can alter body weight.
Patients who gave informed consent	Bariatric surgery done previously
	Severe liver disease
	Severe heart or respiratory disease

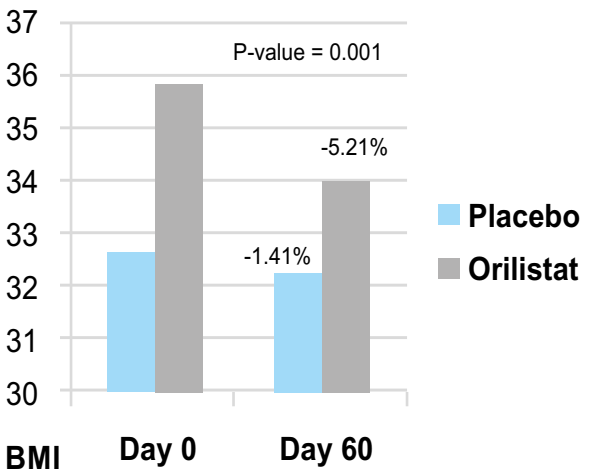

Figure-1.

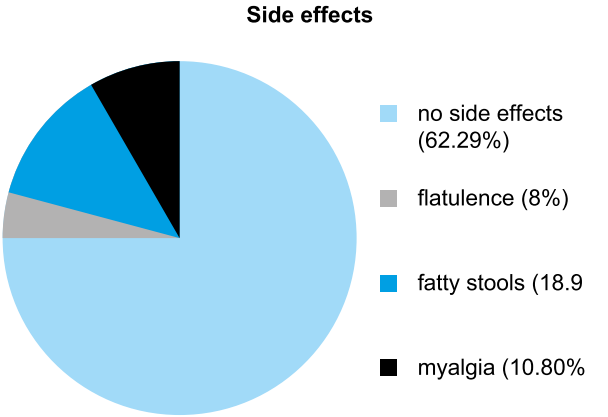

Figure-2.

DISCUSSION

The obesity is a disease of multi factorial dependency and a precursor to number of serious co morbidities with high risk of mortality.

By reducing the body weight, prevalence of associated co morbidities and ultimately mortality can be significantly lowered in the long term. Surgical or bariatric interventions seem to be an effective option for reducing the body weight, however considering low socio-economic status, lack of facilities for such procedures, and fear of surgery among general Pakistani population makes it less viable option. This leaves the health care provider with the pharmacological interventions. The withdrawal of weight reducing drugs like sibutramine and rimonabant has lead us to a huge gap in pharmacotherapy for obesity. Lorcaserin and Phentermine-topiramate combination are two drugs approved by US FDA in 2012. Lorcaserin, a 5HT2C agonist has moderate efficacy with an acceptable safety profile. Clinical trials with Phentermine-topiramate have shown a reasonable efficacy but at the cost of risks such as teratogenicity and psychiatric disturbances. This leaves the physicians with Orlistat, the lipase inhibitor, that significantly lowers the body weight by reducing fat absorption, and if coupled with behavioral changes and life style modifications, can have certain beneficial effects on the well being of obese patients having one or more risk factors as well as overall health status of the society. By reducing the weight and BMI of

obese patients with the use of orlistat, the risk of associated morbidity can be significantly lowered.[11] Especially if the patient has risk factors such as Diabetes as use of orlistat along with anti-diabetic therapies may reduce micro and macro vascular complication.[11] More research is needed to establish the mortality reduction with the use of orlistat. A meta-analysis revealed that the 2 year therapy with the orlistat had no significant reduction on the mortality.[12,13,14,15,16] However the side effects of orlistat observed are high and the patients might suffer from compliance issues as well. Thus, the physician must administer caution while selecting and prescribing orlistat to obese patients. The patients must also be counseled and advised by the physician to improve their lifestyle by daily exercise and proper diet in order to have optimal weight reduction as well as to maintain it in future.

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CONCLUSION

The use of orlistat along with life style modification is beneficial in reducing the weight and BMI of patients significantly as compared to placebo and may be helpful in reducing the morbidity and mortality in the long term. However, caution should be administered by the physician in prescribing orlistat to patients because of associated side effects.

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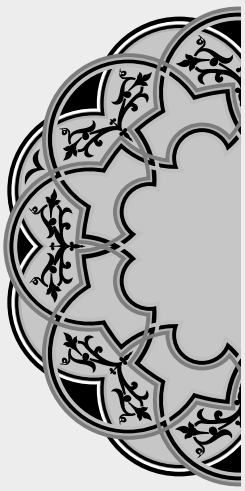

"Nobody's is free until everybody's is free."

Fannie Lou Hamer

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
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2	Bashir-ur-Rehman	Literature search & Questionnaire	
3	Humera Hameed	Substantial, Origin and concept	