

## Effect of Orlistat on blood pressure in overweight/obese hypertensive patients

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**Abstract: Background:** Obesity is an emerging public health problem, associated with an increased risk of serious medical illnesses including hypertension. Behavioral therapy alone has limited role in providing significant and sustained weight loss. If Orlistat, an anti-obesity drug is adequate enough to cause significant decrease in blood pressure, the cost and potential adverse affects of lifelong drug therapy can be avoided.

**Objectives:** To determine the effect of Orlistat on blood pressure in overweight/obese hypertensive patients.

**Materials and methods:** A prospective randomized, open double-blinded study was conducted in a tertiary care hospital. Patients with body mass index  $\geq 23$  with essential hypertension with diastolic blood pressure between 90 to 100 mmHg, who were not on any antihypertensive treatment were selected for this study. Patients were randomly divided into two groups - group I which received Orlistat and group II which received placebo only along with similar hypo-caloric diet in both groups. The patients were serially followed for up to 3 months for change in blood pressure, weight, lipid profile, blood sugar and waist hip ratio.

**Results:** We observed significant reduction in blood pressure, weight, blood sugar, lipid profile and waist hip ratio in group I as compared to group II.

**Conclusion:** We conclude that, Orlistat in combination with diet restriction significantly improve blood pressure in obese hypertensive patients as compared to placebo.

**Keywords:** Obesity, hypertension, anti-obesity drugs

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### I. Introduction

Obesity is a state of excess fat accumulation that is causally related to serious medical illnesses and economic burden on society. It is a leading preventable cause of death worldwide.

According to a global estimate by the World Health Organization (WHO), in 2005 there were about 1.6 billion overweight persons aged 15 years and above and among them at least 400 million adults were obese.<sup>1</sup> The WHO further projects that by 2015, approximately 2-3 billion adults will be overweight and more than 700 million will be obese.<sup>1</sup> Hypertension is one of the most common obesity-related complications, and about 30% of hypertensive individuals can be classified as being obese.<sup>2</sup>

Results from the Framingham Study have shown that high blood pressure and overweight are both independent risk factors for cardiovascular diseases.<sup>3,4</sup> In INTERSALT study<sup>5</sup>, the relationship between body mass index (BMI) and blood pressure was studied in over 10,000 men and women, between 20 and 59 years of age, sampled from 52 centres around the world. In this large study population, BMI was significantly associated with systolic and diastolic blood pressure.

Weight loss has been recommended for the obese hypertensive patient. Behavioral therapy alone has limited success in providing significant and sustained weight loss, which prompted us to conduct this study. Even a modest weight loss produces a positive effect on obesity-related complications including hypertension. If only anti-obesity drug treatment is adequate enough to normalize blood pressure, the cost and potential adverse affects of drug therapy can be avoided.

### II. Materials and Methods

The study was conducted in department of General Medicine, King George's Medical University, Lucknow, India between August 2008-October 2009. The study was a prospective randomized open blinded evaluation (PROBE) design.

Patients between 20 to 60 years of age with body mass index  $\geq 23$  with essential hypertension with diastolic blood pressure between 90 to 100 mmHg, who were not on any antihypertensive treatment were selected for this study.

Patients with endocrinal disorders, renal or hepatic disease, malignancy, medications known to alter blood pressure, body weight or appetite, pregnant and lactating women, severely ill patients and patients not giving consent were excluded from the study

Detailed history regarding complaints, duration, drugs being presently taken, any previous history of hypertension, diabetes mellitus, smoking status, family history of hypertension was carefully elicited in all cases.

A detailed clinical examination was carried out in all the cases. Blood pressure (left arm sitting position), weight, body mass index and waist/hip rate was measured carefully.

Following investigations were carried out:

1. Hemogram
2. Urine: Routine and microscopic
3. Blood sugar: Fasting and postprandial
4. Serum urea and creatinine
5. Serum lipid profile

Cases were randomly categorized into 2 groups:

**Group I:** This group received Orlistat 120 mg twice daily.

**Group II:** This group received placebo twice daily.

A similar dietary chart and dietary advice (hypo-caloric diet – 600 kcal/day deficit) was given to both groups.

Patients were continued on these therapies for three months. Compliance to the drugs was assessed by pill counting. Serial monitoring of weight and blood pressure was done at one month interval in all the cases. Blood sugar, fasting lipid profile and waist hip ratio was re-measured at the end of three month. Occurrence of any side effects were carefully noted.

The statistical analysis was performed using SPSS version 16.0 software. Mean weight and blood pressure in the two groups were compared using student t test. The descriptive values below 5% ( $p < 0.05$ ) were considered statistically significant.

### III. Results

A total of 68 patients were included in the intent to treat (ITT) analysis. The baseline parameters and findings on initial investigations in these patients are summarized in Table 1. These patients were followed up for a period of three months.

**Table 1: Baseline parameters of patients in the two groups**

	Group I	Group II
Number of patients(n)	34	34
Mean age(years) ± SE	45.03±1.08	44.91±1.17
Male: Female	2.5:1	3.6:1
Mean weight(kg) ± SE	95.90±0.77	95.96±0.72
Mean SBP mm Hg ± SE	143.41±0.76	143.59±0.67
Mean DBP mm Hg ± SE	92.75±0.42	92.88±0.39
Mean Fasting blood sugar(mg/dl) ±SE	95.91±0.97	95.88±0.92
Mean Postprandial blood sugar(mg/dl) ± SE	144.69±1.78	145.06±1.79
Mean Total Cholesterol(TC) ±SE (mg/dl)	196.99±2.30	196.32±1.53
Mean Triglycerides(TG) ±SE (mg/dl)	183.31±1.47	183.59±1.15
Mean Low Density Lipoprotein(LDL) ±SE (mg/dl)	120.59±1.01	121.03±0.89
Mean High Density Lipoprotein(HDL) ±SE (mg/dl)	43.50±1.07	43.24±0.95
Mean waist/hip ratio ±SE	0.917±0.004	0.920±0.003

Weight and blood pressure was monitored monthly. The mean reduction of weight, blood pressure (systolic and diastolic) during follow up in the two groups are summarized in Table 2 and depicted graphically in Fig.1

**Table 2: Weight and Blood pressure during follow up in the two groups**

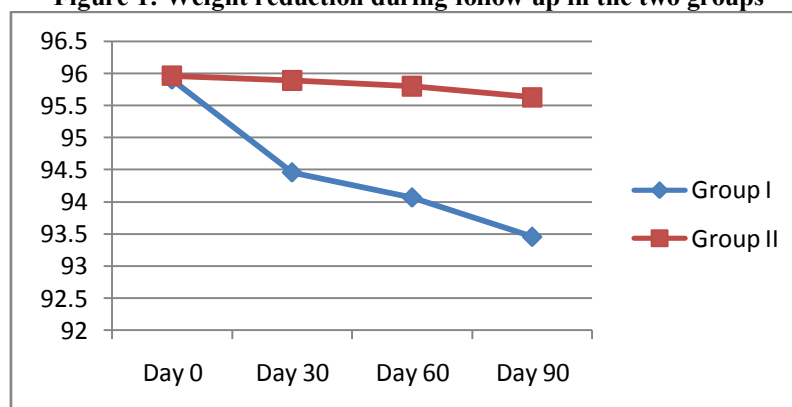
Variables	Groups	Day 0	Day 30	Day 60	Day 90	% change
Weight(kg)	Placebo	95.96 ± 0.72	95.89 ± 0.72	95.80 ± 0.73	95.63 ± 0.73	0.3%
	Orlistat	95.90 ± 0.77	94.96 ± 0.86 <sup>a</sup>	94.07 ± 0.87 <sup>a</sup>	93.46 ± 0.82 <sup>a</sup>	2.6%
SBP(mmHg)	Placebo	143.59±0.67	143.21 ± 0.58	142.91±0.68	142.12 ± 0.67	1.0%
	Orlistat	143.41±0.76	142.72±0.68 <sup>a</sup>	141.34±0.70 <sup>a</sup>	138.91±0.76 <sup>a</sup>	3.1%
DBP(mmHg)	Placebo	94.71 ± 0.44	94.24 ± 0.43	93.94 ± 0.53	93.74 ± 0.42	1.0%
	Orlistat	94.91 ± 0.33	93.16 ± 0.43 <sup>a</sup>	92.50 ± 0.48 <sup>a</sup>	92.25 ± 0.39 <sup>a</sup>	2.8%

a =  $p < 0.05$  in comparison with placebo

At baseline (day 0), there was no significant difference in mean weight and blood pressure in the two groups. During follow up of three months significant reduction of these parameters was observed in group I as compared to group II evident from the first follow up visit.

At the end of three months, there was a significant change in mean weight with Orlistat (2.6%) as compared to placebo (0.3%) (- 2.44 kg versus 0.33 kg ).

**Figure 1: Weight reduction during follow up in the two groups**



Mean systolic blood pressure was reduced to a significantly greater degree with Orlistat(3.1%) compared to placebo (1%) (- 4.5 mm Hg versus -1.47 mm Hg,  $p < 0.05$ ) at the end of three months. Similarly, reductions in mean diastolic blood pressure was greater with Orlistat (2.8%) than with placebo (1%) (-2.66 mm Hg versus - 0.97 mmHg;  $p < 0.05$ ) at the end of three months of therapy.

Blood sugar (fasting and postprandial), fasting lipid profile and waist hip ratio was re-measured at the end of three months. The mean reduction of blood sugar, fasting lipid profile and waist hip ratio during follow up in the two groups are summarized in Table 3.

**Table 3: Blood sugar and lipid profile during follow up in the two groups**

Variables	Groups	Day 0	Day 90	Percentage change
Fasting Blood sugar (mg/dl)	Placebo	95.88 ± 0.92	94.94 ± 0.92	1.0%
	Orlistat	95.91 ± 0.97	93.88 ± 0.98 <sup>a</sup>	2.1%
Postprandial Blood sugar(mg/dl)	Placebo	145.06 ± 1.79	144.15 ± 1.81	0.6%
	Orlistat	144.69 ± 1.78	142.75 ± 1.81 <sup>a</sup>	1.3%
Total Cholesterol (mg/dl)	Placebo	196.32 ± 1.53	196.21 ± 1.57	0.6%
	Orlistat	196.94 ± 2.30	195.84 ± 2.31 <sup>a</sup>	0.1%
HDL (mg/dl)	Placebo	43.24 ± 0.95	43.15 ± 0.90	0.2%
	Orlistat	43.50 ± 1.07	43.37 ± 1.06 <sup>b</sup>	0.6%
LDL (mg/dl)	Placebo	121.03 ± 0.89	120.76 ± 0.88	0.2%
	Orlistat	120.59 ± 1.01	119.41 ± 1.06 <sup>a</sup>	1.0%
VLDL(mg/dl)	Placebo	28.38 ± 0.75	28.24 ± 0.71	0.5%
	Orlistat	28.56 ± 0.79	27.59 ± 0.76 <sup>a</sup>	3.4%
TG (mg/dl)	Placebo	183.59 ± 1.15	183.26 ± 1.16	0.2%
	Orlistat	183.31 ± 1.47	182.66 ± 1.48 <sup>a</sup>	0.4%
WHR	Placebo	0.920 ± 0.003	0.919 ± 0.003	0.1%
	Orlistat	0.917 ± 0.004	0.906 ± 0.004 <sup>a</sup>	1.2%

a =  $p < 0.05$  in comparison with placebo, b=  $p > 0.05$  in comparison with placebo

As evident from table 3, at baseline (day 0), there was no significant difference in these parameters in the two groups. During follow up period of three months, group I showed significantly more reduction in blood sugar, lipid profile and waist hip ratio as compared to group II.

The most common adverse effect observed in group I patients included oily stool (37.5%), diarrhoea (18.8%), nausea (18.8%) and vomiting (12.7%). The proportion of diarrhoea and oily stool were found to be significantly ( $p < 0.05$ ) higher in group I as compared to group II.

#### IV. Discussion

This study evaluates the effect of Orlistat, a lipase inhibitor, on blood pressure in overweight /obese hypertensive individuals. In conjunction with a reduced-calorie diet, treatment with 120 mg of Orlistat twice daily for 90 days significantly decreased blood pressure (systolic and diastolic), weight, blood sugar (fasting and postprandial), fasting lipid profile and waist hip ratio as compared to placebo. This effect is probably due to the decrease in the absorption of fat and its associated calories.<sup>6</sup> Gastrointestinal tract adverse effects were observed more frequently with Orlistat.

In previous studies, Orlistat has been shown to cause significant and sustained reduction in weight, blood pressure, blood sugar, lipid profile and waist hip ratio in overweight or obese adults when given at a dose of 120 mg 3 times daily and combined with a mildly reduced-calorie diet for a longer duration of at least one year.<sup>7,8,9</sup>

In the current study, Orlistat in a lesser dose of 120mg twice daily for a lesser time (three months) was associated with a statistically significant decrease in blood pressure, weight, blood sugar, lipid profile and waist hip ratio in contrast to the placebo group. In this three months trial, Orlistat did not raise any safety issues, and the adverse event profiles except for gastrointestinal tract adverse events as compared to placebo group.

### **V. Conclusion**

We conclude that Orlistat 120 mg twice daily for 90 days, in conjunction with a reduced-calorie diet, significantly improves blood pressure and other cardiovascular risk factors in obese hypertensive patients and should be recommended in every obese hypertensive patient so that the cost and potential adverse affects of lifelong antihypertensive therapy can be avoided.

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