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Original Research Article

Efficacy of orlistat in the treatment of patients with non-alcoholic fatty liver

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ABSTRACT

Background: Nonalcoholic fatty liver disease (NAFLD) is a reversible condition of fat accumulation that is associated with liver inflammation and can disrupt the normal activity of the liver. People with a diagnosis of NAFLD have a higher risk of all-cause mortality than the general population. The purpose of the present study was to determine the efficacy of orlistat in the treatment of patients with NAFLD.

Methods: This semi-experimental study was performed on 45 fatty liver patients of the gastroenterology clinic of Imam Khomeini Hospital in Ardabil city in April 2016 to April 2017. Data was collected by a checklist which included demographic and clinical data such as age, sex, body mass index (BMI), alanine aminotransferase (ALT), aspartate aminotransferase (AST), triglyceride (TG), cholesterol and result of ultrasound before and after orlistat consumption.

Results: The mean decrease in the variables examined was as follows: weight 8.3 kg, BMI 3.5 kg/m², ALT 31.6 U/l, AST 18.1 U/l, cholesterol 15.5 mg/dl and TG 33.1 mg/dl. All of the upper indexes were decreased significantly following received drug.

Conclusions: Orlistat therapy was associated with significant decreases in ALT, AST, TG and cholesterol level. Orlistat is effective in weight loss, body mass index reduction and can be used to treat non-alcoholic fatty liver disease.

Keywords: Ardabil, Fatty liver, Orlistat

INTRODUCTION

Non-alcoholic fatty liver (NAFLD) is a clinic-pathological diagnosis in which more than 5% of hepatocytes demonstrate macrovesicular steatosis in an individual without a significant history of alcohol intake. In recent years NAFLD, the most common form of liver

disease, has been recognized as the hepatic manifestation of the metabolic syndrome.¹ NAFLD occurs across all age groups and ethnicities. The reported prevalence of NAFLD varies widely depending on the population studied and the definition used. The estimated worldwide prevalence of NAFLD ranges from 6.3% to 33% with a median of 20% in the general population, based on a variety of assessment methods.²⁻⁴ Primary NAFLD is

related to insulin resistance and thus frequently appears as part of the metabolic changes that accompany obesity, diabetes, and hyperlipidemia.⁵ The usual management of NAFLD includes gradual weight reduction and physical activity, leading to an improvement in serum liver enzyme levels, reduced hepatic fatty infiltration and in some cases a reduced degree of hepatic inflammation and fibrosis.⁶ Although lifestyle modification is sufficient in many patients, resistant cases of NAFLD may require pharmacologic therapy. Candidate medications for the treatment of NAFLD should lead to weight loss, decreased free fatty acid (FFA) flux to the liver, and improved insulin sensitivity, without hepatotoxic adverse effects.⁷ Orlistat, a gastrointestinal lipase inhibitor, is useful in the treatment of obesity and type 2 diabetes mellitus. Gastric and pancreatic lipases are enzymes that play a main role in the digestion of dietary fat. Orlistat, a semisynthetic derivative of lipstatin, is a potent and selective inhibitor of these enzymes; it exerts its effect within the gastrointestinal (GI) tract. Orlistat acts by binding covalently to the serine residue of the active site of gastric and pancreatic lipases. When administered with fat-containing foods, orlistat partially inhibits hydrolysis of triglycerides, thus reducing the subsequent absorption of monoglycerides and FFA.⁸ Therefore, the purpose of this study was to evaluate the effect of orlistat in the treatment of non-alcoholic fatty liver disease in patients of Ardabil city hospital.

Objectives

The objectives of the present study were to compare the efficacy of orlistat in the treatment of non-alcoholic fatty liver disease in patients with grade II and III fatty liver.

METHODS

Study design

This study was semi experimental study.

Procedure

After approval of the project at the Ethics Committee of Biological Research in Ardebil University, this study was performed on 45 patients with grade II and III fatty liver in ultrasound exam in which were selected by a gastroenterologist from among the patients referred to the Imam Khomeini Hospital in April 2016 to April 2017. An ultrasound examination was carried out at the beginning and at the end of the study by the same person and the same device.

The diet included 100 kJ/day for ideal body weight, with an emphasis on reduced intake of both fat (-25% of daily calories) and simple carbohydrates. All patients were advised to avoid overeating, eating high-fat and high-energy foods during the study and were encouraged to perform physical activity 2 to 3 times a week (30 minutes of walking at 4 to 5 km/h). The nutritionist interviewed

all study participants at the time of their monthly clinic visit. The patients received orlistat (120 mg before lunch and dinner) for three months.

Data was collected by a checklist containing demographical information such as age, sex and weight.

Inclusion criteria

Non-alcoholic fatty liver patients with grade II and III that approved by an ultrasound exam and patients who signed the consent to diet were included in the study.

Exclusion criteria

Patients with diabetes mellitus, chronic viral hepatitis, alcoholic fatty liver disease and pregnant women were excluded.

Efficacy measures

Liver ultrasound condition, body mass index (BMI), serum aspartate and alanine aminotransferase (AST and ALT), cholesterol and triglyceride (TG) levels were assessed at baseline and at the completion of the study.

Statistical analysis

The collected data were analyzed by SPSS software version 22. Data are presented as mean±SD. Paired t-tests were used to evaluate within-group changes from pre and post-treatment. P value less than 5% was considered statistically significant.

RESULTS

Forty-five patients with NAFLD received orlistat. Ninety-three percent of the patients were obese (BMI ≥30 kg/m²), 53.3% of patients were female and the rest were male. The mean age was 45.8±9.7 years. Forty-two percent of the patients were 41 to 50 age (Table 1).

Table 1: Demographic parameter.

Variables	Number	Percentage (%)	
Sex	Female	24	53.3
	Male	21	46.7
Age (in years)	<30	3	6.7
	31-40	9	20
	41-50	19	42.2
	51-60	10	22.2
	>60	4	8.9

Following three months therapy with orlistat, body mass index and weight decreased significantly. The mean decrease in the variables examined was as follows: weight loss 8.3 kg, BMI 3.5 kg/m², ALT 31.6 U/l, aspartate AST 18.1 U/l, cholesterol 15.5 mg/dl and TG 33.1 mg/dl (Table 2). At the beginning of the study, all patients had

grade II or III fatty liver in ultrasound exam. Three months after treatment, 24% had normal ultrasonography,

53% had first grade fatty liver, and 22% had grade II fatty liver (Table 3).

Table 2: Mean BMI, weight and biochemical tests pre- and post-treatment.

Variables	Pre-treatment	Post-treatment	difference	P value
BMI in kg/m² (normal, 20–25)	35.2±3.4 (24-40)	31.8±3.2 (22-37)	3.5±1.2	0.00
Weight in kg	100±14.8 (75-138)	91.8±14.3 (69-116)	8.3±3.4	0.00
Triglyceride level in mg/dl (normal, 50–175)	258.5±68.1 (94-327)	225.3±74.5 (29-313)	33.1±40.1	0.00
Cholesterol level in mg/dl (normal, 150–200)	222.4±61.6 (146-317)	206.8±61.2 (128-312)	15.5±13.3	0.00
ALT level in U/l (normal, 5–39)	73.6±33 (26-216)	42±26.2 (5-154)	31.6±13.7	0.00
AST level in U/l (normal, 5–40)	41.5±14.8 (19-75)	23.4±13.4 (2-57)	18.1±5.8	0.00

Note: For all variables, data are presented as mean ±SD, with the range in parentheses.

Table 3: Frequency of NAFLD grade in pre- and post-treatment.

Time of study	Fatty liver grade								P value
	3		2		1		0		
	N	%	N	%	N	%	N	%	
Base line	23	51.1	22	48.9	-	-	-	-	0.02
End of study	-	-	10	22.2	24	53.3	11	24.4	

DISCUSSION

The prevalence of NAFLD is rapidly increasing worldwide along with the increase in obesity and type 2 diabetes.⁹ Studies show that NAFLD is often associated with insulin resistance, obesity, diabetes mellitus, hyperlipidemia, visceral adiposity and other cardio-metabolic diseases.^{1,10-12}

Orlistat, a reversible inhibitor of gastric and pancreatic lipases, has been approved by the FDA for weight loss. It is not absorbed into the circulation and is mainly excreted unchanged in the feces. Data suggest that when orlistat combined with dietary counseling, approximately 40% of treated patients for one year were able to lose up to 10% of their body weight.¹³ Lipase inhibition by orlistat prevents the absorption of approximately 30% of energy from fat.^{14,15} Orlistat, as an anti obesity drug, reduces lipid levels following a high-fat meal. A study by Gabriel et al identified that administration of orlistat suppressed the postprandial rise of TG levels in healthy adult volunteers following consumption of meals with 50% fats.¹⁶

The present study showed that patients lose up 8.3 kg of their body weight after the use of orlistat and their body mass index decreased significantly too. In a study by Smith et al results showed that orlistat was an effective drug to weight loss and reducing metabolic risk factors associated with abdominal obesity.¹⁷ Other studies showed that treatment with orlistat reduced weight and improved hyperglycemia in diabetic overweight patients.^{14,18} Finer et al in a study on obese patients for one-year, showed that Orlistat group had lower waist circumference than the placebo group and weight loss in Orlistat group was 14% more than the placebo group.¹⁹ In the study by Zelber-Sagi et al Weight loss mean with orlistat treatment was 7.7 kg, and in the study by Harrison

et al Orlistat was associated with a significant reduction in weight, HbA1c, ALT and AST.^{7,13} In meta-analysis by Wang et al the efficacy and safety of orlistat in the treatment of NAFLD and improvements were observed in levels of Alanine aminotransferase, aspartate aminotransferase, gamma-glut amyl transpeptidase and triglycerides. They suggested that orlistat could serve as a therapeutic drug in improving biochemical indicators of liver damage, suggesting a novel palliative drug for the treatment of NAFLD.²⁰

CONCLUSION

Significant decreases in ALT, AST, TG and cholesterol levels were observed following Orlistat therapy and the drug is effective in weight loss and body mass index reduction. It seems that orlistat can be used in treatment of non-alcoholic fatty liver disease. Using an antioxidant such as vitamin E along with orlistat may also help to improve the tissues damages in NAFLD. A clinical trial is recommended using the combination of the two drugs.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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