Effect of weight loss diets on biochemical parameters and anthropometric measurements in prolactinoma patients

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Abstract

Background: The aims of this study were to determine the effect of weight loss on biochemical parameters and anthropometric measurements in prolactinoma patients and to evaluate the effectiveness of weight loss diet along with medical treatment.

Methods: Twenty-two patients with prolactinoma were divided into two groups and one of the groups was applied weight loss diet (diet group) while the other group was diet free (control group). Each participant was interviewed using a structured questionnaire. The biochemical parameters (fasting plasma glucose, fasting plasma insulin, prolactin, leptin, TSH, T4, cortisol, HbA1c, AST, ALT and blood lipids) of participants were analyzed and anthropometric measurements were taken.

Results: There was a significant change in mean BMI after treatment in diet group (p=0.000). The mean level of serum prolactin decreased from 45.1±31.63 ng/dL at baseline to 12.6±8.19 ng/dL after three months in diet group (p=0.006). Despite there being no statistically significant difference between diet and control group in terms of baseline level of prolactin measurement (p=0.800), statistically significant difference between the two groups in terms of final level of prolactin measurement (p=0.027) was observed. There was a significant change in mean level of leptin after treatment in diet group (p=0.001).

Conclusions: In addition to medical treatment, weight loss diets sped up the healing process for hyperprolactinemia and the reduction in body weight had positive effects on the metabolic profiles of prolactinoma patients.

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INTRODUCTION

Prolactinomas are the most common type of pituitary adenomas. Macroprolactinoma is the term used for these tumors when their size is ≥1 cm. If the tumor's size is <1cm, it's referred to as a microprolactinoma.[1,2] Prolactinomas in adults occur more frequently in women (>70%), with the majority in the form of microprolactinoma.[2] Tumor size is generally related with prolactin (PRL) level.[2]

As is well-known, increasing estrogen secretion stimulates the growth and proliferation of the lactotrophs during pregnancy. As a result, PRL secretion increases.[3] PRL is identified as a major stimulating factor for lactation in the postpartum period. Some metabolic effects of PRL comprise of providing pancreatic cell development in the perinatal and postnatal periods to manage insulin release, nutrient uptake and body weight, to stimulating citrate production in prostatic cells, preventing the negative effects of glucocorticoids on the immune system during stress periods, reducing reproductive functions, and suppressing sexual impulsivity.

In addition, PRL hormone induces adipogenesis, which inhibits lipolysis by altering the release of significant adipokines such as leptin, adiponectin, and interleukin (IL)-6.[4] Treatment of hyperprolactinemia reduces cardiovascular disease risk factors, endothelial dysfunction, and insulin resistance.[3,4,5]

Several studies describe a higher body weight in patients with hyperprolactinemia, the exact mechanism of which is not clear.[6,7,8] A combination of factors like decreased dopaminergic tone, low adiponectin, and hypogonadism with or without associated leptin resistance could contribute to weight gain. Also, hyperprolactinemia has been linked to alteration in glucose homeostasis, insulin sensitivity, and lipid parameters.[9] PRL is known to stimulate leptin synthesis and secretion.[10] Leptin, the obese gene product, is synthesized by adipose tissue in the body. Body fat mass and body mass index (BMI) determine serum leptin level. The role of leptin is to regulate nutrient intake on the brain, modulate energy metabolism via negative feedback, and prevent the development of obesity.[11]

The aims of the present study were to determine the effect of weight loss on biochemical parameters and anthropometric measurements in prolactinoma patients and to evaluate the effectiveness of a weight loss diet along with medical treatment. We analyzed the effects of the weight loss diet on the body compositions of prolactinoma patients.

Materials and Methods

Study Design and Participants

The study sample was composed of 22 premenopausal women with prolactinoma between the ages of 20-50 years, who were referred to the outpatient clinic at Başkent University Hospital, Endocrinology and Metabolism Department, Ankara, Turkey. The diagnosis of prolactinoma was established by recording persistently elevated PRL levels (PRL=25-100 ng/ml), coupled with symptoms of hyperprolactinemia, and a positive pituitary adenoma on enhanced magnetic resonance imaging. The participants were enrolled in the study at the time of diagnosis between September 2014 and August 2015 and were receiving dopamine agonist treatment. The major inclusion criteria was to have BMI ≥25 kg/m^2 (overweight and obese). Patients were excluded from the study if they were pregnant, lactating, or planning a pregnancy. As well, participants had no history of pituitary surgery or radiotherapy. The diet group (n=11) recevied both a weight loss diet and started dopamine agonist treatment. The control group (n=11) received only dopamine agonist treatment. The participants' bromocriptine doses were not changed throughout the three months. Group samples were selected randomly. Each participant was interviewed using a structured questionnaire to obtain demographic information about education, occupation, health conditions at entry, nutrition behaviors, and marital status.

This study was approved by the Baskent University Institutional Review Board and Ethics Committee (Project no: KA13/321) and supported by the Baskent University Research Fund.

Anthropometric Measurements

Anthropometric measurements were taken at the beginning and at the third month of the study. Height was measured with a fixed stadiometer with 1 mm precision. Body weight, fat mass, fat, muscle, and water ratios were measured with light indoor clothes, via Bioelectric Impedance Analysis (BIA) (ioi 353, Jawon Medical, S. Korea). BMI was calculated as weight in kilograms divided by the square of the height in meters (kg/m2). Waist and hip circumferences were measured with an inelastic tape measure, halfway between the last rib and the iliac crest. Hip circumference was measured to calculate the waist-to-hip ratio (WHR). Waist to height ratio (WHtR) was determined by dividing waist to height.

Intervention

Weight loss management was planned and controlled by a dietitian for each patient after diagnosis. The diet group's patients had lost a minimum of 5 % of their initial body weight by applying the weight loss diet for three months. Participants who were unable to lose weight were excluded from the study. During the follow-up, patients had multiple outpatient visits where adherence to the diet was checked and regulated. During the course of the study, patients were prescribed a patient-specific balanced diet. The diet plan was individually calculated to provide a reduction from 500 to 1000 kcal/day of the energy needs of the subject. Every two to three weeks, anthropometric measurements were taken and, if necessary, adjustments were made to the diet to improve compliance. Three meals (breakfast, lunch, and dinner) and snacks were recommended. The nutritionist provided personalized instructions by using food exchange lists. Individual preferences for various food items were integrated into the diet plan.

Biochemical Analysis

Blood samples were collected at the beginning and at the third month of the study. Blood samples were obtained after a fast of at least 12 hours and analyzed by the Başkent University Ankara Hospital Biochemistry Laboratory using standardized laboratory procedures. Serum glucose levels were measured by autoanalyzer (Abbott Aeroset, Toshiba, Japan) with the adapted hexokinase method. The hemoglobin A1c (HbA1c) level was measured with high pressure liquid chromatography (HPLC) (DIAMAT; Bio-Rad Laboratories, Milan, Italy). Total and high-density lipoprotein (HDL) cholesterol and triglyceride (TG) levels were measured by routine laboratory techniques using an automated analyzer (Hitachi 912, Roche-Hitachi Modular Analytics, Roche Diagnostics GmbH, Mannheim, Germany). Low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald formula (LDL cholesterol = TC − TG/5 − HDL cholesterol). Very low-density lipoprotein (VLDL) cholesterol was calculated using a formula (VLDL-cholesterol = serum triglyceride/5). Serum PRL, insulin, and cortisol levels were measured with commercially available chemiluminescence kits (Abbott Architect, Toshiba). For evaluating thyroid function, thyroxine (T4), and thyrotrophin-stimulating hormone (TSH) were measured using immunochemiluminescent assays on an automated analyzer (BioDPC, USA). Serum aspartate aminotransferase (AST) and alanine transaminase (ALT) levels were measured using standard clinical methods for automated analysis. Plasma leptin was evaluated by a highly sensitive direct enzyme-linked immunosorbent assay (ELISA) using commercial kits (DIAsource LeptinEASIA Kit, KAP 2281 DIAsource Immunoassays S.A, Nivelles, Belgium).

Statistical Analysis

Statistical analyses were carried out by Statistical Package for Social Sciences (SPSS) for Windows, Release 21.0. Quantitative data were expressed as mean ($\bar{X}$) and standard deviation (SD). Qualitative data were stated as number (n) and percentage (%) values. Normality was tested by Kolmogorov–Smirnov test. Normally distributed data were analyzed using a "*Paired Samples t Test*". Comparison of means between the groups was analyzed using an "*Independent Sample t Test*". The Pearson correlation test was used for correlation analysis. p values < 0.05 were considered statistically significant.

Results

Microadenoma was detected in all participants. The mean age of participants was 37.2±10.21 years. Out of 22 patients, ten (45.5%) were married, 11 (50.0%) were single, and one (4.5%) was widowed or divorced. It was determined that 19 of the participants (86.4%) were graduates of undergraduate and graduate programs. Out of 22 women, 20 had oligomenorrea and 11 had galactorrhea (Table 1).

Anthropometric and biochemical measurements of participants were revealed in Table 2. Although a statistically significant decrease was observed in the mean body weight in the diet group (p=0.000), there was no significant difference observed in the mean body weight in the control group (p=0.192). When the first and last body weight measurements were compared between the groups, no statistically significant differences were found (p^2=0.218, p^3=0.892). At the begining of the study, means of BMI were 31.7±5.88 kg/m^2 and

28.4±5.05 kg/m^2 in the diet and the control groups, respectively. However, after three months, while the mean BMI decreased to 28.9±5.52 kg/m^2 in the diet group (p=0.000), there was no statistical difference in the control group's BMI (28.5±5.00 kg/m^2; p=0.334). When the first and last BMI were compared between the groups, no statistically significant differences were found (p^2=0.180, p^3=0.856). In the diet group, there were statistically significant differences seen in the mean levels of waist circumference, body fat weight and percentage, body water weight, as well as levels of AST, TSH, triglycerides, total cholesterol, and VLDL-cholesterol (p<0.05). Similarly, a statistically significant difference in the mean level of HDL-cholesterol was observed in the control group (p=0.002). The level of total cholesterol decreased significantly in both groups (p=0.004; p=0.005).

It was observed that PRL levels decreased in both groups. The mean level of serum PRL decreased from 45.1±31.63 ng/dL at baseline to 12.6±8.19 ng/dL after three months in the diet group (p=0.006). Also, the mean level of serum PRL decreased from 42.3±17.83 ng/dL at baseline to 22.9±11.68 ng/dL at the end of the study in the control group (p=0.002). Even though there was no statistically significant difference seen between the groups in terms of PRL level at baseline (p=0.800), there was a statistically significant difference in terms of PRL levels after three months (p=0.027). Despite a statistically significant decrease in the mean level of leptin after treatment in the diet group (p=0.001), the decrease was not significant in the control group (p=0.065) (Table 2).

Table 1. Demographic and Disease-Related Characteristics of Participants

Paramenters		Diet Group (n:11)		Control Group (n:11)		Total (n:22)	
		n	%	n	%	n	%
Age ($\bar{X}$ ± SD) (years)		39.8±11.65		34.7±8.31		37.2±10.21	
Marital Status	Single	6	54.5	4	36.4	11	50.0
	Married	4	36.4	7	63.6	10	45.5
	Widow / Divorced	1	9.1			1	4.5
Working status	Officer	3	27.3	3	27.3	6	27.3
	Self-employment	3	27.3	3	27.3	6	27.3
	Unemployed	3	27.3	1	9.1	4	18.2
	Worker			2	18.2	2	9.1
	Academician	1	9.1	1	9.1	2	9.1
	Retired	1	9.1			1	4.5
	Student			1	9.1	1	4.5
Education Status	Primary school	1	9.1	1	9.1	2	9.1
	High school			1	9.1	1	4.5
	License and above	10	90.9	9	81.9	19	86.4
Irregular period	Yes	10	90.9	10	90.9	20	90.9
	No	1	9.1	1	9.1	2	9.1
Galactorrhea	Yes	6	54.5	4	36.4	10	45.5
	No	5	45.5	7	63.6	12	54.5

Table 2. Changes In Anthropometric And Biochemical Measurements In Diet And Control Groups

	Diet Group (n:11)			Control Group (n:11)				
	Before Treatment ($\bar{X}$ ± SD)	After treatment ($\bar{X}$ ± SD)	p^a	Before Treatment ($\bar{X}$ ± SD)	After treatment ($\bar{X}$ ± SD)	p^a	p^b	p^c
Body Weight (kg)	85.5±17.34	78.0±15.94	0.000*	76.4±16.22	77.0±16.03	0.192	0.218	0.892
BMI (kg/m^2)	31.7±5.88	28.9±5.52	0.000*	28.4±5.05	28.5±5.00	0.334	0.180	0.856
Waist circumference (cm)	101.2±13.09	97.0±13.19	0.000*	93.8±13.47	94.8±12.88	0.118	0.206	0.699
Waist / Hip	0.8±0.10	0.8±0.08	0.635	0.8±0.05	0.8±0.08	0.314	0.304	0.915
Waist/ Height	0.6±0.07	0.5±0.07	0.068	0.5±0.12	0.5±0.07	0.399	0.705	0.928
Body Fat Weight (kg)	34.5±12.72	29.6±11.27	0.000*	26.1±10.27	26.6±10.13	0.303	0.107	0.528
Body Fat Percentage (%)	39.3±7.30	36.8±6.67	0.001*	32.7±6.49	33.7±5.71	0.346	0.057	0.259
Fatless Tissue Weight (kg)	49.9±9.65	48.3±6.84	0.328	50.0±7.36	50.3±6.48	0.569	0.975	0.490
Body Water Weight (kg)	38.7±5.80	36.0±4.90	0.029*	37.6±5.42	37.8±5.24	0.649	0.670	0.413
Fasting Glucose (mg/dL)	93.0±12.50	92.1±10.93	0.676	87.0±3.00	87.0±3.56	0.921	0.144	0.168
Fasting Insulin (IU/mL)	9.4±6.16	9.2±7.51	0.966	8.4±3.96	8.5±5.05	0.750	0.659	0.798
HbA1c (%)	5.4±0.40	5.3±0.37	0.284	5.1±0.14	5.1±0.11	0.659	0.016*	0.790
HOMA-IR	2.3±1.91	2.0±1.50	0.709	1.8±0.90	1.8±1.90	0.805	0.441	0.682
AST (U/L)	16.5±3.32	12.5±3.24	0.015*	18.8±3.51	17.7±4.36	0.528	0.135	0.005*
ALT (U/L)	14.0±5.34	13.0±3.83	0.604	18.9±11.92	17.7±8.08	0.749	0.227	0.100
PRL (ng/dL)	45.1±31.63	12.6±8.19	0.006*	42.3±17.83	22.9±11.68	0.002*	0.800	0.027*
Cortisol (μg/dL)	11.4±5.03	8.3±5.34	0.098	9.2±2.51	8.6±2.67	0.527	0.209	0.869
TSH (μIU/L)	2.0±0.70	1.5±0.62	0.005*	1.6±0.51	1.4±0.49	0.563	0.149	0.718
Free T4 (ng/dL)	1.1±0.17	1.1±0.22	0.557	1.1±0.22	1.1±0.23	0.745	0.967	0.898
Triglyceride (mg/dL)	123.1±50.10	95.1±42.45	0.030*	117.8±34.71	115.3±35.33	0.919	0.773	0.198
Total Cholesterol (mg /dL)	202.4±38.52	168.5±38.81	0.004*	205.7±37.93	176.3±23.96	0.005*	0.842	0.577
LDL-Cholesterol (mg/dL)	135.9±36.53	115.8±31.69	0.067	137.0±30.42	124.9±18.36	0.128	0.935	0.420
HDL-Cholesterol (mg/dL)	41.9±3.41	33.7±12.85	0.086	45.0±7.18	28.0±10.69	0.002*	0.200	0.269
VLDL-Cholesterol (mg/dL)	24.6±10.02	19.0±8.49	0.030*	23.5±6.94	22.4±7.06	0.919	0.773	0.198
Leptin (ng/dL)	16.1±8.86	9.7±5.79	0.001*	15.0±8.49	12.2±6.21	0.065	0.768	0.343

*p<0.05
pa: test of significance the difference between the measurements within the group
pb: test of significance between the groups the mean of the first measurement
pc: test of significance between the groups the mean of the last measurement (after 3 months)

Table 3. Correlations Between Prolactin, Leptin Levels and Other Biochemical Parameters, Anthropometric Measurements

		PRL (ng / dL)		Leptin (ng / dL)	
		Diet Group	Control Group	Diet Group	Control Group
Body Weight (kg)	r	-0.103	-0.364	0.267	0.416
	p	0.762	0,272	0.427	0.203
BMI (kg/m^2)	r	-0.117	-0.439	0.274	0.601
	p	0.732	0.177	0.415	0.050
Waist circumference (cm)	r	0.003	-0.223	-0.012	0.695
	p	0.994	0.509	0.972	0.018*
Waist /Hip Ratio	r	0.566	-0.066	-0.173	0.251
	p	0.070	0.847	0.610	0.456
Waist/ Height Ratio	r	0.079	-0.248	-0.044	0.785
	p	0.818	0.462	0.898	0.004*
Body Fat Weight (kg)	r	0.026	-0.176	0.344	0.507
	p	0.940	0.604	0.301	0.111
Body Fat Percentage (%)	r	-0.051	-0.345	0.401	0.633
	p	0.881	0.299	0.222	0.037*
Lean Body Mass (kg)	r	-0.156	-0.364	0.056	0.237
	p	0.646	0,272	0.869	0.483
Fasting Plasma Glucose (mg/dL)	r	-0.098	0.425	0.269	0.035
	p	0.775	0.193	0.425	0.919
Fasting Plasma Insulin (IU/mL)	r	0.154	-0.406	0.051	0.772
	p	0.652	0.216	0.882	0.005*
HbA1c (%)	r	-0.022	-0.252	-0.320	0.482
	p	0.950	0.455	0.337	0.133
HOMA-IR	r	0.148	-0.365	0.119	0.777
	p	0.664	0.270	0.727	0.005
AST (U/L)	r	0.561	0.241	-0.165	0.067
	p	0.073	0.476	0.628	0.845
ALT (U/L)	r	0.267	0.313	-0.179	-0.111
	p	0.426	0.348	0.598	0.746
PRL (ng/dL)	r	1	1	0.538	-0.268
	p			0.088	0.426
Cortisol (μg/dL)	r	0.059	-0,246	0.167	-0.079
	p	0.863	0.466	0.624	0.817
TSH (μIU/L)	r	0.374	-0.051	0.345	0.017
	p	0.258	0.881	0.298	0.961
Free T4 (ng/dL)	r	0.375	0.594	-0.006	-0.125
	p	0.256	0.054	0.985	0.715
Triglyceride (mg /dL)	r	0.115	-0.009	-0.232	0.443
	p	0.736	0.980	0.493	0.172
Total Cholesterol (mg /dL)	r	0.104	0.232	-0.275	0.230
	p	0.761	0.492	0.413	0.496
LDL-Cholesterol (mg /dL)	r	0.276	0.278	-0.249	0.161
	p	0.411	0.408	0.461	0.637
HDL-Cholesterol (mg/dL)	r	-0.444	0.049	-0.064	-0.053
	p	0.172	0.887	0.852	0.876
Leptin (ng/dL)	r	0.538	-0.268	1	1
	p	0.088	0.426		

*p<0.05

Correlations between PRL, leptin levels and other biochemical parameters, and anthropometric measurements were revealed in Table 3. In the present study, there was no statistically significant correlation between BMI and PRL levels in both groups at the end of the study (p=0.732; p=0.177). There were positive and significant correlations between serum leptin levels and waist circumference, waist/ height ratio, body fat percentage, fasting plasma insulin levels and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) values in control group (p<0.05). No correlation was observed between serum leptin and other biochemical parameters in the diet group (p>0.05).

Discussion

Prolactinomas are a type of pituitary adenoma that secrete PRL hormone. The amount of secreted PRL is related to the size of the tumor. Tumor secretion is not the only known cause of hyperprolactinemia. There are also many physiological and pathological reasons for hyperprolactinemia, such as pregnancy, lactation, stress, and multiple drugs which impair the dopamine system.[12] Excessive release of the PRL hormone has various metabolic effects on the body. Hyperprolactinemia is associated with insulin secretion, increased adipokine release, immune system stimulation, increased nutrient intake, and increased body weight. Hyperprolactinemia can also lead to insulin resistance, hyperinsulinemia, endothelial dysfunction, cardiovascular disease, and metabolic syndrome.[4] The aim of this study was to examine metabolic profile improvement by applying a weight loss diet alongside dopamine agonist treatment.

Prolactinomas are more common in women between 20 and 50 years of age.13 The sample of this study consisted of women and the mean age was 37.2±10.21 years. In a recent study, conducted between 2005 and 2007, 53.2% of individuals with pituitary gland tumors were women.[14]

Hyperprolactinemia is a common cause of galactorrhoea, which refers to milk secretion not due to breast-feeding, and has been often accompanied by amenorrhea.[15] The prevalence of hyperprolactinemia in patients with secondary amenorrhea or oligomenorrhorea is 15-20%. Generally, 30% of women with galactorrhoea and infertility have hyperprolactinemia. On the other hand, 75% of women with hyperprolactinemia have amenorrhea and galactorrhea.[16] In this study, 90% of women had menstrual irregularities and 45% of them had symptoms of galactorrhea.

In a study, it was stated that four months of dopamine agonist treatment decreased the level of fasting plasma glucose and HbA1c in obese type 2 diabetic patients.[17] In another study, it was determined that there was a significant increase in serum PRL levels in obese and morbidly obese patients. In addition, serum PRL levels were stated to be significantly related to β-cell index and BMI. However, there was no statistically significant correlation between HOMA-IR values and serum PRL levels.[18] Similarly, in our study, there was no statistically significant correlation seen between serum PRL levels and HOMA-IR in both groups (p=0.664; p=0.270).

Abnormalities in thyroid functions affect the body's energy balance.19 Drugs and hypothyroidism are among other causes of hyperprolactinemia.[20] In this study, there was a significant decrease in TSH levels in the diet group (p=0.005). The decrease seen in the control group was not statistically significant (p=0.563).

Hypothyroidism has similarities with metabolic syndrome. Therefore, low TSH levels have been associated with desired metabolic profiles.[21] Previous studies have shown a significant and positive correlation between serum TSH and PRL levels in hypothyroid patients.[22,23] In our study, a positive correlation was observed between serum PRL and TSH levels of the subjects in the diet group, though insignificant. This result can be possibly attributed to an insufficient sample size.

A randomized clinical trial showed that a 5% weight loss improves lipid profile and reduces inflammation in obese individuals.[24] We observed an 8.7±3.06% decrease in weight in the diet group. Wing et al. demonstrated that 5-10% of body weight loss improved hyperglycemia, blood pressure, triglyceride levels, and HDL-cholesterol levels.[25] In this study, it is intended that the metabolic profile improves by applying the weight loss diet alongside dopamine treatment. A long treatment period is needed to see the effects of dopamine agonist therapy on body weight.[26,27] It has also been reported that weight loss and normalization of serum insulin levels improve PRL response.[28] In our study, at the end of three months follow up, there was a statistically significant decrease in body weight, body fat weight, body fat percentage, body water weight, BMI, and waist circumference in the diet group ($p<0.05$). It is believed that weight loss in a short time has a positive effect on the disease process.

Serum triglycerides, total cholesterol, and VLDL-cholesterol levels were reduced amongst participants of the diet group ($p<0.05$). At the end of the three months, the improvement in lipid profile is thought to be associated with a decrease in body weight and serum PRL levels.

We determined a statistically significant decline in serum PRL levels of all subjects at the end of three months in both groups, which may largely be attributed to dopamine agonist therapy. Though there was no significant difference between the groups in terms of baseline measurements, the final PRL levels were significantly different. This may suggest that implementing the weight loss diet alongside medical treatment in overweight or obese patients with prolactinoma has a positive effect on serum PRL levels. The decrease in prolactin levels may explain the better metabolic profile of the diet group.

Leptin is important in the maintenance of the neuroendocrine system. In a controlled study, the relationship between serum PRL and leptin was investigated. Patients with high PRL levels were compared with normoprolactinemic subjects. There was a strong correlation between PRL and leptin levels. Hyperprolactinemic individuals had higher leptin levels than the control group ($p<0.05$).30 In the present study, there were no statistically significant correlations between serum leptin and PRL levels in both groups. In another study, 40 premenopausal women with prolactinoma or idiopathic hyperprolactinemia were compared to 41 age-matched healthy premenopausal women. There were positive correlations between serum leptin levels and body weight, BMI and waist circumference in the patient group ($p<0.05$).[31] In our study, positive, but insignificant correlations between serum leptin levels and body weight, BMI, waist circumference, waist/hip ratio, waist/height ratio, body fat percentage, and body fat weight in the diet group were observed. Increasing the number of cases may reveal significant results.

Weight loss is observed in patients receiving dopaminergic agonist treatment. Decrease in body weight with dopamine agonist therapy is associated with an increase in dopaminergic tone. In a study, it was shown that two years of treatment with bromocriptine (dopamine agonist) reduced body weight. However, serum leptin levels did not show a statistically significant difference at the end of two years.[27] Furthermore, Silva et al. evaluated 22 patients with prolactinoma.29 After six months of dopamine agonist treatment, serum PRL levels returned to normal, and HOMA-IR values, serum fasting glucose, LDL-cholesterol, and triglyceride levels decreased significantly ($p<0.05$).

In the literature, studies showing the effect of diets that induce weight loss by changing lifestyle and eating habits are insufficient in prolactinoma patients. In the present study, although serum leptin levels decreased in both goups, the change was significant only in the group implementing the diet in addition to medical treatment ($p=0.001$). Although dopamine agonist therapy may be considered as the potential driver of this situation, considering that both groups received that treatment, the significant difference may be attributed to the diet intervention in a relatively short time.

The main limitation of the present study was the small sample size. Besides, dopamine agonist treatment of all patients may be overshadowed by the effects of weight loss.

In the literature, the extent of scientific research conducted thus far is inadequate to truly determine the importance of weight loss in prolactinoma patients. This is the first study in Turkey about this topic. More comprehensive studies with an increased number of cases need to be designed to emphasize the importance of weight loss in prolactinoma patients.

Conclusion

In conclusion, our findings indicate that in addition to medical treatment of prolactinoma, applying a weight loss diet has a positive effect on the recovery process of the disease. The effect of dopamine agonist therapy on the metabolic profile seems to improve more rapidly in the presence of a weight loss diet. Depending on the magnitude of weight loss, patients with prolactinomas may need lower doses with a shorter duration of dopamine agonist treatment, as well as avoiding many obesity-related complications. Consequently, weight loss diet treatment should be offered in addition to medical treatment for overweight and obese patients with prolactinoma.

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