Serum Leptin Levels in Women with Uterine Leiomyomas

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SUMMARY

Objective: The purpose of this study was to examine the influence of leptin in women with uterine myoma.

Materials and Methods: In this study, 38 women with myoma uteri and 30 normal women who applied to the Dr Zekai Tahir Burak Woman Health Research and Education Hospital's gynecology clinic were enrolled. Uterine leiomyomas were proved by pathology postoperatively. In all subjects, FSH, LH, E2, prolactin, hemoglobin, hematocrit, blood urea nitrogen, creatinine, fasting glucose, CA125, and leptin were examined, and body mass index (BMI) was calculated. Data were analyzed by Student's *t* test and Mann-Whitney *U* test.

Results: Although leptin level was higher in the myomatic women (5.73 ± 4.08 ng/mL) than in the normal women, there was no statistically significant difference ($p = 0.303$). Also, no statistical difference in the ratios of leptin/BMI was found in both groups. A significant correlation was found between high E2 level and myoma uteri ($p = 0.021$). Hemoglobin levels were significantly lower in the myomatic women ($p = 0.044$). When we compared the leptin levels according to BMI, leptin levels were higher in patients who had BMI > 30 ($p = 0.02$).

Conclusion: We did not find any significant difference in serum leptin levels between the two groups. But leptin may have an indirect role in the pathogenesis of uterine leiomyoma. So further research is needed to reveal the role of leptin in myoma uteri pathogenesis. [*Taiwanese J Obstet Gynecol* 2007;46(1):33–37]

Key Words: body mass index, serum leptin levels, uterine leiomyoma

Introduction

Leptin is a protein encoded by the ob gene and appears to play an important role in energy expenditure, neuroendocrine-reproductive systems, and immune response [1,2]. Its concentration is related to the mass of adipose tissue [3]. There are several factors influencing circulating leptin levels. Gender and menapouse related differences in leptin levels have been reported [4]. The production of leptin is under a complex hormonal control [5]. Some studies have found that estrogens both *in vivo* [6,7] and *in vitro* [7] increase serum leptin, whereas androgens may show the opposite effect [8]. But some recent studies reported that hypogonadism does not influence serum leptin levels in women if body fat mass is unchanged [9,10].

Uterine leiomyomas are the most common pelvic tumors leading to hysterectomy [11]. Dietary fat intake, high body mass index (BMI), estrogen, and progesterone are well-known risk factors for myoma uteri [12,13]. These risk factors may also affect serum leptin levels [14]. Chan et al [15] reported decreased serum leptin levels in women with myoma uteri, and a recent study by Markowska et al [16] reported expression of the leptin gene both in myomas and in the surrounding myometrium but not in the myometrium of healthy women. In this study, effect of leptin on myoma uteri formation is examined.

Materials and Methods

Thirty-eight women with myoma uteri and 30 normal women who applied to Dr Zekai Tahir Burak Woman

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Health Research and Education Hospital's gynecology clinic were enrolled in this study. A written informed consent was obtained from each women and the study was approved by the Ethics Committee of our hospital. Uterine leiomyomas were proved by pathology after operation. No myoma uteri was detected in normal women by ultrasonographic examination. Women enrolled in this study were questioned carefully about their medical history and women with hypertension, chronic renal failure,diabetes mellitus, or chronic drug usage were excluded.

Serum samples of myomatic women and control group samples were collected in the proliferative phase of menstrual cycle. All samples were stored at −20°C until further analysis. In serum samples FSH, LH, E2, prolactin, hemoglobin, hematocrit, blood urea nitrogen (BUN), creatinine, fasting glucose, CA125, and leptin were examined. In both groups, BMI was calculated.

Serum leptin levels were measured using the BioSource Leptin Easia kit (BioSource Europe SA, Nivelles, Belgium).

Statistical analysis was performed with SPSS version 11.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics are presented as mean ± standard deviation. Intragroup comparisons were performed using Student's *t* test and Mann-Whitney *U* test; $p < 0.05$ was considered significant.

Results

The clinical characteristics and laboratory parameters of myomatic women and control group are shown in Table 1.

There was no significant difference between myomatic and normal women with respect to age, gravidity, parity, BMI, renal function tests, and blood glucose levels. Hemoglobin levels, however, were significantly lower ($p = 0.044$) in the myomatic women. The CA125, E2, FSH, LH, and prolactin levels for both groups are shown in Table 2.

There was no statistical difference in FSH, LH, CA125, and prolactin between the two groups. However, E2 level was significantly higher in the myomatic group ($p = 0.021$).

Serum leptin levels in the myomatic group was 5.73 ± 4.08 ng/mL, while it was 4.75 ± 3.53 ng/mL in the control group. Although leptin level was higher in the myomatic group, there was no significant difference ($p = 0.303$). There was also no statistically significant difference in the ratios of leptin/BMI between the two groups (Table 3).

Serum leptin levels in the myomatic group were evaluated according to the size of myoma uteri. Leptin levels in 21 patients who had myoma uteri < 5 cm were 6.35 ± 4.78 ng/mL. In 10 patients who had myoma

Table 1. Clinical characteristics and laboratory parameters*

	Myomatic group ($n = 38$)	Control group ($n = 30$)	*p*
Age (yr)	45.76 ± 4.12	44.13 ± 3.40	0.085
Gravidity	4.66 ± 1.90	4.60 ± 2.16	0.907
Parity	3.21 ± 1.26	3.10 ± 1.09	0.704
BMI (kg/m^2)	29.14 ± 3.93	27.65 ± 4.06	0.132
Hb (g/dL)	11.41 ± 2.15	12.46 ± 1.99	0.044
Hct (%)	35.83 ± 4.52	37.89 ± 4.64	0.069
BUN (mg/dL)	27.21 ± 6.45	26.67 ± 7.56	0.751
Glucose (mg/dL)	100.89 ± 19.86	94.17 ± 10.87	0.081
Creatinine (mg/dL)†	0.70	0.70	0.415

**Data are presented as mean ± standard deviation (Student's t test); †median value (Mann-Whitney U test). BMI = body mass index; BUN = blood urea nitrogen.*

Table 2. Serum levels of CA125 and hormones

	Myomatic group ($n = 38$)	Control group ($n = 30$)	*p*
CA125 (IU/mL)*	20.34 ± 9.93	17.36 ± 5.97	0.130
E2 (pg/mL)*	116.6 ± 89.16	77.23 ± 45.11	0.021
FSH (mIU/mL)†	9.16 ± 2.07	7.67 ± 1.97	0.309
LH (mIU/mL)†	5.02 ± 2.32	4.08 ± 2.53	0.338
PRL (ng/mL)†	16.05 ± 1.52	14.91 ± 1.79	0.543

**Mean ± standard deviation; †geometric mean ± standard deviation. BMI = body mass index.*

uteri > 5 cm, leptin levels were 5.29 ± 2.81 ng/mL. In seven patients in whom myoma uteri were > 5 cm and < 5 cm in size, leptin level was 4.49 ± 3.38 ng/mL. There was no significant difference among the three groups regarding leptin levels. There was a trend of leptin levels decreasing when the size of myoma uteri was increasing.

Leptin levels according to BMI were also compared. The whole study group was divided into the two groups: BMI > 30 and < 30. Forty-five patients had BMI < 30 and 23 patients had BMI > 30. There was statistically significant difference between the two groups ($p = 0.02$) (Table 4). Leptin levels were higher in patients who had BMI > 30.

Hemoglobin levels in the myomatic group were lower than in the control group. But there was no significant difference when hemoglobin and leptin levels were compared ($p = 0.372$) (Table 5).

Discussion

Uterine leiomyomas are the most common pelvic tumors leading to hysterectomy [11]. There are many known risk factors for myoma uteri such as dietary fat intake, high BMI, estrogen, and progesterone [12,13].

Leptin is a protein encoded by the ob gene and appears to play an important role in reproductive system [1,2]. So risk factors for myoma uteri may be involved in the regulation of leptin [14]. Chan et al reported lower serum leptin levels in the myomatic women than the normal women [15]. Recently, Markowska et al reported expression of the leptin gene both in myomas and in the surrounding myometrium but not in the myometrium of healthy women [16]. In our study, although leptin levels were higher in the myomatic group than in the control group, there was no significant difference. Some factors such as BMI, blood glucose levels, renal function tests, and age, which can affect serum leptin levels, were similar between our two study groups, so that does not explain the situation.

Nowicki et al also had similar results with our report indicating that 12 weeks of goserelin treatment in the myomatic group caused a significant regression of myoma but no change in plasma leptin level even after correction for fat mass [9]. BMI and body fat mass were the major determinants of plasma leptin, especially total body fat mass [6]. So direct measurement of body fat with DEXA would be better. Higher leptin levels in patients with high BMI in our study is consistent with other reports [4,6].

The role of sex steroids in the leptin production has been investigated. Both estrogen and androgen levels have been found to correlate with leptin levels [17,18]. Shimizu et al [19] and Cella et al [20] reported correlation between leptin and estradiol levels throughout the menstrual cycle, while Paolisso et al [21] indicated correlation with plasma progesteron, but not with estradiol. Most human studies that show a link between leptin and estradiol are cross-sectional [17] or observational [22]. In animal experiments in ovariectomized mice, the administration of estradiol did not influence circulating leptin levels, and ovariectomy did not change leptin secretion if it was not accompanied by changes in body fat mass [23]. But in recent reports, there is conflicting data about leptin levels after ovariectomy in rats; Chu et al [24] reported a decline in plasma leptin levels, while Pinilla et al [25] indicated an increase in plasma leptin levels after ovariectomy in rats.

Serum leptin concentrations throughout the menstrual cycle remain controversial. Some authors reported an increase in the luteal phase [19,26,27], while others reported no difference between follicular and luteal phases [28].

Gorden and Gavrilova reported that leptin therapy restores gonadotrophin secretion and menstrual cycle [29]. In our study, some patients from both groups had menstrual dysfunction. This may explain why we did not find a significant difference.

Immunologic factors in myoma uteri etiology have been investigated for years. Malyshkina et al [30] found impairment in differentiation of lymphocytes in rapidly

Table 3. Leptin levels and the ratio of leptin/body mass index (BMI)

	Myomatic group ($n = 38$)	Control group ($n = 30$)	p
Leptin (ng/mL)	5.73 ± 4.08	4.75 ± 3.53	0.303
Leptin/BMI	0.19 ± 0.12	0.17 ± 0.13	0.509

Table 4. Leptin levels according to body mass index (BMI)

	n	Leptin level (ng/mL)
BMI > 30	45	4.27 ± 3.15
BMI < 30	23	7.29 ± 4.38

Table 5. Leptin levels according to the hemoglobin levels of the study group

	n	Leptin level (ng/mL)
Hb < 11 g/dL	20	5.95 ± 4.03
Hb > 11 g/dL	48	5.02 ± 3.79

growing large myomas. Immunoregulatory properties of leptin on CD4+ T cells and immune system reconstitution by leptin therapy in leptin deficient patients have been reported [31]. So leptin administration may take place in myoma uteri treatment in the future.

In the literature, the leptin effect on myoma uteri formation is still uncertain. This may be due to many factors affecting leptin levels. In further research, all known factors affecting leptin levels, such as menstrual phase, age, BMI, total body fat, dietary, and exercise habits, must be matched very carefully with the control group with a large sample size. A study containing these strict criteria is still absent in the literature.

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