The effect of buserelin on plasma lipid and lipoprotein concentration during treatment of endometriosis

Nedim ÇİÇEK[1], Turhan ÇAĞLAR[1], Gülnur ÖZAKŞİT[1], Perran MÖRÖY[1], Ali HABERAL[2], Sertaç BATIOĞLU[1], Oya GÖKMEN[1]

[1] Dr.Zekai Tahir Burak Women's Hospital,
[2] Social Security Administration, Etlik Obst. and Gyn. Hospital, Ankara, TURKEY

The plasma changes of lipid and lipoprotein concentrations in patients with endometriosis were evaluated before treatment, every two months during 6 months course of medical treatment with buserelin and one month thereafter. In this study 103 patients with endometriosis laparoscopically diagnosed and staged according to the revised American Fertility Society (AFS) classification were given buserelin 800 pgr/day intra-nasally during a course of 6 months of medical treatment. Plasma levels of triglycerides, total cholesterol, low-density lipoprotein (LDL), very low density lipoprotein (VLDL) and high-density lipoprotein (HDL) concentrations were obtained in intervals mentioned above. Body weight was also followed. Buserelin had no adverse effects on serum lipoprotein concentrations and on body weight. [Turk J Med Res 1995; 13(2): 71-73)

Key Words: Buserelin, Endometriosis, Lipids, Lipoproteins

Endometriosis is a frequent disorder associated with infertility, pelvic pain, dysmenorrhea and dyspareunia. Therapy is determined by the reproductive goals and the extend of the disease. Various agents are used for the medical treatment.

Recent medical agent which produce hypoestrogenic environment are gonadotropin-releasing hormone analogues (GnRHa) (1). Buserelin (D-ser-CBu)-des-Gly[10]-LHDH) is a membt. of GnRH which is a decapeptide.

Since hormonal treatment of endometriosis and similar disorders extend over several months possible alterations in serum lipids must be taken into account. Lipoprotein metabolism is influenced in several ways by both estrogens and androgens. Androgenic steroids reduce the HDL apoprotein synthesis and induces hepatic lipase activity (2). GnRH analogues supress ovarian production of both androgens and estrogens. This difference in the androgenic millue may explain the difference in the lipid profile (3).

The present study was designed to evaluate the changes in serum lipids and lipoproteins in patients with pelvic endometriosis during and after the treatment with a GnRH analogue "Buserelin".

Received: Dec. 10,1994 **Accepted:** Jan. 10,1995

Correspondence: Nedim ÇİÇEK
Dr.Zekai Tahir Burak Women's Hospital,
Ankara, TURKEY

MATERIALS AND METHODS

103 women aged 29+0.8 SD years with laparoscopically diagnosed and staged endometriosis were studied. Characteristics of the study population are given in Table 1. Following diagnostic laparoscopy they received buserelin 4x200 mgr/day intranasally. Amenorrhea was observed in all patients and ovarian supression was confirmed by serial serum E2, LH and FSH measurements. Treatment was continued for six months. FSH, LH and E2 levels were evaluated using RIA. Phospho tungstic acid and magnesium ion precipitating method was used to determine HDL, VLDL, VDL levels.

Plasma levels of trigliserid, total cholesterol, LDL, VLDL and HDL concentrations were measured before the start of treatment and after 2, 4 and 6 months ^f therapy and one month thereafter. At the end of six months course of therapy a second-look laparoscopy was performed for restaging of endometriosis. At each visit weight was also recorded. Student's T test for dependent groups was used in the statistical evaluation of consective measurement of plasma lipids.

RESULTS

Before the initation of therapy the plasma lipid concentrations were within the normal range.

The serum total triglyceride concentration increased 2.7% after 2 months of treatment with buserelin, and remained unchanged after 4 months

Table 1. Characteristics of the study population

	MeaniSEM
No of women	103
Age (yr.)	29±0.8
Smokers	17
Endometriosis scores	29.0±7.0
Weight (kg)	
Before treatment	61.4±2.3
After treatment	62.7±3.3

Table 2. Plasma lipid concentrations

Test	Pretreatment	2nd month	4th month	6th month	Post treatment
Total cholesterol (mg/dl)	184±25	186±24	187+19	187±17	187±11
Trigliserid (mg/dl)	74i19	76±21	76±15	75±16	75±11
LDL (mg/dl)	87±9	86±8	88+11	87±9	86±8
VLDL (mg/dl)	24±6	23±7	25±5	25±9	22±9
HDL (mg/dl)	63±12	67±11	68±10	67±13	64±7

and decreased 1.3% after 6 months of treatment (Table 2). All of these changes were reflected as a statistically insignificant rise in total trigliserid concentrations.

The serum total cholesterol concentrations remained unchanged during the treatment. The serum level of total HDL cholesterol increased 6.2% in the second month, 7.8% in the fourth month and 6.2% in the sixth month of the treatment. In the post treatment period it returned to the baseline levels (Table 2).

In the LDL and VLDL fractions a slight decrease was observed in the second month of treatment but rose slightly above the baseline values in the fourth month and sixth month then fell below the baseline values in the post treatment period (Table 2). All of these changes were statistically insignificant.

DISCUSSION

The efficacy of buserelin acetate in endometriosis derives from a rapid "down regulation" of gonadotropin secretion and "medical oophorectomy" that is achieved within 1 month of therapy (4). This therapeutically induced hypoestrogenism is associated with temporary and reversible "menopausal" adverse effects, the most predominant of which is hot flush.

Danazol is an effective treatment for endometriosis but induces metabolic disturbances in lipid (5) and carbohydrate risk markers (6) for coronary heart disease. As an alternative GnRH agonists have the advantage of avoiding these metabolic changes.

In this study buserelin treatment was accompanied by a slight rise in the levels of antiatherogenic HDL but no change or slight decrease in the concentrations of LDL and VLDL. This had a favorable effect on the predictors of ischemic heart disease. Two of four previous investigations on the lipid effects of GnRH agonists in women were carried out with naferelin (7,8), one with buserelin (9) and one with leuprolide (10). Similar to the findings in all of these studies HDL cholesterol or total HDL rose during treatment with buserelin in our work. It is worth noticing that GnRHa treatment produced an increase in HDL cholesterol in men also (11). Treatment of endometriosis with GnRHa in this study revealing no difference is in LDL accordance with the findings of Henzl et al (7), but contrasts with the data of Johansen et al which found elevations in total and LDL cholesterol (8).

Dlugi et al (3), also found similar results in their study with buserelin. In principle GnRHa should operate by the same mechanism, but in theory there might be minor differences in their pharmacological and biochemical properties. Androgens rather than estrogens may determine the final effect of buserelin on lipoproteins. Buserelin use was accompanied by reduction in androgen levels (3).

Androgenic steroids reduce the HDL apoprotein synthesis rate in animal and humans while inducing hepatic lipase (2). This explains the induction of HDL concentration in danazol treatment. On the other hand reduced androgen levels in GnRHa treatment proceeds an increase in HDL concentration.

In conclusion GnRH analogues seems to be a good alternative to other medications for the treatment of endometriosis with no adverse effect on lipid profile.

Endometriosis tedavisinde buserelin'in plasma lipid ve lipoprotein seviyeleri üzerine etkisi

Buserelin ile tedavi edilen endometriosisli hastalarda plasma lipid ve lipoprotein konsantrasyonlarındaki değişmeler tedaviye başlamadan önce, 6 aylık tedavi süresince 2 ayda bir ve tedaviden 1 ay sonra değerlendirildi. Bu çalışmada laparoskopik olarak tanı konmuş ve revised American Fertility Society Klassifikasyonuna göre sınıflandırılmış 103 hastaya 6 ay süreyle 800 ngr/gün intranasal olarak "Buserelin" verildi. Yukarıda belirtilen intervallerle plasma trigliserid, total cholesterol, low-density lipoprotein (LDL), very low density lipoproteinler (VLDL) ve high density lipopro-

tein (HDL) konsantrasyonları ölçüldü. Vücut ağırlığı da takiplerde alındı. Sonuçlar; buserelinin vücut ağırlığı ve plasma lipoprotein konsantrasyonları üzerinde olumsuz bir etkisi olmadığını göstermektedir. [TurkJMedRes 1995; 13(2): 71-73]

REFERENCES

1. Steingold KA, Cedars M, Lu JKH et al. Treatment of endometriosis with a long acting gonadotropin-releasing hormone agonist. Obstet Gynecol 1987; 69:403-11.
2. Haffner SM, Kushwaka RS, Faster DM et al. Studies on the metabolic mechanism of reduced HDL during anabolic steroid therapy. Metabolism 1983; 32:413.
3. Dlugi AM, Rufo S, D'Amico JF et al. A comparison of the effect Buserelin versus Danazol on plasma lipoproteins during treatment of pelvic endometriosis. Fertil Steril 1988; 49:913.
4. Schriock E, Monroe SE, Henzl M et al. Treatment of endometriosis with a potent agonist of gonadotropin releasing hormone. Fertil Steril 1985; 44:583-8.
5. Valimaki M, Nilsson G, Rome R et al. Comparison between the effects of nafarelin and danazol on serum lipids and lipoproteins in patients with endometriosis. J Clin Endocrinol Metab 1989; 69:1097.
6. Bruce R, Godsland J, Stevenson JC et al. Danazol induces resistance to both insulin and glucagon in young women. Clin Sci1992; 82:211.
7. Henzl MR, Corson SL, Moghissi K et al. Administration of nasal nafarelin as compared with oral danazol for endometriosis: A multicenter double-blind comparative clinical trial. N Engl J Med 1988; 318:485.
8. Johansen JS, Riis BJ, Hassager C et al. The effect of a gonadotropin releasing hormone agonist analog on bone metabolism. J Clin Endocrinol Metab 1988; 67:701.
9. Fedele L, Bianchi S, Bocciolone L et al. Buserelin acetate in the treatment of pelvic pain associated with minimal and mild endometriosis; a controlled study. Fertil Steril 1993; 59:516.
10. Friedman AJ, Barbieri RL, Doubilet PM et al. A randomized, double blind trial of a gonadotropin releasing hormone agonist with or without medroxyprogesterone acetate in the treatment of leiomyoma uteri. Fertil Steril 1988; 49:404.
11. Goldberg RB, Rabin D, Alexander AN et al. Supression of plasma testesterone leads to an increase in serum total and HDL cholesterol and apoproteins A-1 and B. J Clin Endocrinol Metab 1987; 50:203.