

## laser vaporization

1

1

### The endocrine changes and alteration of the ovarian response to clomiphene citrate after laparoscopic laser vaporization in patients with polycystic ovary syndrome

Lee SJ · Kim JY · Park KH1

Department of Obstetrics and Gynecology, Kangbuk Samsung Medical Center, Sungkyunkwan  
University School of Medicine, Department of Obstetrics and Gynecology, Yonsei University School of  
Medicine1

corresponding address:

108

) 110-102

Tel: 02-2001-2194

Fax: 02-2001-2187

E-mail: jinyeongk@netscape.net

**Objectives:** Polycystic ovary syndrome(PCOS) has the feature of excessive LH, hyperandrogenism and disturbance of folliculogenesis. Also, insulin, IGF-I and IGFBP-1 are involved in the pathogenesis of PCOS. Various surgical and medical therapies have been used and the action mechanisms are related to the endocrine effect. Laparoscopic ovarian electrocautery or laser vaporization is effective in the restoration of ovulation and normal menstrual cycle with minimal invasive procedure especially in the patients resistant to medical therapy. Clomiphene citrate(CC) is used for the ovulation induction in PCOS and the resistance is known to be related to insulin, IGF-I, IGFBP-1 levels.

This study was performed to evaluate the effect of the laparoscopic laser vaporization on the levels of LH, FSH, testosterone, IGF-I and IGFBP - 1 and on the ovarian response to clomiphene citrate in patients with CC-resistant PCOS.

**Materials and Methods:** The fasting basal serum LH, FSH, testosterone, IGF-I and IGFBP - 1 level were measured in 10 PCOS patients with CC-resistance and 7 normal controls with regular menstrual cycle. In PCOS, after laparoscopic CO<sub>2</sub> laser vaporization, endocrine levels were measured in 1 week interval for 4 weeks and then compared with preoperative levels.

**Results:** In PCOS group, mean serum LH/FSH ratio, testosterone, IGF-I levels were higher and IGFBP-1 level was lower than control. LH/FSH ratio decreased from  $2.51 \pm 0.67$  to  $1.7 \pm 0.6$ ( $P < 0.05$ ) in 2 weeks, to  $0.56 \pm 0.2$ ( $P < 0.01$ ) in 3 week and to  $1.41 \pm 0.3$ ( $P < 0.01$ ) in 4 week after operation. Testosterone level decreased from  $1.51 \pm 0.82$ ng/ml to  $0.65 \pm 0.34$ ng/ml( $P < 0.05$ ) in 2 weeks, to  $0.56 \pm 0.67$ ng/ml( $P < 0.01$ ) in 3 weeks after operation. IGF-I level also decreased from  $436 \pm 47.5$   $\mu$ g/l to  $187 \pm 38$   $\mu$ g/l( $P < 0.01$ ) in 1 week, to  $167 \pm 42$   $\mu$ g/l( $P < 0.01$ ) in 2 weeks,  $179 \pm 55$   $\mu$ g/l( $P < 0.01$ ) in 3 weeks and to  $120 \pm 43$   $\mu$ g/l( $P < 0.01$ ) in 4 weeks after operation. IGFBP-1 level showed no significant change. In 8 of 10 PCOS patients, ovulation was induced with low dose clomiphene citrate.

**Conclusion:** Laparoscopic CO2 laser vaporization restores normal menstrual cycle and ovulation through endocrine effect of decreasing LH/FSH ratio, testosterone and IGF-I level and increases the response to CC. Therefore it is useful for restoration of normal menstruation and induction of ovulation in CC resistant PCOS patients.

---

**Key words :** Laparoscopic laser vaporization, Endocrine effect, CC response, Polycystic ovary syndrome

(Polycystic ovary syndrome, PCOS) ,

(hyperandrogenism), ,

.1),2) (LH)

thecal cell (androgen) 가

(folliculogenesis) 가 ,3) Stein (1935)4)

wedge resection ,

가 LH

.5),6) wedge resection (ovarian electrocautery) ,7)

laser LH androstenedione, testosterone (sex hormone binding globulin, SHBG) 가 ,8)-12)

가 .13)

PCOS (insulin) (insulin like growth factor, IGF), factor) system (insulin like growth factor binding protein, IGFBP) (growth ,14)15) PCOS IGF-I 가, IGFBP-1 ,16),17) IGF-I IGFBP-1 가 PCOS androgen ,18) , SHBG IGFBP-1 가 IGF-I .19) (clomiphen citrate) antiestrogen gonadotropin 가 , antiestrogen 가 obesity IGF, IGFBP .20)

PCOS CO2 laser vaporization LH, IGF-I, IGFBP-1

10 PCOS , PCOS  
 , LH, FSH LH/FSH 2.0 ,  
 hirsutism . 28.2 ( : 23-39 ),  
 3.5 , 150mg  
 LH, FSH, testosterone, IGF-I IGFBP-1  
 . LH, FSH Amerelex LH, FSH kit(American International Plc, U.K.)  
 , testosterone RIA , IGF-I, IGFBP-1  
 immunoenzyme assay(Medix Biochemica, Kannainen, Finland)  
 7  
 , laser vaporization 1 4  
 t-test Tukey-Kramer  
 multiple comparisons test  
 2 puncture technique , coupler CO2 laser set  
 , 25W CO2 laser 5-10 1mm focal diameter  
 vaporization , hole diameter 2-4mm 25-40 hole  
 Ringer's lactate irrigation  
 가 5 50mg 5  
 , 3 가  
 가 150mg  
 E2, progesterone

LH/FSH , testosterone, IGF-I 가

IGFBP-1 (Table 1).

(Body mass index, BMI) 가 1, 2, 3,

4 Fig.1 , LH/FSH

2.51 ± 0.67(Mean ± SD) 2 1.7 ± 0.6 (P<0.05),

3 0.56 ± 0.2(P<0.01), 4 1.41 ± 0.3(P<0.01) . testosterone

1.51 ± 0.82 2 0.65 ± 0.34(ng/ml) (P<0.05),

3 0.56 ± 0.67(ng/ml) (P<0.01). IGF-I 436 ± 47.5(μ g/l)

1 187 ± 38(μ g/l) (P<0.01), 2 167 ± 42 μ g/l(P<0.01), 3

179 ± 55 μ g/l(P<0.01), 4 120+43 μ g/l(P<0.01) . IGFBP-1

(Fig.1). 10 7 4-6

가 50mg 5 5

. 3 3 가

가

7 3 1 8

2 150mg .

Table 1. Endocrine characteristics of control and PCOS

	Control	PCOS
No. of patients	7	10
LH/FSH	1.15 ± 0.32	2.51 ± 0.67
Testosterone(ng/ml)	0.61 ± 0.37	1.51 ± 0.82
BMI(Kg/m <sup>2</sup> )	21.9 ± 0.7	22.9 ± 1.1
IGF-I( g/l)	287.4 ± 27.1	436 ± 47.5
IGFBP-1( g/l)	8.8 ± 2.4	2.7 ± 0.2

PCOS: polycystic ovary syndrome

Mean ± SD(standard deviation)

p< 0.01

Fig. 1. Comparison of endocrine level of control and PCOS and changes before and after laparoscopic CO2 laser vaporization in PCOS (Mean  $\pm$  SD, \*P<0.05, \*\*P<0.01)

PCOS ovarian wedge resection 4)

LH, testosterone, androstenedione  
.5),6) wedge resection

,  
,7)

wedge resection  
laser vaporization 83-92% .7),21)

wedge resection LH androgen  
inhibin  
androgen level

,8) PCOS testosterone, androstenedione, LH, DHEA-S 가  
22),23) laser 가  
, SHBG 가 ,8)24) negative feed back

.8)-11),21),25) 70-90%

.8)-11) GnRH FSH/LH 가 25)  
hMG 가 .26)

androgen negative feedback LH가 가  
가 estradiol 가 negative feed back 가 LH 가  
FSH negative feedback inhibin 가

.27) inhibin level  
.12) androgen LH

, 1-2 가 ,7)

Gjonnaess (1998) 18-20  
.24)

LH가 가 , LH  
가가 ,8),12),28)

PCOS LH ,13)

가  
.29)

(diathermy point) 3-8 point7) 8-10 point21)  
Naether (1993) testosterone

가 ,30) Armar (1990) 4 point 가

.11) unipolar electrocautery

가

PCOS insulin IGF(insulin-like growth factor) IGFBP(insulin-like growth  
factor binding protein)가 ,31) hyperinsulinemia IGF-I 가  
IGFBP-1 , insulin IGFBP-1 SHBG level

level , hyperinsulinemia IGFBP-1  
PCOS IGFBP-1 . IGFBP-1 IGF-I

가 insulin IGF-I thecal cell LH androgen  
. antiestrogen 가 PCOS ,32)

75-85% , , insulin, IGF-I,  
IGFBP-1 level .33) PCOS

GnRH-agonist 29)

, LH androgen 가 ,  
 가 FSH LH 가  
 .29) PCOS IGF-I IGFBP-1 가, SHBG  
 가 androgen  
 가 estrogen 가 granulosa cell IGFBP-1  
 가 ,18) androgen SHBG 가 가  
 .34) insulin IGFBP-1  
 ,18) PCOS insulin .35)  
 , insulin SHBG IGFBP-1 가  
 , insulin .36)  
 insulin, IGF IGFBP  
 insulin IGFBP-1 level insulin  
 LH 가  
 .36)  
 PCOS LH, testosterone 가 , IGF-I 가,  
 IGFBP-1 , laser vaporization 1-2 LH  
 testosterone 가 . laser vaporization  
 , resource  
 .10),37) IGFBP -1 level 가 IGF-I level  
 36) , IGF-I tropic hormone local  
 factor , IGF-I thecal-interstitial cell granulosa cell IGF-II mRNA가  
 , IGF-I thecal-interstitial cell insulin thecal cell  
 steroidogenesis ,38) local factor 가  
 IGF-I level 가 ,  
 가 IGFBP-1 theca-stroma cell steroidogenesis  
 IGFBP-1 insulin level ,39)  
 PCOS insulin level  
 insulin IGFBP-1 가 가 .  
 IGFBP-1 가 LH/FSH testosterone, IGF-I level ,  
 10 8  
 , laser vaporization LH, testosterone IGF-I  
 가 , laser  
 vaporization IGFBP-1 insulin .  
 testosterone IGF-I laser vaporization LH,  
 , PCOS  
 , laser vaporization PCOS IGF IGFBP  
 가 .



1. Dunaif A, Segal KR, Futterweit W, Dobrjansky A. Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. *Diabetes* 1989;38:1165-74.
2. Barbieri RL. Hyperandrogenism, insulin resistance and acanthosis nigricans: Ten years of progress. *J Reprod Med* 1994;39:327-36.
3. Baird DT, Corker CS, Davidson DW, Hunter WM, Michie EA, VanLook PDA. Pituitary-ovarian relationships in polycystic ovary syndrome. *J Clin Endocrinol Metab* 1977;45:798-809.
4. Stein KF, Leventhal ML. Amenorrhea associated with bilateral polycystic ovaries. *Am J Obstet Gynecol* 1935;29:181-91.
5. Lloyd DW, Lobotsky J, Segre EF, Kobayaski T, Taymor ML, Batt RE. Plasma testosterone and urinary 17-ketosteroids in women with hirsutism and polycystic ovaries. *J Clin Endocrinol Metab* 1966;26:314-24.
6. Judd HL, Figg LA, Anderson DC, Yen SS. The effects of ovarian wedge resection on circulating gonadotropin and ovarian steroid levels in patients with polycystic ovary syndrome. *J Clin Endocrinol Metab* 1976;43:347-55.
7. Gjonnaess H. Polycystic ovarian syndrome treated by ovarian electrocautery through the laparoscope. *Fertil Steril* 1984;41:20-5.
8. Aakvaag A, Gjonnaess H. Hormonal response to electrocautery of the ovary in patients with polycystic ovarian disease. *Br J Obstet Gynecol* 1985;92:1258-64.
9. Gjonnaess H, Norman N. Endocrine effects of ovarian electrocautery in patients with polycystic ovarian disease. *Br J Obstet Gynecol* 1987;94:779-83.
10. Daniell JF, Miller W. Polycystic ovaries treated by laparoscopic laser vaporization. *Fertil Steril* 1989;51:232-6.
11. Armar NA, Holownia P, McGarrigle HHG, Jacobs HS, Honour J, Lachelin GCL. Laparoscopic ovarian diathermy in the management of anovulatory infertility in women with polycystic ovaries: endocrine changes and clinical outcome. *Fertil Steril* 1990;53:45-49.
12. Kovacs G, Buckler H, Bangah M, Outch K, Burger H, Healy D, et al. Treatment of anovulation due to polycystic ovarian syndrome by laparoscopic ovarian electrocautery. *Br J Obstet Gynecol* 1991;98:30-35.
13. Balen AH, Jacobs HS. A prospective study comparing unilateral and bilateral laparoscopic ovarian diathermy in women with the polycystic ovary syndrome. *Fertil Steril* 1994;62:921-5.
14. Barbieri RL, Smith S, Ryan KJ. The role of hyperinsulinemia in the pathogenesis of ovarian hyperandrogenism. *Fertil Steril* 1988;50:197-212.
15. Iwashita M, Mimuro T, Watanabe M, Setoyama T, Matsuo A, Adachi T, et al. Plasam levels of insulin-like growth factor-I and its binding protein in polycystic ovary syndrome. *Horm Res* 1990;33(suppl.2):21-6.
16. Urdl W. Polycystic ovarian disease : endocrinological parameters with specific reference to growth hormone and somatomedin-C. *Arch Gynecol Obstet* 1988;243:13 - .
17. Suikkari AM, Ruutiainen K, Erkkola R, Seppala M. Low levels of low molecular weight insulin-like growth factor-binding protein in patients with polycystic ovarian disease. *Hum Reprod* 1989;4:136-9.
18. Suikkari AM, Seppala M, Tiitinen A, Laatikainen T, Stenman UH. Oral contraceptives increase insulin-like growth factor binding protein-1 concentration in women with polycystic ovarian disease. *Fertil Steril* 1991;55:895-9.
19. Kiddy DA, Hamilton-Fairley D, Seppala M, Koistinen R, James VHT, Reed MJ, et al. Diet-induced changes in sex hormone binding globulin and free testosterone in women with normal or polycystic ovaries: correlation with serum insulin and insulin-like growth factor-I. *Clin Endocrinol* 1989;31:757-63.
20. Tiitinen AE, Laatikainen TJ, Seppala MT. Serum levels of insulin-like growth factor binding protein-1 and ovulatory responses to clomiphene citrate in women with polycystic ovarian disease. *Fertil Steril* 1993;60:58-62.
21. Greenblatt E, Casper RF. Endocrine changes after laparoscopic ovarian cautery in polycystic ovarian syndrome. *Am J Obstet Gynecol* 1987;156:279-85.
22. Lobo RA, Kletzky OA, Campeau JD, diZerega GS. Elevated bioactive luteinizing hormone in women with the polycystic ovary syndrome. *Fertil Steril* 1983;39:674-8.
23. Lobo RA, Shoupe D, Chang SP, Campeau J. The control of bioactive luteinizing hormone secretion in women with polycystic ovary syndrome. *Am J Obstet Gynecol* 1984;148:423-8.
24. Gjonnaess H. Late endocrine effects of ovarian electrocautery in women with polycystic ovary

syndrome. *Fertil Steril* 1998;69:697-701.

25. Gjonnaess H, Norman N. Endocrine effect of ovarian electrocautery in patients with polycystic ovary syndrome. *Br J Obstet Gynaecol* 1987;94:779-783.

26. Gadir AA, Alnaser HMI, Mowafi RS, Shaw RW. The response of patients with polycystic ovarian disease to human menopausal gonadotropin therapy after ovarian electrocautery or a luteinizing hormone-releasing hormone agonist. *Fertil Steril* 1992;57:309-13.

27. Sakata M, Terakawa N, Tasaka K, Miyake A, Kurachi H, Tanizawa O. Changes of bioactive luteinizing hormone after laparoscopic ovarian cautery in patients with polycystic ovarian syndrome. *Fertil Steril* 1990; 53:610-13.

28. Kovacs G T, Pepperell RJ, Evans JH. Induction of ovulation with human pituitary gonadotropin(HPG)-the Australian experience. *Aust NZ J Obstet Gynaecol* 1989;29:315-8.

29. Gadir AA, Khatim MS, Mowafi RS, Alnaser HMI, Alzaid HGN, Shaw RW. Hormonal changes in patients with polycystic ovarian disease after ovarian electrocautery or pituitary desensitization. *Clin Endocrinol* 1990;32:749-54.

30. Naether OGJ, Geiger-Kotzler L, Fischer R, Delfs T, Weise HC, Rudolf K. Laparoscopic electrocoagulation of the ovarian surface in infertile patients with polycystic ovarian disease. *Fertil Steril* 1993;30:88-94.

31. Insler V, Lunenfeld B. Pathophysiology of polycystic ovarian disease : new insights. *Hum Reprod* 1991;6:1025-9.

32. Franks S, Adams J, Mason H, Polson D. Ovulatory disorders in women with polycystic ovary syndrome. *Clin Obstet Gynaecol* 1985;12:605-33.

33. Tiitinen AE, Laatikainen TJ, Seppala MT. Serum levels of insulin-like growth factor binding protein -1 and ovulatory responses to clomiphene citrate in women with polycystic ovarian disease. *Fertil Steril* 1993;60:58-62.

34. Gjonnaess H. Comparison of ovarian electrocautery and oral contraceptives in the treatment of hyperandrogenism in women with polycystic ovary syndrome. *Acta Obstet Gynecol Scand* 1999;78:530-3.

35. Geffner ME, Kaplan SA, Bersch N, Golde DW, Landaw EM, Chang RJ. Persistence of insulin resistance in polycystic ovarian disease after inhibition of ovarian steroid secretion. *Fertil Steril* 1986;45:327-33.

36. Tiitinen A, Tenhunen A, Seppala M. Ovarian electrocauterization causes LH-regulated but not insulin-regulated endocrine changes. *Clin Endocrinol* 1993; 39:181-84.

37. Cohen BM. Laser laparoscopy for polycystic ovaries. *Fertil Steril* 1989;52:167-8.

38. Bergh C, Carlsson B, Olsson JH, Selleskog U, Hillensjo T. Regulation of androgen production in cultured human thecal cells by insulin-like growth factor I and insulin. *Fertil Steril* 1993;59:323-31.

39. Mason H, Davis SC, Franks S, Holly JMP. Insulin-like growth factor I and II(IGF I and II) and IGF binding proteins are produced by normal and polycystic human ovaries(abstract 33). *J Endocrinol* 1991;131(suppl).

: LH, insulin, IGF-I IGFBP-1 , 가 laser vaporization insulin, IGF IGFBP CO2 laser vaporization LH, FSH, testosterone, IGF-I IGFBP-1

: 10 7 LH, FSH, testosterone, IGF-I IGFBP-1 level CO2 laser vaporization 1 4

: LH/FSH , testosterone, IGF-I IGFBP-1 LH/FSH 2.51 ± +0.67 2 1.7 ± 0.6(P<0.05) , 3 0.56 ± 0.2(P<0.01), 4 1.41 ± 0.3(P<0.01) Testosterone 1.51 ± 0.82ng/ml 2 0.65 ± 0.34ng/ml(P<0.05), 3 0.56 ± 0.67ng/ml(P<0.01) IGF-I 436 ± 47.5 μ g/l 1 187 ± 38 μ g/l(P<0.01) , 2 167 ± 42 μ g/l(P<0.01), 3 179 ± 55 μ g/l(P<0.01), 4 120+43 μ g/l(P<0.01) IGFBP-1 가 . 10 8

: CO2 laser vaporization LH/FSH , testosterone IGF-I 가 가