

The Effect of Laparoscopic Ovarian Electrocautery in Pregnancy Rate in Metformin- and Clomiphene Citrate-Resistant Infertile Women

Zahra Rezaei¹, Mehrnaz Valadan, Pooneh Shojaee Asl*

Department of Obstetrics and Gynecology, Yas Women General Hospital, Tehran University of Medical Sciences, Tehran, Iran



Article Info

doi [10.30699/jogcr.5.3.84](https://doi.org/10.30699/jogcr.5.3.84)

Received: 2020/09/30;

Accepted: 2020/10/19;

Published Online: 25 Nov 2020;

Use your device to scan and read the article online



Corresponding Information:

Pooneh Shojaee Asl,

Department of Obstetrics and Gynecology,
Yas Women General Hospital, Tehran
University of Medical Sciences, Tehran, Iran
Email: shojaee.pooneh@yahoo.com

ABSTRACT

Background & Objective: Insulin resistance can be seen in most overweight women with polycystic ovary syndrome (PCOS). Insulin resistance seems to play a key role in the pathophysiology of PCOS and infertility. This study aimed to evaluate the effects of insulin resistance on pregnancy rate and regulation of the menstrual cycle following laparoscopic ovarian electrocautery (LOE).

Materials & Methods: This prospective cohort study was conducted on 54 infertile metformin- and clomiphene citrate-resistant women with PCOS at Yas Hospital in 2007. These patients initially took a glucose tolerance test and then classified into two groups (i.e., insulin-resistant and non-insulin-resistant) based on the obtained results. Both groups, then, underwent LOE. Patients were evaluated for pregnancy rate and regulation of the menstrual cycle up to six months.

Results: Out of 54 patients, 37 patients (68.5%) were non-insulin-resistant, and 17 patients (31.5%) were insulin-resistant. In the insulin-resistant group, after six months, menstrual cycles were less regular than those of the non-insulin-resistant group (OR=0.2; 95%CI, 0.07-0.87).

Conclusion: Insulin resistance can be an important marker of the poor outcomes of PCOS infertility treatment, and LOE significantly improves insulin resistance in women with PCOS.

Keywords: Polycystic ovary syndrome, Insulin resistance, Laparoscopic ovarian electrocautery, Pregnancy



Copyright © 2020. This is an original open-access article distributed under the terms of the Creative Commons Attribution-noncommercial 4.0 International License which permits copy and redistribution of the material just in noncommercial usages with proper citation.

Introduction

Polycystic ovary syndrome (PCOS) is the most prevalent reason for anovulatory infertility in reproductive-age women (1-3). The first-line treatment in PCOS patients is clomiphene citrate (CC); however, 20%-25% of the women do not respond to CC treatment (4-7).

At present, the recombinant follicle stimulation hormone (rFSH) is broadly prescribed, but it has some disadvantages, including high costs, necessity for extensive monitoring, and risk of multiple pregnancies. Laparoscopic approaches, including biopsy, electrocautery, and laser, are alternative treatments with very little morbidity, and minimum risk of multiple pregnancies (8).

In addition, insulin resistance is seen in most overweight patients with PCOS, and it is estimated that up to 65% of these patients suffer from this problem. Conversely, its prevalence is estimated to be nearly 20% among normal-weight patients with PCOS (9-12).

Some researchers have suggested that hyperinsulinemia occurred as a result of this condition may increase the luteinizing hormone (LH)-stimulated androgen production from ovarian theca cells (13-15). This effect may be due to the direct influences of insulin on theca cells (16) or biological activity of growth factors, such as insulin-like growth factor (IGF)-I/II or binding proteins (17, 18).

The current study aimed to determine the effect of insulin resistance on pregnancy rate and regulation of the menstrual cycle following laparoscopic ovarian electrocautery (LOE) in metformin- and clomiphene citrate-resistant patients with PCOS referred to Yas Hospital, Tehran, Iran (2007).

Materials and Methods

This prospective cohort study was conducted on 54 infertile metformin- and clomiphene citrate-resistant women with PCOS at Yas Hospital in 2007.

Inclusion criteria included being diagnosed with PCOS and having a history of treatment with CC up to 150 mg for five days with not responding to the treatment, as well as having a history of treatment with metformin 500 mg three times a day for three months with normal thyroid function and prolactin level, normal hysterosalpingography, and normal semen analysis of the patients' husbands according to the World Health Organization (WHO) criteria.

Women with underlying diseases or chronic diseases, such as Cushing's syndrome, androgen-secreting tumors, hyperprolactinemia, and diabetes mellitus, were excluded. Also, patients who withdrew to participate at any time during the study were excluded.

This research was conducted in compliance with the Helsinki Declaration and approved by the local ethics committee. All the patients signed informed consent.

According to a study conducted by Dale *et al.* (19), pregnancy rate in the insulin-resistant and non-insulin-resistant groups were 18% and 50%, respectively. Their sample size included 17 patients in each group (a total of 34 patients) with a power of 80% and type I error of 0.05.

Then, the eligible patients underwent the glucose tolerance test performed by assessing two-hour glucose and insulin after the administration of 75 g of glucose. Patients with an insulin level of more than or equal to 150 mIU/L were regarded as the insulin-resistant group, and patients with an insulin level of less than 150 mIU/L were considered as the non-insulin-resistant group.

Next, patients had LOE by undergoing general anesthesia (by diathermy of 1.75 MHz and a power of 60 W), and eight points were pierced in each ovary. The follow-up time was six months, and primary outcomes were the regulation of menstrual cycles and occurrence of clinical pregnancy.

Data analysis was carried out in SPSS version 16 (SPSS Inc., Chicago, Ill., USA), the independent

samples *t* test or the Mann-Whitney U test was used to compare the means in the two groups. The chi-squared test or Fisher's exact test was utilized to compare the ratios. The logistic regression test was employed to evaluate the effect of variables in predicting pregnancy. A P-value of less than 0.05 was considered significant.

Results

Out of these 54 women, 37 patients (68.5%) were non-insulin-resistant, and 17 patients (31.5%) were insulin-resistant.

There was no significant difference between the two groups in baseline characteristics, including age, body mass index (BMI), frequency of BMI<25 and BMI≥25, type of primary or secondary infertility, hirsutism, and pre-treatment cycle status. Only, the duration of infertility in the insulin-resistant group was significantly ($P=0.020$) higher than that of the non-insulin-resistant group (Table 1).

In the insulin-resistant group, after six months, menstrual cycles were less regular than those of the non-insulin-resistant group (OR=0.2; 95% CI, 0.07-0.87).

Fifteen (40.5%) women in the non-insulin-resistant group became pregnant; one pregnancy ended in miscarriage, one pregnancy was preterm, five pregnancies were term, and eight pregnancies continued. In addition to LOE, two cases underwent in vitro fertilization (IVF), and one case had intrauterine insemination (IUI). The pregnancy rate that occurred because of LOE alone was 32.4%.

In contrast, three (17.6%) women in the insulin-resistant group became pregnant; one pregnancy ended in miscarriage, one pregnancy was term, and one pregnancy continued.

In the logistic regression analysis, the results demonstrated that age, duration of infertility, BMI, and insulin resistance had no significant effects on pregnancy rate (Table 2).

Table 1. A comparison of the insulin-resistant and non-insulin-resistant groups

Variables	Insulin-resistant	Non-insulin-resistant	P-value
Age	29±4.4	27.2±3.7	0.100
Duration of infertility	7.1±4.01	4.5±2.8	0.020
BMI	27.6±3.8	26.8±3.6	0.400
Hirsutism	13 (76.5%)	26 (70.3%)	0.600
Regulation of the cycle after the treatment	6 (35.3%)	25 (67.6%)	0.020
BMI≥25	13 (76.4%)	24 (64.8%)	0.300
Pregnancy rate	3 (17.6%)	15 (40.5%)	0.090

BMI: body mass index.

Table 2. The logistic regression analysis considering the effects of age, duration of infertility, BMI, and insulin resistance on pregnancy rate

Variables	P-value	OR	95% C.I. for OR	
			Lower	Upper
Constant	0.040	1474.5		
Age	0.070	0.8	0.6	1.08
Duration of infertility	0.056	1.2	0.9	1.6
BMI	0.100	0.8	0.7	1.05
Insulin resistance	0.060	0.2	0.04	1.1

Discussion

In this study, out of 54 women, 37 patients (68.5%) were non-insulin-resistant, and 17 patients (31.5%) were insulin-resistant. In the insulin-resistant group, after six months, menstrual cycles were less regular than those of the non-insulin-resistant group (OR=0.2; 95% CI, 0.07-0.87).

Dale *et al.* (19) examined the effect of insulin resistance on pregnancy rate in 64 infertile women with PCOS treated with LOE (28 insulin-resistant patients and 36 non-insulin-resistant patients). Their results showed that after LOE, the non-insulin-resistant group achieved a regular menstrual cycle, and ovulation was more frequent than the insulin-resistant group. Subsequently, 18 patients (50%) of the non-insulin-resistant group became pregnant, while only five patients (18%) achieved successful pregnancies in the insulin-resistant group. Finally, following the LOE and IVF treatment, 27 non-insulin resistant patients (75%) achieved successful pregnancies compared to 13 insulin-resistant patients (46%) who became pregnant. They concluded that insulin resistance might be one of the key markers of the poor outcome of treatment in PCOS infertility.

Moreover, Seow *et al.* (20) demonstrated that LOE significantly improves insulin resistance in women with PCOS. Before LOE, two-hour glucose, fasting, and two-hour insulin levels of the insulin-resistant group were significantly higher than those of the control group; however, after the surgery, the glucose and insulin levels were significantly reduced.

In this study, the total pregnancy rate was 33.3% after LOE. In former studies, pregnancy rates ranged from 41% to 80% (21). The causes of the lower pregnancy rate in our study could be the effect of other parameters, including the type of infertility, age at menarche, cycle history, size of the ovary, and LH/FSH ratio that we did not evaluate them. Speaking of which, the LH/FSH ratio is the most predictive factor for ovarian response after electrocautery (8).

This study had some limitations; we did not measure alteration in serum LH and FSH levels after LOE;

further, the limited sample size and lack of consideration to other infertility concurrent causes in participants (such as endometriosis) were the other limitations.

Conclusion

Insulin resistance can be an important marker of the poor outcomes of PCOS infertility treatment, and LOE significantly improves insulin resistance in women with PCOS. Although the pregnancy rate was higher in the non-insulin-resistant group, no significant difference was observed in the two groups. Accordingly, more studies are needed to evaluate the effects of different treatments for insulin-resistance and hyperinsulinemia on ovulation induction.

Acknowledgments

The authors thank all those who helped them writing this article.

Conflict of Interest

Authors declared no conflict of interests.

References

1. Adams J, Polson DW, Franks S. Prevalence of polycystic ovaries in women with anovulation and idiopathic hirsutism. *Br Med J (Clin Res Ed)*. 1986;293(6543):355-9. [DOI:10.1136/bmj.293.6543.355] [PMID] [PMCID]
2. Nardo LG, Patchava S, Laing I. Polycystic ovary syndrome: pathophysiology, molecular aspects and clinical implications. *Panminerva Med*. 2008 Dec;50(4):267-78.
3. Mortada R, Williams T. Metabolic Syndrome: Polycystic Ovary Syndrome. *FP Essent*. 2015 Aug;435:30-42.
4. Imani B, Eijkemans MJ, te Velde ER, Habbema JD, Fauser BC. Predictors of patients remaining anovulatory during clomiphene citrate induction of ovulation in

- normogonadotropic oligoamenorrheic infertility. *J Clin Endocrinol Metab.* 1998;83(7):2361-5. [DOI:10.1210/jc.83.7.2361] [PMID]
5. Shoham Z, Weissman A. Polycystic ovarian disease: obesity and insulin resistance. In: Kempers RD, Cohen J, Haney AF, Younger JB, eds. *Fertility and reproductive medicine.* Amsterdam, New York, Oxford, Shannon, Singapore, Tokyo: Elsevier, 1998:263-72.
 6. Franks S. Polycystic ovary syndrome. *N Engl J Med* 1995;333:853-61.[Erratum, *N Engl J Med* 1995;333:1435.] [DOI:10.1056/NEJM199509283331307] [PMID]
 7. Franks S, Adams J, Mason H, Polson D. Ovulatory disorders in women with polycystic ovary syndrome. *Clin Obstet Gynecol* 1985;12:605-32
 8. van Wely M, Bayram N, van der Veen F, Bossuyt PM. Predictors for treatment failure after laparoscopic electrocautery of the ovaries in women with clomiphene citrate resistant polycystic ovary syndrome. *Hum Reprod.* 2005;20(4):900-5. [DOI:10.1093/humrep/deh712] [PMID]
 9. Dale PO, Tanbo T, Djoseland O, Jervell J, Abyholm T. Persistence of hyperinsulinemia in polycystic ovary syndrome after ovarian suppression by gonadotropin-releasing hormone agonist. *Acta Endocrinol (Copenh).* 1992;126(2):132-6. [DOI:10.1530/acta.0.1260132] [PMID]
 10. Dale PO, Tanbo T, Haug E, Abyholm T. The impact of insulin resistance on the outcome of ovulation induction with low-dose follicle stimulating hormone in women with polycystic ovary syndrome. *Hum Reprod.* 1998;13(3):567-70. [DOI:10.1093/humrep/13.3.567] [PMID]
 11. Gjonnaess H. Ovarian electrocautery in the treatment of women with polycystic ovary syndrome (PCOS). Factors affecting the results. *Acta Obstet Gynecol Scand.* 1994 May; 73(5): 407-12. [DOI:10.3109/00016349409006253] [PMID]
 12. Gjonnaess H, Norman N. Endocrine effects of ovarian electrocautery in patients with polycystic ovarian disease. *Br J Obstet Gynaecol.* 1987; 94(8): 779-83. [DOI:10.1111/j.1471-0528.1987.tb03726.x] [PMID]
 13. Gadir AA, Khatim MS, Mowafi RS, Alnaser HM, Alzaid HG, Shaw RW. Hormonal changes in patients with polycystic ovarian disease after ovarian electrocautery or pituitary desensitization. *Clin Endocrinol (Oxf).* 1990; 32(6): 749-54. [DOI:10.1111/j.1365-2265.1990.tb00921.x] [PMID]
 14. Barbieri RL, Makris A, Randall RW, Daniels G, Kistner RW, Ryan KJ. Insulin stimulates androgen accumulation in incubations of ovarian stroma obtained from women with hyperandrogenism. *J Clin Endocrinol Metab.* 1986; 62(5): 904-10. [DOI:10.1210/jcem-62-5-904] [PMID]
 15. 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(1): 58-62. [DOI:10.1016/S0015-0282(16)56036-1]
 16. Barbieri RL, Makris A, Ryan KJ. Insulin stimulates androgen accumulation in incubations of human ovarian stroma and theca. *Obstet Gynecol.* 1984; 64(3 Suppl): 73S-80S. [DOI:10.1097/00006250-198409001-00019] [PMID]
 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(2): 136-9. [DOI:10.1093/oxfordjournals.humrep.a136858] [PMID]
 18. Hernandez ER, Resnick CE, Holtzclaw WD, Payne DW, Adashi EY. Insulin as a regulator of androgen biosynthesis by cultured rat ovarian cells: cellular mechanism(s) underlying physiological and pharmacological hormonal actions. *Endocrinology.* 1988; 122(5): 2034-43. [DOI:10.1210/endo-122-5-2034] [PMID]
 19. Dale PO, Tanbo T, Ertzeid G, Bjerkke S, Oldereid N, Fedorcsak P, et al. The impact of insulin resistance on the outcome of laparoscopic ovarian electrocautery in infertile women with the polycystic ovary syndrome. *Gynecol Endocrinol.* 2004; 19(4): 182-9. [DOI:10.1080/09513590400012093] [PMID]
 20. Seow KM, Juan CC, Hsu YP, Hwang JL, Huang LW, Ho LT. Amelioration of insulin resistance in women with PCOS via reduced insulin receptor substrate-1 Ser312 phosphorylation following laparoscopic ovarian electrocautery. *Hum Reprod.* 2007; 22(4): 1003-10. [DOI:10.1093/humrep/del466] [PMID]
 21. Kriplani A, Manchanda R, Agarwal N, Nayar B. Laparoscopic ovarian drilling in clomiphene citrate-resistant women with polycystic ovary syndrome. *J Am Assoc Gynecol Laparosc.* 2001;8(4):511-8. [DOI:10.1016/S1074-3804(05)60613-5]

How to Cite This Article:

Rezaei Z, Valadan M, Shojaee Asl P. The Effect of Laparoscopic Ovarian Electrocautery in Pregnancy Rate in Metformin- and Clomiphene Citrate-Resistant Infertile Women. *J Obstet Gynecol Cancer Res.* 2020; 5 (3) :84-87

Download citation:

[BibTeX](#) | [RIS](#) | [EndNote](#) | [Medlars](#) | [ProCite](#) | [Reference Manager](#) | [RefWorks](#)