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ORIGINAL ARTICLE

Gestagen versus oral contraceptive pills to induce withdrawal bleeding before induction of ovulation by clomiphene citrate in polycystic ovary syndrome

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KEYWORDS

Gestagen;
Oral contraceptive pills;
PCO;
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Abstract *Objective:* To compare between gestagen versus oral contraceptive pills to induce withdrawal bleeding before induction of ovulation by clomiphene citrate in polycystic ovary syndrome.

Design: Randomized controlled trial.

Setting: Integrated Fertility Center and Agial Fertility Center.

Sample: Fifty PCO female patients.

Methods: The patients were subdivided in 2 groups according to computer generated randomized program:

Group I: Twenty five PCO female patients treated by cidolut nor 5 mg tablets (two tablets every day for 5 days).

Group II: Twenty five PCO female patients treated by cilest tablets (one tablet every day for 21 days).

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All patients were observed until withdrawal bleeding followed by ovulation induction by clomiphene citrate from the second day of menses (100 mg per day for 5 days). The patients were then followed up by:

- transvaginal ultrasound follicular scanning in days 10, 12, and 14 of withdrawal bleeding until ovulation was detected with additional evaluation of the endometrial thickness and pattern
- serum progesterone was measured 7 days after the expected day of ovulation
- pregnancy test 15 days after ovulation to detect pregnancy and 2 weeks later by U/S to detect fetal pulsation.

Main outcome measures: Endometrial thickness, number of mature follicles and serum progesterone level on day o f ovulation, and clinical pregnancy rate.

Results: There was no significant difference between the two groups regarding pregnancy rate.

Conclusions: A few studies show an apparent use of oral contraceptive pills in the improvement of ovulation induction by clomiphene citrate. Despite this, from the available data a causal relationship is not confirmed, so large prospective studies using larger sample size, and longer duration of treatment are needed. Meanwhile, close clinical surveillance of patients being treated with oral contraceptive pills is required.

1. Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age and is the most frequent cause of hyperandrogenism and oligoanovulation, both of which have substantial psychological, social, and economic consequences. An increased awareness of this disorder in the general population and medical communities has taken place in recent years with the knowledge that women with polycystic ovary syndrome are susceptible to metabolic syndrome and its associated co morbidities. Therefore, polycystic ovary syndrome is a persisting challenge for clinical and basic research scientists (1–5).

Three key diagnostic features of polycystic ovary syndrome are hyperandrogenism, chronic anovulation, and polycystic ovaries on ultrasonography. Importantly, other conditions like congenital adrenal hyperplasia, Cushing's syndrome, and androgen-secreting tumors which are known to cause or to mimic the features of polycystic ovary syndrome must be excluded prior to diagnosis. Although obesity, insulin resistance, and metabolic syndrome are frequently present in women with polycystic ovary syndrome, they are not regarded as intrinsic disturbances of the disorder. The prevalence of polycystic ovary syndrome, as defined by the 1990 National Institutes of Health (NIH) criteria, in unselected populations of women of reproductive age is between 6.5% and 8%. Adoption of the 2003 Rotterdam criteria for the diagnosis of this disorder will presumably increase the prevalence of polycystic ovary syndrome because the scope for inclusion is broader than it is with the 1990 NIH criteria (6–10).

Women with polycystic ovary syndrome form the largest group of women with ovulatory dysfunction, which is characterized by chronic anovulation in the presence of normal follicular stimulating hormone (FSH) and estradiol concentrations. Induction of ovulation is the first-line treatment for this class of anovulation and is aimed at introducing an endocrine milieu that promotes growth and ovulation of a single dominant follicle with consequent singleton pregnancy. According to the National Institute of Clinical Excellence (NICE) guidelines, the recommendations for ovulation induction are as follows (11):

- Anti-estrogens: women with World Health Organization Group II ovulation disorders (hypothalamic pituitary dysfunction) such as polycystic ovary syndrome should be offered treatment with clomifene citrate (or tamoxifen) as the first line of treatment for up to 12 months because it is likely to induce ovulation. Women should be informed of the risk of multiple pregnancies associated with both clomifene citrate and tamoxifen.
- Metformin: anovulatory women with polycystic ovary syndrome who have not responded to clomifene citrate and who have a body mass index of more than 25 should be offered metformin combined with clomifene citrate because this increases ovulation and pregnancy rates. Women prescribed metformin should be informed of the side effects associated with its use (such as nausea, vomiting, and other gastrointestinal disturbances).
- Ovarian drilling: women with polycystic ovary syndrome who have not responded to clomifene citrate should be offered laparoscopic ovarian drilling because it is as effective as gonadotropin treatment and is not associated with an increased risk of multiple pregnancies.
- Gonadotropin: women with World Health Organization Group II ovulation disorders such as polycystic ovary syndrome who do not ovulate with clomifene citrate (or tamoxifen) can be offered treatment with gonadotropins. Human menopausal gonadotropin, urinary follicle-stimulating hormone, and recombinant follicle-stimulating hormone are equally effective in achieving pregnancy, and consideration should be given to minimizing cost when prescribing.
- Gonadotropin-releasing hormone analogs: women with polycystic ovary syndrome who are being treated with gonadotropins should not be offered treatment with gonadotropin-releasing hormone agonist concomitantly because it does not improve pregnancy rates, and it is associated with an increased risk of ovarian hyperstimulation.

Like NICE guidelines, the Society of Obstetricians and Gynecologists of Canada (SOGC) also provides guidelines for ovulation induction. The recommendations are as follows (12):