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ORIGINAL ARTICLE

Impact of dexamethasone on pregnancy outcome in PCOs women candidate for IVF/ICSI, a single-blind randomized clinical trial study

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KEYWORDS

Polycystic ovary syndrome;
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Abstract *Objective:* Infertile women with polycystic ovary (PCOs) involve with anovulatory cycles. Various adjuvant treatments have been suggested to improve ovarian response in these patients. In this study, we aimed to evaluate the role of dexamethasone in the outcome of IVF/ICSI in PCOs infertile women. *Study design:* 129 PCOs infertile women undergone IVF/ICSI were enrolled for this single blind clinical trial study in 2012–2013. *Setting:* Fatemezahra Infertility and Reproductive Health Research Center, Babol University of Medical Sciences, Babol, Iran. *Method:* 43 patients who underwent IVF received dexamethasone (0.5 mg, 4 tab/day) in the treatment group and 74 patients were considered as the placebo group. *Main outcome measure:* Pregnancy rate was compared between the two groups. In addition, number of dominant follicle, oocytes retrieved, embryos transferred, and number of gonadotropin ampoule were evaluated. *Results:* The pregnancy rate in the group receiving dexamethasone was 17.5% significantly higher versus 4.3% in the placebo group ($P < 0.05$). The mean number of embryos in the patients received dexamethasone was 6.7 ± 4.3, significantly greater than placebo which was 4.9 ± 4.9 ($P < 0.05$). The mean number of gonadotropin ampoules used in the group received dexamethasone was 3.5 ± 1.6, significantly lower versus the placebo which was 5.3 ± 2.5 ($P < 0.05$). The mean number of oocytes in the group received dexamethasone was 11.8 ± 8 and in the placebo group was 9.6 ± 5.8 that was not significant. *Conclusion:* Dexamethasone enhances embryos and pregnancy rate; in addition, it reduces gonadotropines ampoule used for stimulation, hence, and we recommend using of dexamethasone in women with PCOs undertreatment of IVF/ICSI.

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1. Introduction

Incidence of polycystic ovarian syndrome (PCOs) according to Rotterdam criteria is 19.5%. It protests as infertility, menstrual problems, hirsutism, acne, obesity and worsened health-related quality of life (1,2). In this syndrome, by increasing the concentrations of estrogen and probably reducing SHBG, hypothalamus and pituitary sensitivity change and level of LH enhances, however the FSH remains normal or diminishes (3). Both autosomal and X-linked dominant modes of inheritance need to describe the familial clustering of PCOs women (4).

Although patients with polycystic ovary respond adequately to ovulation, some of them require Assisted Reproductive Technology (ART) (5). However, there are some reports on other possible ways of influencing ovarian function by gonadotropin, growth hormone, glucocorticostroids, low dose aspirin, metformin and also dexamethasone (6–11). Dexamethasone was used for the first time in 1953. It inhibits the estradiol activity directly, affects the pituitary gland and lessens adrenal androgen level, therefore increases the follicular growth (3).

It seems dexamethasone reduced the influences of adrenal androgenism on follicle growth (12). Harlow et al. showed the significant increase of intra follicle cortisol after ovulation explains the role of steroids in oocyte maturation and ovulation (13). However, it is believed that stromal blood flow at the follicular phase in women with polycystic ovary is greater than women with normal ovaries (14). Also, it has been shown that the increased blood flow in follicles stroma at the ovulation phase is associated with increasing gonadotropin reception by the target cells of ovary which results in ovulation (15).

Keay et al. concluded that the higher intrafullicular cortisol indicates oocytes maturation and embryo implantation in a natural unstimulated IVF (8). In a study conducted by Ashrafi et al., gonadotropin consumption in the combined group was significantly lower than the placebo group (6).

This study evaluates the effect of dexamethasone on ovarian response in infertile PCOs women candidate for IVF/ICSI compared to the control group.

2. Methods

This single-blind clinical trial study was conducted in Fatemezahra Infertility and Reproductive Health Research Center of Babol (north of Iran) in March 2012 to September 2013. The ethic permission was received from ethic committee of Babol University of Medical Science. This paper was registered in Iran clinical registry with the number, 201207031760N19.

The study population included the infertile patients with polycystic ovary which candidate for ICSI. The formula samples obtained by 5.0 = a, 8.0 = B, 6.41 = X1, 3.18 = S1, 6.30 = X2 and 3.13 = S2, 35 case in each group and for increasing the accuracy of the study, 40 patients for the case and 70 patients in the placebo group were analyzed according to previous similar studies (16,17). In this study, the initial assessment consists of hormonal and biochemical tests, and ultrasound and hysterosalpingography were performed before the study.

Women with one ovary, uterine problems such as fibroids, intrauterine septum or a history of ovarian surgery, endometrioma, and male factor infertility were excluded. In addition, patients underwent IVF treatment during previous three months prior to the study were excluded. All patients had BMI $\leqslant 28$ and were enrolled from PCO clinic of our center based on Rotterdam criteria (18). All participants signed a consent form and entered the study. A computer generated sequence (19) concealed from the gynecologist was randomly assigned to the patients receiving either dexamethasone or placebo. The data collector (a medical student) administered the drugs. All processing was conducted by the same gynecologist. Both groups were matched in age and duration of infertility.

To stimulate the follicles, ovulation induction protocol using agonists GnRh (Superfact, Aventis Pharma Deutschland, Germany) was begun in the mid-luteal phase of the cycle. At the initiation of the agonist GnRh, the patients were divided in a treatment group and a placebo group. For the placebo group Folic acid (400 μg, 2 tab/day, Nature Made, USA) and for the treatment group dexamethasone (0.5 mg, 4 tab/day, Daroupakhsh, Iran) were administered. We chose dexamethasone 2.0 mg (high dose) for lack of side effects as well as more affectivity than 0.5 mg, according to Beck (20). From the third day of subsequent menstrual cycle, injection of gonadotropin (75 IU, IVF-M, Menotropin, LG life Science, Jeonbuk-do, Korea) was initiated. Then, follicles monitoring was performed by serial TVS and if needed, the stimulation was continued. According to our ICSI routine, Human Chorionic Gonadotropin 10,000 IU (HCG, Daroupakhsh, Iran) was injected when at least 3 oocytes $\geqslant 16$ mm were seen at the TVS.

Oocytes picked up 34–36 h following injection of HCG (Daroupakhsh, Iran) in the operating room under a slight anesthesia. Dexamethasone and folic acid were continued until the day of oocyte picking up. Oocytes fertilized through intra cytoplasmic injection method and embryo in good quality (up to 3 embryos) was transferred on the third day following picking up guiding by TVS. The rest of qualified embryos were cryopreserved. After embryo transfer, vaginal suppository Cyclogest 400 mg (Actavis Group, Iceland) twice/daily was recommended for both groups to support the luteal phase.

Chemical pregnancy rate defined as serum B-hCG level was checked on the sixteenth day after embryo transfer to clarify the pregnancy outcome (21).

The number of retrieved oocytes, formed embryos, and pregnancy rate in both groups was compared with each other.

Data were entered into the computer. Software SPSS 17 was used. Data analysis was done with *T*-test and fisher exact test. *P*-value < 0.05 was considered as significant.

3. Results

Out of 129 ICSI patients who were eligible, three women were excluded; six women had no inclusion criteria, one woman declined to participate and one woman met the exclusion criteria. 118 women were randomized in two groups; 42 women received dexamethasone. One woman showed psychological problem and did not receive that. In control group, 74 women received placebo and two women did not receive for no contribution. One woman in the case and one woman in control group lost to follow-up for hyperstimulation. One woman discontinued placebo for non-attendance at follow-up in the control group. No patient in the study group was excluded from analysis. In control group, one patient was excluded from