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ORIGINAL ARTICLE

Effects of human chorionic gonadotropin combined with clomiphene on Serum E_2, FSH, LH and PRL levels in patients with polycystic ovarian syndrome

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KEYWORDS

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Abstract *Objective:* Effects of human chorionic gonadotropin combined with clomiphene on serum E_2, FSH, LH and PRL levels in patients with polycystic ovarian syndrome were analyzed.

Methods: 90 patients with polycystic ovarian syndrome treated from January 2015 to March 2016 were randomly and evenly divided into control group and observation group. Patients in the control group were only treated with clomiphene. On the basis of the treatment in control group, human chorionic gonadotropin was added in the treatment of observation group. The changes of E_2, FSH, LH, PRL levels were compared between two groups before and after the treatment. Clinical curative effects of patients in the two groups was evaluated. Adverse reactions during treatment in two groups were observed and recorded. The incidence of adverse reactions was calculated.

Results: Serum E_2, FSH, LH and PRL levels in the two groups decreased significantly after treatment compared with that before treatment. The difference is statistical significant ($P < 0.05$). After the treatment, E_2, FSH, LH and PRL levels in the observation group were lower than that in the control group and the difference is statistical significant ($P < 0.05$). Total effective rate was 64.44% in the control group and 93.33% in the observation group. There were statistically significant difference in clinical curative effects in the two groups ($P < 0.05$). Different degrees of adverse reactions were found in both groups during treatment, such as nausea, vomiting, anorexia, liver dysfunction. There were 2 cases of nausea, 2 cases of vomiting, 3 cases of anorexia and 1 case of liver dysfunction from the 45 patients in control group. The total incidence of adverse reactions was 17.78% (8/45). There were 1 case of nausea, 1 case of vomiting, 1 case of anorexia and no liver dysfunction from the 45 patients in observation group. The total incidence of adverse reactions was

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6.67% (3/45). The total incidence of adverse reactions in the observation group was significantly higher than that in the control group and the difference was not statistically significant ($P > 0.05$).

Conclusion: Combined use of human chorionic gonadotropin can significantly reduce serum E_2, FSH, LH and PRL levels, improve clinical curative effects and reduce the incidence of adverse reactions. Human chorionic gonadotropin has high application value on the treatment of polycystic ovary syndrome.

1. Introduction

Polycystic ovary syndrome (PCOS) is a common disease of obstetrics and gynecology. It was mainly caused by anovulation endocrine disorders with clinical manifestations of diversity, including irregular menstruation, infertility, and so on. According to statistics (Shi and Quan, 2015; Jiang et al., 2012; Wei et al., 2013), the incidence of polycystic ovary syndrome in women of childbearing age was as high as 10% and it brings seriously negative affect to the healthy and family life of patients. Drug treatment is the common method of clinical treatment. Analysis on effects of human chorionic gonadotropin combined with clomiphene on serum E_2, FSH, LH and PRL levels during the treatment was conducted in this study. The results are reported as follows.

2. Materials and methods

2.1. General information

90 patients with polycystic ovarian syndrome treated from January 2015 to March 2016 were randomly and evenly divided into control group and observation group. Patient enrollment criteria: patients clinically diagnosed with polycystic ovary syndrome, not using hormonal drugs recently. Exclusion criteria: patients with liver and kidney dysfunction. This study was agreed by the patients and approved by our hospital ethical committee. There were no significant difference between the two groups in general clinical materials, including age, weight, height, infertility type and BMI, and so on ($p > 0.05$), and it was strongly comparable. Data are shown in Table 1.

2.2. Methods

Treatment in the control group: Patients were only treated with clomiphene. Clomiphene was given orally with the dose of 100 mg/d (specification: 50 mg × 20particle/box, approval number: national medicine approved number H31021107, manufacturer: Shanghai Hengshan Pharmaceutical Co., Ltd.). The treatment was stopped after 12 d of continuous medicine taken. It would be extended to three menstrual cycles, if the patient was not pregnant. Treatment in the observation group: Clomiphene was combined with human chorionic gonadotropin in the treatment. Clomiphene was given orally with the dose of 100 mg/d. The diameter of follicular was observed and if it is larger than 18 mm, intramuscular injection of 100 mg human chorionic gonadotropin was given. If the patient was not pregnant, the treatment was continued for three menstrual cycles.

Serum E_2, FSH, LH and PRL levels was determined by immune analyzer after patients in the two groups taking drug for 3 menstrual cycles.

2.3. Observed indicators

2.3.1. E_2, FSH, LH and PRL were chosen as observed indicators

Venous blood was extracted from all patients at 9 am in their fasting state. After centrifuge separation, the separated serum was placed in a thermostat of −40 °C for storage. Enzyme linked immunosorbent assay (ELIA) method is applied to determine the levels of E_2, FSH, LH, PRL in serum.

2.3.2. Clinical curative effect criterion (Chen et al., 2013; Li and Wu, 2015; Chen and Wei, 2015; Wang et al., 2014; Liu, 2014)

According to the menstrual recovery degree, curative effects could be divided into the following four grades. Healing-Menstruation returned to normal level during treatment or one year later, and the patient got pregnant successfully. Excellent-Menstruation returned to normal level during treatment or one year later, but the patient were failed to get pregnant. Improved-The function of ovulation was normal, but the amount of menstruation is less than normal during treatment or within one year. Failure-menstrual cycle was serious

Table 1 Comparison of general clinical materials in two groups.

Materials	Control group ($n = 45$)	Observation group ($n = 45$)	t/χ^2 Value	P Value
Average age (years)	35.46 ± 4.12	35.02 ± 4.57	0.4797	0.6326
Average height (cm)	168.23 ± 3.42	167.09 ± 4.18	1.4160	0.1603
Average weight (kg)	64.18 ± 4.02	65.04 ± 3.17	1.1269	0.2629
Infertility type				
Primary infertility	33 (73.33)	30 (66.67)	3.7479	0.0529
Secondary infertility	12 (26.67)	15 (33.33)		
BMI (kg/cm^2)	25.02 ± 2.69	25.97 ± 2.49	1.7386	0.0856

delayed and no ovulation was found. Total effective rate = (Healing cases + Excellent cases + Improved cases)/total cases × 100.00%.

2.4. Statistical analysis

Data were analyzed using SPSS 18.0. Data were represented as mean ± standard deviation ($\bar{x} \pm s$). Measurement data were compared using *T*-test. Count data were compared using chi-square (χ^2) test. Grade data were compared using rank sum test. Result of $P < 0.05$ was considered to be statistically significant.

3. Results

3.1. Changes of E2, FSH, LH, PRL levels in the two groups after treatment

Serum E_2, FSH, LH and PRL levels in two groups decreased significantly after treatment. The difference is statistical significant ($P < 0.05$. The levels of E_2, FSH, LH and PRL in observation group were lower than that in the control group and the difference was statistical significant ($P < 0.05$). Detail data is listed in Table 2.

3.2. Evaluation of clinical curative effects in the two groups

The total effective rate was 64.44% in control group and 93.33% in observation group. The difference of clinical curative effects in the two groups was statistically significant ($P < 0.05$). Detail data is listed in Table 3.

3.3. Comparison of adverse reactions in the two groups

Different degrees of adverse reactions were found in both groups during treatment, such as nausea, vomiting, anorexia, liver dysfunction and ovarian hyper-stimulation. There were 2 cases of nausea, 2 cases of vomiting, 3 cases of anorexia, 1 case of liver dysfunction and 2 cases of ovarian hyper-stimulation from the 45 patients in control group. The total incidence of adverse reactions was 17.78% (8/45). There were 1 case of nausea, 1 case of vomiting, 1 case of anorexia, no liver dysfunction and no ovarian hyper-stimulation from the 45 patients in observation group. The total incidence of adverse reactions was 6.67% (3/45). The total incidence of adverse reactions of the observation group was significantly higher than that of the control group and the difference was not statistically significant ($P > 0.05$).

4. Discussion

At present, with the accelerating pace of social life, more and more women suffer from polycystic ovary syndrome, a common clinical gynecological syndrome (Zhao, 2012; Deng, 2012; Chen et al., 2013; Xu et al., 2013; Zhang et al., 2013; Guo et al., 2015). It's a type of metabolic syndrome with clinical features like endocrine disorder, high androgen and chronic anovulation. The infertility symptom causes various problems to the patients and their family and affects their happiness severely. The main treatments for polycystic ovary syndrome in practice are behavioral therapy, surgery and medicine, supplemented with proper adjustments to diet structure. Among them, medical therapy is the most often applied treatment (Hu et al., 2012; Li and Qiao, 2012; Wang et al., 2012; Mo and Yang, 2013; Fan et al., 2013). Clomiphene is a hormone-like biological agent. It can promote the secretion of gonadotropin from hypothalamus. With estrogen index improved, resistance to androgen is enhanced and hypothalamic releasing of GnRH is increased, then the LH and FSH levels in serum is raised. However, a number of clinical practice (Zhu, 2013; Gao et al., 2014; Jiang et al., 2015; Geng and Xu, 2015; Kuang et al., 2013) show that due to the anti-estrogen effects of clomiphene, endometrial gets thinner and sperm pass rate gets lower. After the treatment, the pregnancy rate is low and the miscarriage rate is high. Human chorionic gonadotropin is a kind of glycoprotein secreted by placental trophoblast cells. It can accelerate the secretion of androstenedione and progesterone. In addition, it is similar to LH with respect to property and activity and can improve the ovulation rate partly (Jin et al., 2014; Liu et al., 2014; Lin et al., 2014). The combination of clomiphene and human chorionic

Table 2 Changes of E_2, FSH, LH and PRL levels in the two groups before and after treatment.

Indicators	Control group ($n = 45$)		Observation group ($n = 45$)	
	Before treatment	After treatment	Before treatment	After treatment
E_2 (pmol/L)	196.23 ± 43.26	176.23 ± 30.23	197.02 ± 45.16	158.40 ± 32.07
FSH (u/L)	7.46 ± 1.48	6.72 ± 1.21	7.39 ± 1.50	5.46 ± 1.09
LH (u/L)	13.52 ± 2.14	10.36 ± 2.01	13.46 ± 2.42	8.45 ± 1.75
PRL (ng/L)	28.74 ± 11.02	16.12 ± 5.04	28.19 ± 12.91	14.46 ± 3.72

Table 3 Evaluation of clinical curative effects in the two groups [*n* (%)].

Groups	Healing	Excellent	Improved	Failure	Total effective rate
Control group ($n = 45$)	3 (6.67)	12 (26.67)	14 (31.10)	16 (35.56)	29 (64.44)
Observation group ($n = 45$)	11 (24.44)	19 (42.22)	12 (26.67)	3 (6.67)	42 (93.33)
χ^2 Value					11.2750
P Value					0.0008

gonadotropin can effectively prevent excessive luteinizing and promote follicle rupture ovulation. This study investigated the effects of human chorionic gonadotropin combined with clomiphene on serum E_2, FSH, LH and PRL levels in patients with polycystic ovarian syndrome based on 90 patients.

The study shows that the serum E_2 level in patients treated with clomiphene alone decreased from 196.23 ± 43.26 pmol/L before treatment to 176.23 ± 30.23 pmol/L, while the decreased level was still higher than that in patients treated with clomiphene combined with human chorionic gonadotropin (158.40 ± 32.07 pmol/L). Serum FSH, LH and PRL levels in patients treated by both the two methods showed a downward trend after the treatment, while the levels in patients treated with clomiphene combined with human chorionic gonadotropin were higher than that in patients treated with clomiphene alone. It suggested that human chorionic gonadotropin can significantly reduce serum E_2, FSH, LH and PRL levels. This result is consistent to the reported results (Chen et al., 2015; Yuan et al., 2015). Out of the 45 patients treated with clomiphene alone, 29 of them were effectively treated. The total effective rate was 64.44%. In contrast, 42 patients were effectively treated, from the total 45 patients treated with the combinative method. Its total effective rate was 93.33%, significantly higher than that of the former one. Human chorionic gonadotropin significantly improved the clinical curative effect. Different degrees of adverse reactions were found in all patients, such as nausea, vomiting, anorexia and liver dysfunction. There were 8 patients with adverse reactions from 45 patients treated with clomiphene alone and the total incidence of adverse reactions was 17.78%. There were 3 patients with adverse reactions from 45 patients treated with clomiphene combined with human chorionic gonadotropin and the total incidence of adverse reactions was 17.78%. No liver dysfunction and ovarian hyper-stimulation were found.

Combined use of human chorionic gonadotropin and clomiphene for the treatment of polycystic ovary syndrome can significantly reduce levels of E_2, FSH, LH and PRL in serum, improve clinical curative effect and reduce the incidence of adverse reactions. Human chorionic gonadotropin has high application value on the treatment of polycystic ovary syndrome.

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