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ORIGINAL ARTICLE

Correlation of progesterone level on the day of human chorionic gonadotropin injection in intrauterine insemination cycle and fertility rate

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ABSTRACT

Background: Intrauterine insemination (IUI) is one of the assisted reproductive techniques widely used in infertility treatment. This must be done at a specific time, and progesterone plays an important role in the implantation process, a prerequisite for embryonic attachment and invasion. This study aimed to evaluate the relationship between progesterone levels on the day of human chorionic gonadotropin (hCG) injection in the IUI cycle and fertility.

Methods: In this cross-sectional descriptive study, patients referred to the Infertility Center of Ardabil University of Medical Sciences for IUI during 2019-2020 were included. The pattern of the menstrual cycle, history of medical or surgical diseases, history of dyspareunia, number of previous IUIs, causes of infertility, and duration of infertility were entered in the relevant checklists. On the day of the hCG injection, a blood sample was taken, and the level of progesterone and estrogen were measured and evaluated.

Results: A total of 85 patients were included in the study. The IUI result was negative in 67 (78.8%) patients. The mean total IUI history of patients was 1.71 ± 0.8 years. The mean duration of infertility was 35.11 ± 18.31 months. The highest fertility rate was observed in the serum level of 1.21-1.6 progesterone. The mean serum level of estradiol was 816.46 ± 651.00 months.

Conclusion: The results of this study showed that the highest fertility rate was observed in the serum level of 1.21-1.6 progesterone in the IUI cycle.

Keywords: Progesterone, IUI, human chorionic gonadotropin.

Introduction

Intrauterine insemination (IUI) means the injection of washed sperm into the uterine cavity and is one of the methods of assisted reproduction that increases the probability of ovum contact with sperm in the uterine environment and increases the chance of pregnancy [1]. IUI is a straightforward method that is widely used in the treatment of infertility [2]. Performing the IUI method requires ovulation, at least one open fallopian tube and a semen sample containing healthy sperm [3]. Sperm insemination into the uterus should be done at a certain time compared to ovulation. For this purpose, the time of ovulation should be determined [4]. In some cases, human chorionic gonadotropin (hCG) injection may be prescribed to release the egg at a certain time [5]. Ovum release usually occurs 36 hours after the injection of this ampoule, and usually, 24 to 48 hours after hCG injection, IUI is performed [2,6]. Progesterone plays an important role in implantation by creating significant

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changes in endometrial morphology, a prerequisite fetal connection. Progesterone is the dominant hormone during the luteal phase, and the endometrial implantation cycle occurs mainly by progesterone, and the gene induced by progesterone firmly controls this cycle [1]. Patients with a high concentration of estradiol also have a significantly high concentration of progesterone, which indicates that at least one of the mechanisms leading to an increase in the level of progesterone during the follicular phase is related to the ovarian response during ovarian stimulation [7].

Although IUI with ovarian stimulation is one of the first treatments for infertility, the pregnancy rate results vary from 10% to 25% [8]. One of the reasons for the low pregnancy rate may be premature peaks in luteinizing hormone (LH) surge during assisted reproductive treatments, which is associated with luteinization of follicles at the end of ovarian stimulation [1,9]. Early LH surge occurs in 25%-30% of stimulated IUI cycles and may theoretically conflict with the timing of IUI or lead to the failure of this treatment [10,11]. The effect of an early rise in progesterone levels in stimulated IUI cycles has not been well-studied. However, this information can be useful for timing sperm injection for insemination in IUI cycles.

On the other hand, studies show that the increase in serum progesterone level in the middle of the luteal phase was not associated with an increase in the clinical pregnancy rate in women undergoing controlled ovarian stimulation in the IUI cycle [12]. However, a low progesterone level in the middle of the luteal phase was suggested to predict treatment failure [13]. According to the above study and considering the importance of predicting the fertility rate in each IUI cycle, the purpose of this study is to measure the relationship between the progesterone level on the day of hCG injection in the IUI cycle, and the pregnancy rate in women referred to the infertility center of Ardabil University of Medical Sciences.

Subjects and Methods

A cross-sectional descriptive stud was conducted from October 2018 to September 2019 on 85 women candidates for IUI treatment referred to the infertility center of Ardabil University of Medical Sciences. The samples were selected by a simple and accessible random sampling method of all women referred to the infertility center. The studied women were first asked questions about menstrual cycle patterns, history of medical or surgical diseases, history of dyspareunia, number of previous IUIs, causes of infertility, and duration of infertility and recorded in a checklist. Then, before hCG injection, blood samples were taken from them, progesterone and estrogen levels were measured, and the patients entered IUI cycles. The success of this cycle was checked according to the results of b-hCG tests 10 days after IUI. After obtaining written consent, women aged 18 to 35 years with a history of infertility candidates for IUI and having at least one fallopian tube were included in the study. Women with active pelvic infection, ovarian cysts (using baseline ultrasound), smoking, history of ectopic pregnancy, and failure to visit the infertility center for follow-up treatment were excluded from the study. Information related to progesterone and estrogen serum level, age, infertility duration, number of follicles and endometrial thickness were expressed as mean ± SD. Statistical Package for the Social Sciences version 25 software was used to perform statistical calculations, and Excel software was used to draw graphs. According to the Kolmogorov–Simonov test, the serum level of progesterone and estrogen, the number of follicles and the thickness of the blood endometrium had an abnormal distribution, and the age and duration of infertility had a normal distribution. A comparison of two groups was made using the Mann–Whitney test and independent *t*-test. A significance level of $p < 0.05$ was considered.

Results

The average age of all women was 28.45 ± 4.48 years, with an age range between 18 and 38. The result of IUI was negative in (78.8%) of 67 patients and positive in 18 (21.2%) patients. Menstruation was regular in 48 patients (56.5%) and irregular in 37 (43.5%). 69 (81.2%) patients had no history of disease, and 12 (14.12%) patients had a history of hypothyroidism. Depression, factor seven deficiency, MS, and nephrolithiasis were reported only in the history of one patient (1.12%). Seventy-three patients (85.9%) had no history of surgery, four patients (4.7%) had a history of cholecystectomy, and eight patients (9.4%) had a history of appendectomy. 18 patients (21.2%) had a history of dyspareunia, 54 patients (63.5%) had infertility due to female reasons, and 31 patients (36.5%) had infertility problems due to male reasons. Forty-three patients (50.6%) had a 1-time history of IUI, 24 patients (28.2%) had a 2-time history of IUI, and 18 patients (21.2%) had a 3-time history of IUI. All patients' average number of previous IUIs was 1.71 ± 0.8 times.

The average period of infertility among all patients was 35.11 ± 18.31 months. No significant relationship was observed between the duration of infertility and the treatment outcome. The average number of follicles in the patients was 2.85 ± 0.97 from 1 to 5. There was a statistically significant difference between the numbers of follicles based on the treatment outcome. The average thickness of the endometrium of the patients was 7.68 ± 0.68 mm in the range of 6.3 to 9.7. A statistically significant difference was observed between the viscosity of the endometrium based on the treatment result. The mean serum progesterone level of the patients was 0.83 ± 0.59 ng/dl in the range of 0.05 to 2.7. There was a statistically significant difference between serum progesterone levels based on treatment outcome. The average serum estradiol level of the patients was 816.46 ± 651.00 ng/dl in the range of 30 to 3,125. There was a statistically significant difference between serum estradiol levels based on treatment outcome (Table 1).

Table 1. *Relationship between the studied variables and the treatment outcome in the studied women.*

Variables	The result of the treatment		Meaning
	Positive	negative	
Frequency of IUI	0.81 ± 1.73	0.78 ± 1.61	0.58
Infertility period	13.65 ± 36.00	19.45 ± 34.87	0.83
Number of follicles	0.67 ± 3.72	0.90 0 ± 2.61	0.001
Endometrial thickness	0.82 ± 8.26	0.55 ± 7.53	0.001
Serum progesterone levels	0.33 ± 1.28	0.58 ± 0.70	0.001
Serum estradiol levels	344.98 ± 1,335.56	644.6 ± 676.99	0.001

Discussion

In the present study, the result of IUI was negative in (78.8%) of 67 patients and positive in 18 (21.2%) patients. The overall pregnancy rate in the present study shows a high percentage of IUI success. The survey of Basirat et al. [14], with a pregnancy rate of 19.8%, was similar to the present study [14]. Other studies mentioned the pregnancy rate following IUI from 4.7% to 14.8% [15-17]. The possible effect of the average number of mature follicles in the study population can cause a high pregnancy rate in the present study. Among the characteristics of infertile women, age is of particular importance because the effect of ageing on the reduction of oocyte quality has been well-proven, and even more effective infertility treatments than IUI are not able to eliminate the adverse impact ageing on the treatment outcome [18,19]. However, in the present study, no significant relationship was observed between the age of infertile women and the success of IUI in pregnancy. The studies conducted in other places also aligned with the present research [15,20]. In the studies conducted elsewhere, like the present study, there was no significant relationship between the duration of infertility and the occurrence of pregnancy in IUI cycles [21-24]. However, in the study of Basirat et al. [17], this relationship was significant. In the present study, there was no significant relationship between the number of IUI cycles and the occurrence of pregnancy in IUI cycles, which was inconsistent with Yavuz's et al. [25] study, probably due to the different sample sizes and statistical population. This study observed a statistically significant relationship between the progesterone serum level and the treatment result. Based on the classified serum level, the highest fertility rate was observed at the serum level of 1.21-1.6. In the study of Kutlu et al. [13] the increase in serum progesterone level in the middle of the luteal phase was not associated with an increase in the clinical pregnancy rate in women undergoing controlled ovarian hyperstimulation (COH) in IUI. However, a low progesterone level in the middle of the luteal phase was suggested as a predictor for treatment failure and the highest fertility rate was observed in serum progesterone levels between 1.21 and 1.6 [13]. Zarei et al. [26] study also concluded that progesterone level has no relationship with embryo transfer day or fertility outcomes. This relationship was confirmed in the study of Mascarenhas et al. [27] similar to the present study. The study by Weedin et al. [12] shows that the increase in serum progesterone level in the middle of the luteal phase was not associated with an increase in the clinical pregnancy rate in women undergoing COH in IUI. The lower fertility rate at a higher progesterone serum level may be due to the negative effect of progesterone on oocyte quality [28].

In this study, a significant relationship was observed between the thickness of the endometrium and the result of treatment, so in cases where the thickness of the endometrium was greater, the pregnancy rate was also high. In other studies, the relationship between endometrial thickness and pregnancy rate similar to the present study has been confirmed [21,29]. The present study found a significant relationship between the number of mature follicles and the pregnancy rate in IUI cycles. Despite the higher number of mature follicles, the pregnancy rate increases significantly in IUI cycles.

Conclusion

The results of the present study showed that follicle number, endometrial thickness, serum estradiol level and progesterone serum level had a positive effect on pregnancy rate. Therefore, it is recommended to carefully adjust the progesterone level to obtain a better result in women who are candidates for IUI. Also, consider the thickness of the endometrium and the number of follicles. According to progesterone level and fertility results, it is recommended that IUI be performed earlier than 36 hours, and the results were checked. Conducting a study with more cases in the future is also recommended.

List of Abbreviations

hCG	Human chorionic gonadotropin
IUI	Intrauterine insemination
SPSS	Statistical package for social science

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent to participate
All participated completed the consent form before study.

Ethical approval
The study was approved by the Ethics Committee of Ardabil University of Medical Sciences, Ardabil, Iran with the approval number IR.ARUMS.REC.1398.201 at 2019.

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