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Pregnancy Rate by Human Chorionic Gonadotropin Administration Versus Urinary Luteinizing Hormone Surge Method in Patients Undergoing Intrauterine Insemination

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Abstract

Background: Infertility is becoming a world-wide concern in developed and developing countries. Multiple causes are responsible for the situations and various therapies have been developed to overcome this problem in infertile couples, as in the case of intrauterine insemination (IUI), with considerable variations between pregnancy rates in relation to the method employed.
Objectives: To compare pregnancy rate, by human chorionic gonadotropin (HCG) administration and urinary luteinizing hormone (LH) surge method, for insemination in patients undergoing IUI.
Patients and Methods: The present study included 309 infertile women, candidate for IUI, randomly divided into LH surge and HCG groups (each participant was assigned a number from 1 to 309, of which odd numbers were for LH and even numbers for HCG groups, respectively). All patients were subjected to baseline ultrasound and received clomiphene citrate before undergoing serial transvaginal sonography. The LH was measured using LH kit, when 2 - 5 follicles (18 - 20 mm) appeared in LH surge group, and, if positive, IUI was performed after 24 hours. In HCG group, the patients received HCG 1000 units and underwent IUI after 36 hours. The pregnancy rate was then compared in LH and HCG groups.
Results: We found no significant differences in pregnancy rates between the two groups. Also, we compared pregnancy rates between the two groups based on age, infertility cause, number of follicles, number of previous IUI and previous abortions. We found no significant differences between the subgroups, in terms of pregnancy rate.
Conclusions: The urinary LH surge and HCG administration methods for IUI timing are similar and none had any considerable advantages over the other. However, the use of the urinary LH surge has no side effects or injection pain, in relation to HCG administration methods

Keywords: Chorionic Gonadotropin, Clomiphene Citrate, Luteinizing Hormone, Insemination, Artificial, Pregnancy

1. Background

Giving birth to a child is an important event in the lifetime of any couple. Infertility is defined as the inability to become pregnant after 1 year of sexual intercourse, without using any methods of prevention of pregnancy (1, 2). In our country (Iran), about-25% of couples are faced with infertility (3). In 10% of cases, infertility involves both partners and in other 10%, the causes remain unknown. The Infertility of unknown causes refers to the situations where the results of all clinically standard evaluations are normal (4). Globally, the prevalence of infertility is 16.7% (5).

The studies performed in the US showed that 10% of women aged 15 - 44 years suffer from infertility, of which 49% had primary and 51% had secondary infertility (6). Different causes of infertility are reported in developed and developing countries (7). Diagnosing the main causes of infertility and suitable treatment method, in terms of expenses and time, is very important for designing treatment programs and preferential treatment (2).

In recent years, the demand of infertile couples to have a child has increased and various studies have also been performed in the field of infertility and treatment; therefore, different assisted reproductive technologies (ART)

have been created. Intrauterine insemination (IUI) is the first line of treatment for most infertility causes, such as infertility with male causes, Infertility with unknown causes and ovulation disorders. The moment for performing IUI is determined by two methods: administration of chorionic gonadotropin (HCG) and performing IUI after 36 hrs, or the urinary luteinizing hormone (LH) surge by LH kit. Several studies have shown no significant differences in pregnancy rate between the groups receiving HCG and the cases on LH kit, before undergoing IUI. Lewis et al., in 2006, performed IUI on 150 cases, divided into two groups of HCG administration and LH surge, and found no significant differences in the rate of pregnancy between them (8).

Multiple studies, with inconsistent results, were performed to compare pregnancy rate between HCG administration and urinary LH surge, in subjects undergoing IUI.

Since there are limited studies in this field, in Iran, and most infertility centers in Iran use HCG before IUI (although the use of LH kit is cheap and safe for patient) different results have been reported by the researchers.

2. Objectives

We aimed to perform this study to compare pregnancy rates by HCG administration versus urinary LH surge method for insemination of subjects, in patients undergoing IUI.

3. Patients and Methods

This study was a randomized clinical trial which included 320 infertile women candidate for IUI, referred to Montaserieh (infertility) fertility research & treatment center, Mashhad University of Medical Sciences, Mashhad, Iran, in 2009. The sample volume in each group was calculated according to previous studies (4). The first group included 85 subjects, with 15.2% pregnancy success rate in each cycle. The second group comprised 86 cases, with 27.7% success rate of pregnancy in each cycle. The final sample size was calculated as 160 subjects in each group, considering 5% rejection with α =.05 and β = 0.2.

Only infertile women candidate for IUI were included in the study. The exclusion criteria were women with negative urinary LH surge, which required HCG administration, and those with more than five follicles who had to use LH kit and did not receive HCG to avoid ovarian hyperstimulation.

Approval from the institutional review board and the ethics committee of Mashhad University of Medical Sciences, Mashhad, Iran, was obtained prior to the start of the study (number: 88032). This study has been successfully registered with the clinical trials service of the US national institutes of health (clinicaltrials.gov identifier: NCT02638285). All participants provided written informed consents.

At first, all conditions of the study were fully explained to the patients and they were assured about the privacy of the data and, if willing to participate in the study, they provided a written informed consent.

All the infertile women received 50 mg/day clomiphene citrate tablet (Iran hormone pharmaceutical Co., Tehran, Iran), then underwent serial transvaginal sonography on the 9th day of the menstrual cycle, which was repeated every other day until two to five follicles measuring 18 - 20 mm appeared. Transvaginal sonography was performed by five specialists from Montaserieh (infertility) fertility research & treatment center.

When two to five follicles, measuring 18 - 20 mm, appeared, the patients were randomly divided into two groups. Each patient was assigned a number from 1 to 309, even numbers for HCG group and odd numbers for LH. The patients in the HCG group received an injection of 1000 units of HCG (Darou Pakhsh pharmaceutical Mfg. Co., Tehran, Iran) and underwent IUI after 36 hours. In the second group, LH was measured by LH kit LH-TEST-H (Farafan diagnostics Co., Tehran, Iran). Patients were given explanations on how to use the tests to check urinary LH and, if positive, IUI was performed after 24 hours. Two weeks after IUI, we checked serum b-HCG [through enzyme-linked immunosorbent assay (ELISA)] to diagnose pregnancy.

Age, infertility causes, the number of previous IUI, the number of abortions and the number of follicles measuring 18 - 20 mm and pregnancy rates were separately evaluated and compared, in each group. Data were analyzed by SPSS version 13 (SPSS Inc., Chicago, IL, USA), with the Chi-square and Fisher-exact tests. A $P < 0.05$ was considered significant.

4. Results

This study comprised 309 infertile women, of which 152 subjects (49.2%) were in the HCG groups and 157 (50.8%) cases in urinary LH groups.

As shown in Table 1, no significant difference in pregnancy rates was observed between HCG and urinary LH groups (P = 0.58).

The two groups were not significantly different in terms of age (P = 0.45). Also, pregnancy rate was not significantly different between the age subgroups of HCG and LH groups.

There was no significant difference observed between the groups in terms of infertility causes (P = 0.24). Regarding the number of follicles of 18 - 20 mm, a significant difference was found between the two groups (P = 0.001).

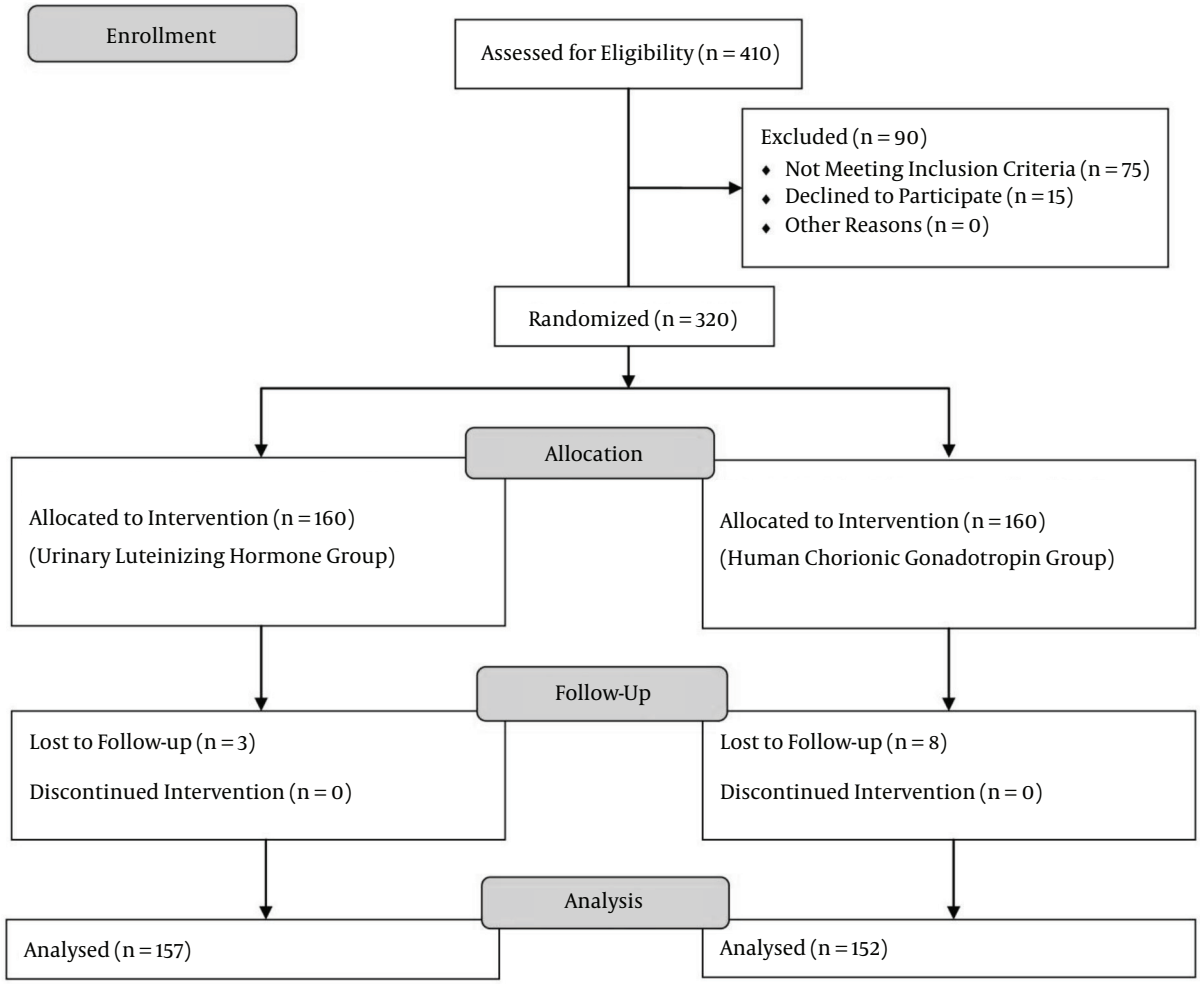

Figure 1. Study Protocol and Flowchart of the Participants

However, the pregnancy rate was not significantly different between HCG group and LH group, with respect to the number of follicles of 18 - 20 mm (Table 1).

The distribution of the number of previous IUI was not significantly different between the two groups (P = 0.43). Moreover, the pregnancy rate was not significantly different between HCG and LH groups, in relation to the number of previous IUI. Also, no significant difference was observed in the number of abortions among the two groups (P = 0.63) (Table 1). Moreover, pregnancy rate was not significantly different with respect to the number of abortions between HCG and LH groups.

5. Discussion

The results of the present study showed that pregnancy rate was not significantly different between HCG (12.8%) and urinary LH (12.1%) groups. The two groups were similar in terms of age, infertility causes, number of previous IUI and previous abortions. The only significant difference observed between the groups was related to the number of follicles of 18 - 20 mm (P = 0.001).

In the study performed in 1995 by Guttmacher, pregnancy rate was compared between different age groups and showed higher rate of pregnancy in age group of 20 - 25 years (9). In our study, the pregnancy rate was not significantly different between age subgroups of HCG and LH. The pregnancy rate was higher in those aged 20 - 25 years, in both HCG and LH groups, next to age group 25 - 30 years.

Table 1. Distribution of Pregnancy Rate, Infertility Causes, Number of Follicles, Number of Previous intrauterine Inseminations and Number of Previous Abortions in Chorionic Gonadotropin and Luteinizing Hormone Groups

	LH Surge (No = 157) N (%)	HCG Administration (No = 152) N (%)	P Value
Age, y			0.450
20 - 25	53 (33.8)	50 (32.9)	
26 - 30	63 (40.1)	55 (36.2)	
30 - 35	25 (15.9)	36 (27.3)	
More than 35	16 (10.2)	11 (7.3)	
Pregnancy rate			0.580
Negative	138 (87.9)	131 (86.2)	
Positive	19 (12.1)	21 (13.8)	
Infertility causes			0.240
Male	50 (32.1)	33 (22)	
Unknown	44 (28.2)	47 (31.3)	
Pelvic	15 (9.3)	24 (15.3)	
Ovulation disorder	37 (23.7)	35 (23.3)	
Male and female	11 (7.1)	13 (8.7)	
Number of follicles 18 - 20 mm			0.001
Two follicles	140 (89.2)	114 (75.0)	
Three follicles	14 (8.9)	24 (8.15)	
Four follicles	3 (1.9)	11 (7.2)	
Five follicles	0 (0.0)	3 (2.0)	
Number of previous IUI			0.430
No history	88 (56.1)	86 (56.6)	
Once	41 (26.1)	46 (30.3)	
Twice	20 (12.7)	17 (11.2)	
Three times	8 (5.1)	3 (2.0)	
Number of previous abortions			0.630
No history	128 (81.5)	132 (86.8)	
Once	21 (13.4)	15 (9.9)	
Twice and more	8 (5.1)	5 (3.3)	

Abbreviations: HCG, chorionic gonadotropin; IUI, intrauterine insemination; LH, luteinizing hormone.

In another study performed by Randall et al. in 2008, single IUI was compared with double IUI. The pregnancy rate was significantly higher in the double IUI group. In both single and double IUI groups, HCG administration and urinary LH groups were employed before IUI (10), whereas we only used single IU in our study.

In the study performed by Mitwally et al. in 2004, pregnancy rate was compared between three groups of urinary LH, HCG administration and urinary LH followed by HCG administration. They reported that pregnancy rate was significantly higher in the group using urinary LH plus HCG administration, while no significant difference was observed in pregnancy rates between urinary LH and HCG administration groups (11). The results of their study were consistent with our findings, with respect to urinary LH and HCG administration, as our study did not include the group with urinary LH and HCG administration.

Another study, performed by Cantineau et al. in 2007, reported that pregnancy rates was lower in the group that had LH surge before HCG administration, compared to those who only had HCG administration, although the difference was not statistically significant (12). This was simi-

lar to our finding, where the pregnancy rate was 13% in LH surge group and HCG administration group; the discrepancy may be due to the difference in sample volume.

Different methods for IUI timing were evaluated in a review article by Cantineau et al. in 2010. These methods included serum or urinary LH surge, HCG administration and sonography to determine ovulation and normal body temperature. They showed no significant differences between different methods for IUI timing in terms of live birth, although the highest rate of live birth was observed in urinary LH surge and HCG administration methods (13).

The meta-analysis, performed by Cantineau et al. in 2014, reported no evidence of a difference between HCG injection versus LH surge, in rates of pregnancy (14).

The urinary LH surge and HCG administration methods for IUI timing are similar and none showed any considerable advantage over the other, even though the use of urinary LH surge has no side effects and injection pain as the HCG administration methods.

Footnote

Conflict of Interest: No potential conflict of interest relevant to this article was reported

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