Original Article

Single versus Double Intrauterine Insemination in Controlled Ovarian Hyperstimulation Cycles: A Randomized Trial

Ziba Zahiri Sorouri MD[1], Romina Rashid Shomali MD•[1], Davoud Pourmarzi MSc[1]

Abstract

Background: There are many factors that affect intrauterine insemination (IUI) success rate and identifying those factors can be helpful. This study aimed to investigate the single versus double IUI in controlled ovarian hyperstimulation cycles.

Methods: This is a randomized clinical trial with equal randomization (1:1) conducted on 580 women who underwent IUI in a private infertility clinic from May 2013 to November 2014 in Rasht, Iran. Women were randomly assigned to single (n = 290) or double (n = 290) IUI groups. Women in the single group underwent IUI performed 36 hours after human chorionic gonadotropin (HCG) administration. Women in the double group underwent two IUIs performed 18 and 40 hours after HCG administration. The main outcome was clinical pregnancy confirmed by evidence of fetal cardiac activity. Data were analyzed by SPSS software. Comparisons of frequencies were done using the Fisher exact test and Chi-square test. For comparing means between the two groups, the independent *t*-test was used. The *P*-value < 0.05 was considered to indicate statistical significance.

Results: Pregnancy rate was 11.7% (34/290) in the single IUI group and 13.4% (39/249) in the double IUI group. The difference between the two groups was not statistically significant (*P* = 0.617, OR = 1.17, 95% CI: 0.72 – 1.91). Also, we could not show significant difference between single and double IUI groups in different cause of infertility groups regarding the success rate.

Conclusion: Based on findings, double versus single IUI did not increase the pregnancy rate of IUI and further investigations are recommended.

Keywords: Controlled ovarian hyperstimulation, intrauterine insemination, pregnancy rate, single and double insemination

Cite this article as: Zahiri Sorouri Z, Rashid Shomali R, Pourmarzi D. Single versus double intrauterine insemination in controlled ovarian hyperstimulation cycles: A randomized trial. *Arch Iran Med*. 2016; **19(7):** 465 – 469.

Introduction

Various medical modalities have been used to treat infertility. Intrauterine insemination (IUI) is an inexpensive and low invasive method of assisted reproduction technologies (ART).[1] Controlled ovarian hyperstimulation with IUI is approved, cost effective, efficient, and the first-line of choice for infertility treatment with unexplained cause, mild male factors, and ovulation disorders.[2,3] Previous investigations reported 10% – 20% success rate for clinical pregnancy by IUI.[3] There are many factors such as: causes of infertility, age, number of dominant follicles, the history of pelvic inflammatory diseases, endometrial thickness, and duration of infertility that can have a significant effect on the success rate of IUI.[4–7] Moreover, it seems that considerable changes done in the protocol of IUI including timing and the frequency can enhance the success rate.[8,9] Double IUI is a method with increased frequency and change in timing versus single IUI. Recommending the double IUI has been done because it has been reported that the longer period of adjacency between the sperm and oocyte may result in an elevated success rate.[10]

However, there is no confirming consensus on the preference of double IUI versus single IUI. Previous studies have reported conflicting findings regarding the success rate by single and double IUI.[11–17] Based on a systematic review and a meta analyses, there is no significant preference of the double IUI versus the single one.[18,19] However, in some studies higher pregnancy rate were reported by the double IUI than the single one.[13,15,17]

According to the conflicting results and the limited knowledge regarding the success rate of the double IUI, in this study we aimed to compare the success rate of the single and double IUI in the controlled ovarian hyperstimulation cycles.

Materials and Methods

Trial design and setting

Ethical approval was received from the ethical committee of the Guilan University of Medical Sciences. Before inclusion in this trial, written informed consent were obtained from all patients.

This study was a parallel randomized clinical trial with equal randomization (1:1) that was conducted on all eligible IUI candidates who attended a private infertility clinic in Rasht, Iran, from May 2013 to November 2014.

Patients

Eligible patients were all IUI candidate women with mild male factor infertility, unexplained infertility, and polycystic ovary syndrome (PCOS) who could not become pregnant even after being inducted six times and producing dominant follicle. Women with 2 – 5 dominant follicles ≥ 18 mm in size and basal Follicle-stimulating hormone (FSH) levels 12 mIU/L were included.

Authors' affiliations: [1]Reproductive Health Research Center, Department of Obstetrics and Gynecology, Alzahra Hospital, Guilan University of Medical Sciences, Rasht, Iran.

•Corresponding author and reprints: Romina Rashid Shomali MD, Reproductive Health Research Center, Department of Obstetrics and Gynecology, Alzahra Hospital, Guilan University of Medical Sciences, Rasht, Iran, P. O. Box: 4144654839, Tel: +98-911-1834561, E-mail: Rominashomali@gmail.com

Accepted for publication: 11 May 2016

Patients with blocked fallopian tubes and endometriosis were not included and cervical factor was not assessed. Each participant received one cycle of IUI treatment.

For infertility causes detection and classification, a gynecologist used the patients' history, physical examination, laboratory tests, hysterosalpingography, and laparoscopy. In this study, unexplained infertility was indicated in couples with normal sperm parameters, unblocked fallopian tubes, and defined ovulation. Male infertility determined by the sperm count and its motility based on the World Health Organization criteria, in which the baseline feature of normal sperm is ≥ 20 million/mL with ≥ 50% progressive motility after one hour collection. Oligospermia and asthenospermiaor both in combination with ≤ 10 million progressive sperm indicated mild male infertility.[20] Polycystic ovary syndrome was noted by rolling out pregnancy hypothalamic-hypopituitarism disorders and other causes of hyperandrogenism. Also, 2 out of 3 criteria including Oligo ovulation or anovulation, hyperandrogenism, polycystic ovaries that were defined by ultrasound indicated PCOS.[21]

Randomization and interventions

During the first to third day of their menstrual cycle, transvaginal ultrasound was performed for all participants and ovarian inductions were done for women who did not have ≥15 mm cysts. Ovarian inductions were done using clomiphene citrate (Iran Hormone, Iran) or letrezol (Iran Hormone, Iran) with or without human menopausal gonadotropin (HMG) (Merional, IBSA, Switzerland). Type and dose of administrated medications were used based on the response of patients that was chosen by the physician. Follicle monitoring was performed by serial transvaginal ultrasonography and when there were 2 – 5 dominant follicles ≥ 18 mm in size, 5000 IU human chorionic gonadotropin (HCG) (IBSA, Switzerland) was administered. On the HCG injection day, participants were randomly assigned to two single and double IUI groups. Random sequence was generated by a co-worker with no clinical involvement in the trial using the block randomization method.

Semen specimens were obtained a few hours before the scheduled time of insemination. In this study, the standard swim-up technique was used for semen preparation. Liquefaction of the seminal sample with buffer solution was performed in a sterile tube and centrifuged slowly at 200 g – 300 g for 10 min and the supernatant was discarded. This step was repeated 2 – 3 times and the final remaining sperm was over layered with 0.5 – 1 cc of culture medium and stored inside an incubator at 37°C for 30 – 60 min to cause sperms with the most motility migrate to supernatant in order to be used for IUI. Sperm count and motility was calculated by a gynecologist who was infertility fellowship and had about 10 years expertise in this area using the final swim-up sample. The IUI was indicated in cases with at least 1 million sperms.

For the single IUI group, IUI was performed 36 hours after HCG injection and for the double IUI group it was performed 18 and 40 hours after HCG injection. Excess mucus was removed to prevent catheter blockage. An injection catheter with 0.5 mL sample was entered for 10 – 30 seconds in the cervical orifice and driven directly into the uterine cavity. According to protocol the patients remained supine for 15 min after IUI. All participants were educated about prohibition of intercourse, NSAIDs, and antihistamine use for 72 hours previous until 72 hours after insemination.

Data collection and outcomes

Clinical pregnancy that was defined as detection of fetal cardiac activity (FCA) after IUI was the primary outcome of this trial. Serum beta human chorionic gonadotropin (BHCG) was assessed 15 days after IUI for women who experience a missed menstrual period. Transvaginal sonography was performed for participants with a positive result of BHCG at the seventh week of gestation for evaluation of FCA. All FCA evaluations were performed by the study's principle investigator.

Baseline data including the women's age, their husbands' age, women's body mass index (BMI), level of FSH and luteinizing hormone (LH), cause and type of infertility, duration of infertility, motility and sperm count, the number of dominant follicle during HCG injection, endometrial thickness, and endometrial pattern were collected. Also the incidence of miscarriage, ectopic pregnancy, and multiple pregnancies were recorded.

Statistical analysis

To detect at least 7% difference in pregnancy rate between the two groups with an alpha error level of 5% and a power of 80%, 290 participants in each group were recruited. Data were analyzed by SPSS software (Statistical Package for the Social Sciences, version 21.0, SPSS Inc, Chicago, Illinois, USA). Intention to treat analysis was used and involved all women who underwent IUI. Comparisons of frequencies were done using the Fisher exact test and Chi-square test. For comparing means between the two groups, the independent *t*-test was used. The *P*-value < 0.05 was considered to indicate statistical significance.

Results

During the study duration 627 women were eligible to participate and of these 47 patients refused to be included into the study. Five hundred and eighty patients were randomly assigned equally into two groups: single IUI (n = 290) and double IUI (n = 290). Two women in the single IUI group and three women in the double IUI group were lost to follow-up (Figure 1).

There were no significant difference between the groups regarding women's age, their husbands' age, women's BMI, duration of infertility, causes and types of infertility, the level of FSH and LH, the number of dominate follicles, endometrial thickness, endometrial pattern, and the sperm character ($P > 0.05$) (Table 1).

In the single and double groups, 15.2% and 17.9% of female had a positive B-HCG test, respectively ($P = 0.434$). Furthermore, 11.7% (34/290) in the single and 13.4% (39/290) in the double IUI groups had positive FCA and this difference was not statistically significant ($P = 0.617$, OR = 1.17, 95% CI: 0.72 – 1.91) (Table 2).

In further analysis, the difference between success rates in the single and double groups in women with primary ($P = 0.512$) and secondary ($P = 0.999$) infertility were not significant. Also, these differences were not significant in any of the fertility cause and type groups. There was no significant difference in the success rate in patients with normal sperm ($P = 0.680$), asthenospermia ($P = 0.999$) and oligospermia ($P = 0.751$) (Table 2).

In the single IUI group, 2 subjects (4.5%) and in the double IUI group, 8 subjects (15.4%) experienced miscarriage ($P = 0.103$). Ectopic pregnancy in the single group occurred in 4 (9.1%) patients and in the double group in 4 (7.7%) patients ($P = 0.999$). Also, incidence of multiple pregnancy in the single IUI was

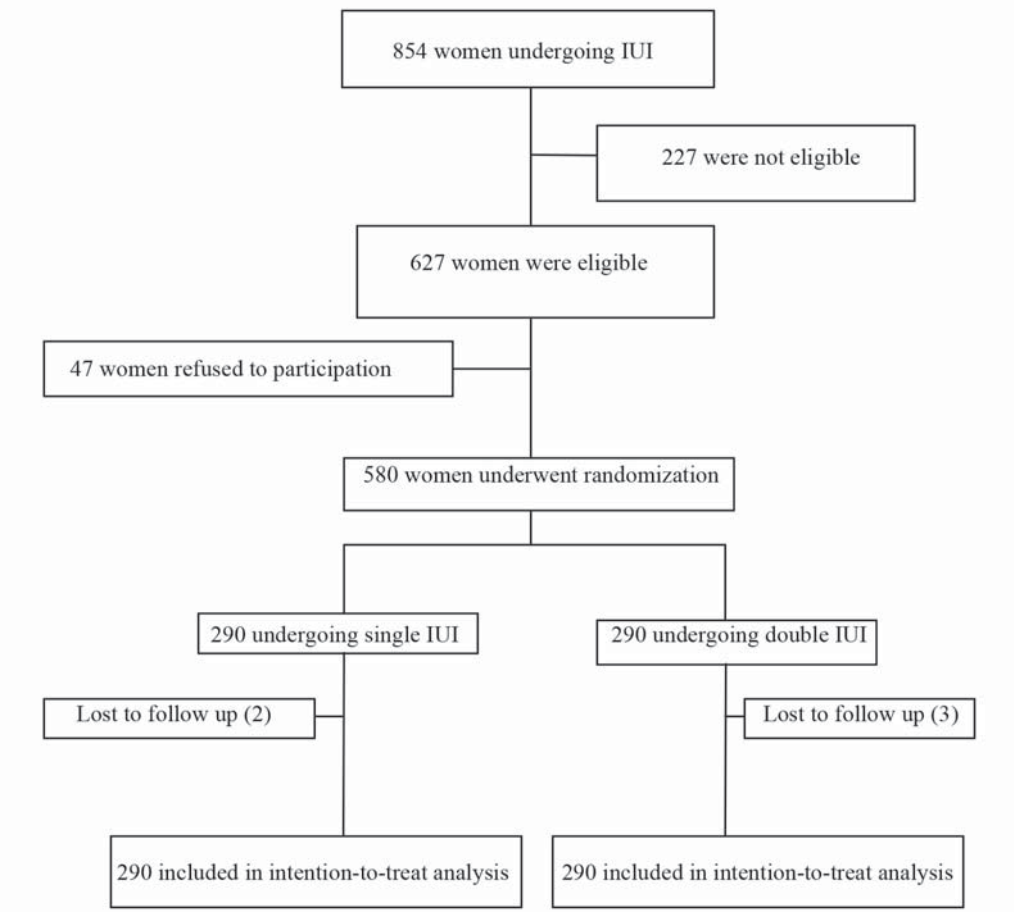

Figure 1. Flowchart of participants

Table 1. Baseline characteristics of patients

Characteristics	Single IUI (n = 290)	Double IUI (n = 290)	*P*-value
Women's age (year)	30.57 ± 5.46	29.77 ± 5.31	0.077[a]
Husband's age (year)	34.31 ±5.74	34.47 ± 6.25	0.746[a]
BMI	27.90 ± 4.99	27.54 ± 4.43	0.357[a]
Infertility duration (year)	4.04 ± 3.67	3.70 ± 2.77	0.210[a]
FSH (mg/dl)	6.27 ± 3.64	6.14 ± 4.96	0.726[a]
LH (mg/dl)	7.12 ± 5.56	7.95 ± 7.87	0.141[a]
Dominant follicle numbers	3.35 ± 1.09	3.51 ± 1.08	0.062[a]
Type of infertility			
Primary	255 (87.9)	261 (90)	0.508[b]
Secondary	35 (12.1)	29 (10)	
Cause of infertility			
Unexplained	98 (33.8)	89 (30.7)	0.610[c]
Male factor	41 (14.1)	38 (13.1)	
PCOS	118 (40.7)	134 (46.2)	
Both male and PCOS	33 (11.4)	29 (10)	
Endometrial thickness (mm)			
≥ 7	9 (3.1)	5 (1.7)	0.418[b]
7 <	281 (96.9)	285 (98.3)	
Endometrial pattern			
Homogen	38 (13.1)	25 (8.6)	0.109[b]
Triple	252 (86.9)	265 (91.4)	
Sperm count (×10 ^{6} P/ml)			
Normal	216 (74.5)	223 (76.9)	0.561[b]
Oligospermia	24 (8.3)	22 (7.6)	0.878[b]
Asthenospermia	50 (17.2)	45 (15.5)	0.654[b]

*Data are Mean ± SD or numbers (%); a: Independent t-test was used; b: Fisher exact test was used; C: Chi-square test was used.

Table 2. Comparison of IUI success rate between two single and double IUI

Variables	Single IUI (n = 290)	Double IUI (n = 290)	OR (95% Confidence Interval)	*P*-value
FCA*	34 (11.7)	39 (13.4)	1.17 (0.72–1.91)	0.617[a]
FCA in unexplained group	10 (10.2)	9 (10.1)	0.99 (0.38–2.56)	0.999[a]
FCA in mild male infertility group	3 (7.3)	3 (7.9)	1.09 (0.21–5.74)	0.999[a]
FCA in POCS group	18 (15.3)	23 (17.2)	1.15 (0.59–2.26)	0.734[a]
FCA in both mild male and PCOS group	3 (9.1)	4 (13.8)	1.60 (0.33–7.83)	0.696[a]
FCA in Normal Sperm morphology	28 (13.0)	32 (14.3)	1.17 (0.72–1.91)	0.680[a]
FCA in oligospermia	1 (4.2)	1 (4.5)	1.10 (0.06–18.64)	0.999[a]
FCA in asthenospermia	5 (10)	6 (13.3)	1.38 (0.39–4.89)	0.751[a]
FCA in primary infertility	30 (11.8)	36 (13.8)	1.20 (0.74–2.02)	0.512[a]
FCA in secondary infertility	4 (11.4)	3 (10.3)	0.89 (0.183–436)	0.999[a]

a: Fisher exact test was used; *FCA: fetal cardiac activity.

detected in 2 cases (4.5%) and in double IUI groups was detected in 6 (11.5%) and this difference was not significant ($P = 0.282$). Furthermore, 2 patients (3.8%) in the double IUI group had triple pregnancy ($P = 0.498$).

Discussion

Controlled ovarian hyperstimulation with IUI is the common modality for infertility treatment. Also, due to its cost-effectiveness and low invasiveness, it is indicated as the first line of treatment for several causes of infertility.[2,3]

There have been many attempts to improve the chance of fertility by IUI. Some studies emphasized the appropriate selection of patients and others focused on changes in the IUI process.[5–9] Also, clinicians were concerned about the changes in frequency and time of IUI and mentioned them as significant factors.[8,9] Although, the effect of the double IUI as ART has been investigated, various investigations reported inconsistent findings.[18,19] It seems that these different findings could be justified due to differed inclusion criteria and timing.

Based on our findings the success rates in the single and double IUI groups were 11.7% and 13.4%, respectively and this difference was not statistically significant. Also, we could not show significant difference between single and double IUI groups in different cause of infertility groups regarding the success rate.

Our findings are consistent with most of the previous studies. In a meta-analysis by Osun, et al. it was reported that the success rate by double IUI (14.9%) was not significantly higher than by single IUI (11.4%).[19] Bagis, et al. in a study evaluated 228 women with at least 2 dominate follicles. In that study only unexplained and male infertility causes were included. They performed single IUI at 36 hours and double IUI at 18 and 40 hours after HCG administration and reported 10.7% and 12.3% success rates in the single and double IUI, respectively and the difference was not statistically significant.[12] Furthermore, Alborzi, et al. assessed 486 controlled ovarian hyperstimulations in 110 patients with male infertility, cervical disorders, or unexplained infertility. Single IUI was performed at 34 hours and double IUI was performed at 12 and 34 hours after HCG injection. Clinical pregnancy in single and double IUI was noted in 7.9% and 9.4% of cycles, respectively, and no significant difference was mentioned.[11] In other study, Tongue, et al. assessed infertile couples in three groups: group I (single IUI at 24 hours after HCG injection), II (double IUI at 12 and 36 hours after HCG administration), and III (single IUI at 36 hours after administration).The success rate in groups I, II and III were 11.3%, 14% 17.2%, respectively, and the differences among the groups were not statistically significant.[16] Also, Geznic, et al. assigned 100 infertile women randomly as single (at 36 hours after HCG administration) and double IUI groups (at 24 and 48 hours after HCG administration). They assessed 75 and 78 cycles in the single and double IUI groups, respectively. Clinical pregnancy rate between single (10%) and double (6.4%) IUI groups was not statistically significant.[2] Rahman, et al. assessed 160 infertile couples with unexplained cause. Single (at 34 hours after HCG injection) and double (at 12 and 34 hours after HCG injection) IUI were been performed for 195 and 204 cycles, respectively. The success rate difference between the single (13.3%) and double (11.8%) IUI groups was not statistically different.[14] Furthermore, Ghanem, et al. assessed 106 and 192 cycles in the double and single IUI groups, receptively. All patients underwent single IUI at 34 to 38 hours after HCG injection. Also, double IUI was performed at 24 hours after the first step. There was no significant difference between the single (9.4%) and double (5.05%) IUI regarding success rate. In addition, success rate in the single and double groups with male infertility (2.8% versus 13.3%), unovulation (8% versus 12.5%), and unexplained cause (5.5% versus 6.6%) was not significantly different.[4]

Although, consistent with our finding, the majority of studies reported no significant difference between single and double IUI, there are some studies that reported the superiority of double IUI.[13,15,17] Liu, et al. assigned 1257 couples with male factors and unexplained cause into two groups of single (at 34 hours) and double IUI (at 18 and 48 hours after HCG administration). Success rate in the double IUI group (19.9%) was significantly higher than in the single IUI group (11.1%). But further analysis showed significant difference only in the male infertility in which the success rates were 24.9% by double and 11.3% by single IUI. In the unexplained infertility group, the success rates were 11.9% in the double and 10.5% in the single IUI groups, respectively and there was not any significantly different.[13] Moreover, Randall, et al. assessed 595 couples with ovulation disorders, endometriosis, male infertility, unexplained infertility or with combined types of infertility. Patients were assigned non-randomly into single and double IUI groups. Single IUI was performed at 36 hours and double IUI was performed at 18 and 36 hours after HCG administration. Success rate by double IUI was 16.2% and by single IUI was 11% and this difference was statistically significant.[15] In other study by Ragni, et al. 273 patients with male and unexplained infertility undergoing controlled ovarian hyperstimulation and IUI were included. Pregnancy rate were reported at 14.4% by single IUI 34

hours after HCG administration, 30.4% by double IUI 12 hours and 34 hours after HCG administration, and 10.9% by double IUI 34 hours and 60 hours after HCG administration. Success rate in the double IUI 12 hours and 34 hours after HCG administration group was significantly higher than the two other groups.[17]

It seems that these different results might be a result of different timing of IUI, frequency of cycles, the inclusion criteria, and randomization. In Liu, et al.'s[13] study, patients with mild and moderate male infertility and unexplained infertility were included. However, in our study patients with PCOS, mild male infertility and unexplained infertility were included, and we did not include patients with moderate male infertility. In addition, we assessed patients for one cycle of IUI while Randall, et al.[15] and Ragni, et al.[17] evaluated multiple cycles of ovulation hyperstimulation. In Randall, et al.'s study, patients with infertility induced by endometriosis were included, which was inconsistent with our study. Randall, et al. did not assign patients into the groups randomly, which can lead to biased results.[15] Also, we did not assess the cycle with one dominant follicle due to the hypothesis that cycles including one follicle can decrease the rate of success in double IUI.

We had some limitations in this study. In this study we did not evaluate the final result of pregnancy. Therefore, we suggest a follow up period for further investigations to assess live birth rate. Performing further trials with higher sample size is recommended. Also, higher success rate in some subgroups of infertility by double IUI and further investigations with sufficient sample size are recommended to compare subgroups.

In conclusion, based on our findings, there was no significant difference between single IUI performed 36 hours after HCG administration and double IUI performed 18 and 40 hours after IUI in regard to clinical pregnancy rate.

Conflict of interest

The authors report no conflict of interest related to this study.

RCT registration number: *IRCT201307231306N7.*

Acknowledgments

This study was based on a thesis submitted by the Romina Rashid Shomali at the Guilan University of Medical Sciences. The authors acknowledge with grateful appreciation the financial support provided by the Research voice chancellorship at the Guilan University of Medical Sciences. We sincerely appreciate the participation of women in this project.

References

1. Mukherjee GG, Pal B, Sarkar M. IUI: Intrauterine Insemination. Jaypee brothers medical publishers, India, 2012.
2. Guzick DS, Carson SA, Coutifaris C, Overstreet JW, Factor–Litvak P, Steinkampf MP, et al. Efficacy of superovulation and intrauterine insemination in the treatment of infertility. *N Engl J Med*. 1999; 340(3): 177 – 183.
3. Duran HE, Morshedi M, Kruger T, Oehninger S. Intrauterine insemination: a systematic review on determinants of success. *Hum Reprod Update*. 2002; 8(4): 373 – 384.
4. Yavuz A, Demirci O, Sözen H, Uludoğan M. Predictive factors influencing pregnancy rates after intrauterine insemination. *Iran J of Reprod Med*. 2013; 11(3): 227 – 234.
5. Merviel P, Heraud MH, Grenier N, Lourdel E, Sanguinet P, Copin H. Predictive factors for pregnancy after intrauterine insemination (IUI): an analysis of 1038 cycles and a review of the literature. *Fertil Steril*. 2010; 93(1): 79 – 88.
6. Barros DJ, Rojas RJ, Molina MA, Villalobos AS, Sánchez SV, Barroso VG, et al. Prognostic factors of pregnancy in intrauterine insemination. *Ginecol Obstet Mex*. 2006; 74(12): 611 – 625.
7. Ibérico G, Vioque J, Ariza N, Lozano JM, Roca M, Llácer J, et al. Analysis of factors influencing pregnancy rates in homologous intrauterine insemination. *Fertility and Sterility*. 2004; 81(5): 1308 – 1313.
8. Ragni G, Somigliana E, Vegetti W. Timing of intrauterine insemination: where are we? *Fertil Steril*. 2004; 82(1): 25 – 26.
9. Ransom M, Blotner M, Bohrer M, Corsan G, Kemmann E. Does increasing frequency of intrauterine insemination improve pregnancy rates significantly during superovulation cycles? *Fertil Steril*. 1994; 61(2): 303 – 307.
10. Andersen A, Als – Nielsen B, Hornnes P, Andersen LF. Time interval from human chorionic gonadotrophin (HCG) injection to follicular rupture. *Hum Reprod*. 1995; 10(12): 3202 – 3205.
11. Alborzi S, Motazedian S, Parsanezhad ME, Jannati S. Comparison of the effectiveness of single intrauterine insemination (IUI) versus double IUI per cycle in infertile patients. *Fertil Steril*. 2003; 80(3): 595 – 599.
12. Bagis T, Haydardedeoglu B, Kilicdag EB, Cok T, Simsek E, Parlakgumus AH. Single versus double intrauterine insemination in multi–follicular ovarian hyperstimulation cycles: a randomized trial. *Hum Reprod*. 2010; 25(7): 1684 – 1690.
13. Liu W, Gong F, Luo K, Lu G. Comparing the pregnancy rates of one versus two intrauterine inseminations (IUIs) in male factor and idiopathic infertility. *J Assist Reprod Genet*. 2006; 23(2): 75 – 79.
14. Rahman SM, Malhotra N, Kumar S, Roy KK, Agarwal A. A randomized controlled trial comparing the effectiveness of single versus double intrauterine insemination in unexplained infertility. *Fertil Steril*. 2010; 94(7): 2913 – 2915.
15. Randall GW, Gantt PA. Double vs. single intrauterine insemination per cycle: use in gonadotropin cycles and in diagnostic categories of ovulatory dysfunction and male factor infertility. *J Reprod Med*. 2008; 53(3): 196 – 202.
16. Tonguc E, Var T, Onalan G, Altinbas S, Tokmak A, Karakaş N, et al. Comparison of the effectiveness of single versus double intrauterine insemination with three different timing regimens. *Fertil Steril*. 2010; 94(4): 1267 – 1270.
17. Ragni G, Maggioni P, Guermandi E, Testa A, Baroni E, Colombo M, et al. Efficacy of double intrauterine insemination in controlled ovarian hyperstimulation cycles. *Fertil Steril*. 1999; 72(4): 619 – 622.
18. Cantineau A, Heineman M, Cohlen B. Single versus double intrauterine insemination in stimulated cycles for subfertile couples: a systematic review based on a Cochrane review. *Hum Reprod*. 2003; 18(5): 941 – 946.
19. Osuna C, Matorras R, Pijoan JI, Rodríguez–Escudero FJ. One versus two inseminations per cycle in intrauterine insemination with sperm from patients' husbands: a systematic review of the literature. *Fertil Steril*. 2004; 82(1): 17 – 24.
20. Dickey RP, Pyrzak R, Lu PY, Taylor SN, Rye PH. Comparison of the sperm quality necessary for successful intrauterine insemination with World Health Organization threshold values for normal sperm. *Fertil Steril*. 1999; 71(4): 684 – 689.
21. ESHRE TR, Group A–SPCW. Revised 2003 consensus on diagnostic criteria and long–term health risks related to polycystic ovary syndrome. *Fertil Steril*. 2004; 81(1): 19 – 25.