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Journal of the Chinese Medical Association 80 (2017) 366–370

www.jcma-online.com

Original Article

Does intrauterine insemination timing matter for achieving pregnancy during ovulation induction using gonadotropins? A retrospective cohort study

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Received May 14, 2016; accepted June 16, 2016

Abstract

Background: Intrauterine insemination (IUI) is a commonly used procedure to increase the infertile couples' chance of pregnancy. Single or double insemination and different timing choices are modifications of this intervention. The aim of this study was to elucidate the effect of the IUI procedure on clinical pregnancy rates when performed at 24 hours or 36 hours after ovulation triggered by human chorionic gonadotropin (hCG) following ovulation induction with gonadotropins.

Methods: One hundred and thirteen women diagnosed with polycystic ovarian syndrome (PCOS) (as per Rotterdam's criteria) or unexplained infertility, who were treated using gonadotropins for ovulation induction and IUI for increasing fertilization potential, were recruited from the medical records of the infertility clinic. Demographic features, cycle outcomes, and clinical pregnancy rates of the patients were compared based on two different timing strategies of IUI (24 hours and 36 hours) following ovulation trigger using hCG.

Results: Clinical pregnancy rates per cycle were 22.9% in the PCOS group and 26.9% in the unexplained group. The clinical pregnancy rates according to the timing of IUI were found to be similar for PCOS patients, unlike patients with unexplained infertility whose clinical pregnancy rates were significantly better when the IUI procedure was performed 24 hours following the hCG trigger. The cycle day of hCG trigger was also found to be significantly related to clinical pregnancy rate as utilizing a later hCG trigger day appeared to positively affect the odds of clinical pregnancy establishment.

Conclusion: IUI performed at either 24 hours or 36 hours after ovulation triggered by hCG injection does not change clinical pregnancy rates for PCOS patients. Patients with unexplained infertility seem to benefit from earlier IUI procedures, which increases their fertility potential during ovulation induction with gonadotropins. Avoiding earlier than physiologically needed artificial-hCG triggering before IUI procedures results with better pregnancy rates.

Keywords: clinical pregnancy; gonadotropin; infertility; intrauterine insemination

1. Introduction

Intrauterine insemination (IUI) with or without ovarian stimulation is a common treatment for infertility. Despite the popularity of this assisted reproductive technique, IUI is widely used to improve pregnancy rates with mild male factor, unexplained infertility, cervical factor, anovulation, and

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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http://dx.doi.org/10.1016/j.jcma.2016.06.005

minimal and mild endometriosis.[1] It is a simple and relatively less invasive and less expensive procedure than other forms of assisted reproductive technology.[2] The minimum requirements for performing the procedure are: (1) ovulation in the IUI cycle; (2) patency of at least one fallopian tube; (3) insemination with an adequate number of motile sperm; and (4) the absence of documented or suspected active cervical, intrauterine, or pelvic infection.[1]

Stimulated IUI is much more effective than natural cycle or controlled ovarian hyperstimulation treatment. In four randomized trials of patients with unexplained subfertility, pregnancy rates were higher when IUI was performed in stimulated cycles than in natural cycles [odds ratio (OR): 2.14; 95% confidence interval (CI): 1.26−3.61; pregnancy rates: 25% vs. 14% for stimulated and natural cycles, respectively, where 26 patients received clomiphene citrate, and 370 patients received gonadotropins].[3] According to the 2009 European Society of Human Reproduction and Embryology Capri Workshop, the pregnancy rates with clomiphene citrate and IUI were 7%, and with follicle stimulating hormone (FSH) ovarian stimulation and IUI they were 12% per cycle.[1] However, there are various criteria affecting the success rate of IUI including age, indications of IUI, the optimal procedures for sperm preparation, insemination methods, and timing.[1,4]

There is not a consensus on the optimal timing of IUI. In the large majority of published studies, insemination is performed 32−36 hours following human chorionic gonadotropin (hCG) administration. A 2014 systematic review compared the optimum time interval from hCG injection to IUI, comparing different time frames ranging from 24 hours to 48 hours, and found no difference in the pregnancy rate per couple.[5] Luciano et al[6] showed that ultrasound-confirmed follicle rupture occurred on Day +1 of the luteinizing hormone (LH) surge in 6% of patients, on Day +2 in 72%, and on Day +3 in 21%. In light of this finding, it seems probable that IUI on Day +1 after hCG injection, plus properly timed intercourse, could achieve results similar to those obtained with IUI on Day +2 after hCG injection in infertile couples with normal spermiograms. The clinical effect of IUI on pregnancy rates for different infertility etiologies such as polycystic ovary syndrome (PCOS) and unexplained infertility has not yet been extensively evaluated. Although the efficiency of IUI procedures for unexplained infertility in patients has been proven, the clinical benefit of this procedure is not clear for PCOS patients whose central problem is anovulation rather than fertilization. The primary aim of this study was to elucidate the effect on clinical pregnancy rates of the IUI procedure performed at 24 hours or 36 hours after ovulation triggered by hCG, following ovulation induction with gonadotropins. The secondary aim of the study was to compare the clinical pregnancy rates for PCOS and unexplained infertility that is associated with the timing of IUI procedures, during ovulation induced by gonadotropins.

2. Methods

This retrospective study was approved by the ethics committee of the Zekai Tahir Burak Women's Health Research and Education Hospital, Ankara, Turkey. One hundred and thirteen women diagnosed with PCOS (as per Rotterdam's[7] criteria) or unexplained infertility were recruited from the medical records of the infertility clinic. Couples were evaluated with semen analyses, hysterosalpingogram and/or laparoscopy, and transvaginal sonographic screening performed in the early follicular phase of cycle and midluteal serum progesterone. The husbands of all patients had normal spermiogram results based on at least two semen analyses according to the World Health Organization 2010 criteria. All women had at least one tubal patency, documented by hysterosalpingogram and in some cases also by laparoscopy. Early follicular phase hormone assay (basal FSH, LH, estradiol (E2), prolactine (PRL), and thyroid stimulating hormone (TSH)) measurements were made on Day 3 of the cycle. Couples with endometriosis, uterine or tubal factor, poor ovarian reserve, and male infertility were excluded. Patients were classified into two groups according to their infertility diagnosis: unexplained ($n = 78$) and PCOS ($n = 35$). A couple was considered to have unexplained infertility when the results of semen analysis, hormonal assay, hysterosalpingography, and/or laparoscopy were normal.[8]

Controlled ovarian hyperstimulation was initiated with 37.5−150 IU of pure FSH or human menopausal gonadotropin (hMG) starting on Day 2 or Day 3 of the cycle. Transvaginal USG was performed with serum E2 levels starting on Day 6 for the follicular development. A dose of 10,000 IU urinary hCG or 250 μg recombinant hCG was administered when at least one follicle of $\geq$ 18 mm was seen on transvaginal ultrasonography.

Patients were divided randomly into two groups at the time of hCG administration. Patients in Group 1 ($n = 38$; 33.6%) underwent IUI 24 hours after hCG administration. Group 2 ($n = 75$; 66.4%) underwent IUI 36 hours after hCG administration. All patients were instructed to have intercourse when the dominant follicle reached a diameter of approximately 16 mm and 12 hours after insemination. Following the transfer, the patients received 200 mg/day vaginal progesterone supplementation for luteal support until 12 weeks of gestational age if the patient conceived. Qualitative serum β-hCG test was performed 14 days after insemination if menstruation had not started. A clinical pregnancy was defined as the presence of a gestational sac with accompanying fetal cardiac activity by ultrasound at least 4 weeks after insemination. The demographic features, infertility types, dominant follicle number, endometrial thickness on hCG day, timing of intrauterine insemination, and clinical pregnancy rates of the patients have been evaluated. Statistical analysis was performed as follows: normal distribution of data was evaluated using the Kolmogorov−Smirnov test. The continuous variables were presented as means ± standard deviation and compared using the independent samples t test. The nonparametric variables and data without normal distribution were tested using the Mann−Whitney U test, and correlation analysis was performed using Spearman's correlation test. The comparison of categorical values was made utilizing Fisher's exact test or Chi-square test. A p value < 0.05 were considered statistically significant.

3. Results

The cycle outcomes of patients who underwent IUI procedures 24 hours and 36 hours following hCG trigger after ovulation induction with gonadotropin treatment are presented in Table 1. Basic characteristics of patients according to the infertility etiology, PCOS, or unexplained infertility, are shown in Table 2. Clinical pregnancy rates were found to be similar between the urinary and recombinant hCG trigger procedures ($p = 0.06$).

Clinical pregnancy rates per cycle were 22.9% in the PCOS group, and 26.9% in the unexplained group ($p = 0.64$). The clinical pregnancy rate of the patients who underwent IUI procedures 24 hours and 36 hours following hCG trigger was 39.5% and 17.4%, respectively ($p = 0.017$; OR = 2.84, 95% CI = 1.18–6.79). When the same analysis was performed separately on the subgroups, PCOS patients, and patients with unexplained infertility, the clinical pregnancy rate when IUI procedures were performed at 24 hours or 36 hours was found to be similar for PCOS patients. However, in the unexplained infertility group, the clinical pregnancy rates were significantly better when the IUI procedure was performed 24 hours following hCG trigger ($p = 0.011$; OR = 3.73, 95% CI = 1.11–10.60).

Table 1
Cycle outcomes of patients who have undergone IUI procedures 24 hours and 36 hours following hCG trigger after ovulation induction with gonadotropin treatment.

Parameter (mean ± SD)	IUI 24 hours following hCG trigger (mean ± SD) $n = 35$	IUI 36 hours following hCG trigger (mean ± SD) $n = 78$	p
Age (y)	28.3 ± 4.5	30.1 ± 5.4	0.09[a]
BMI (ratio)	26.0 ± 5.0	25.5 ± 4.4	0.37[b]
Infertility duration (y)	3.8 ± 2.9	4.1 ± 2.8	0.45[b]
Day 3 FSH (mIU/mL)	7.4 ± 8.1	7.2 ± 2.1	0.79[a]
LH (mIU/mL)	6.9 ± 4.8	7.3 ± 6.4	0.43[a]
E2 (pg/mL)	36 ± 12	42 ± 15	0.03[a,*]
Cycle day of gonadotropin commencement (d)	2.7 ± 0.6	2.7 ± 0.5	0.88[b]
hCG trigger day of cycle (d)	12.7 ± 3.3	11.8 ± 3.0	0.17[b]
>17 mm follicle number (*n*)	1.9 ± 0.9	1.6 ± 0.9	0.08[b]
Largest diameter of leading follicle (mm)	17.7 ± 1.3	18.0 ± 1.1	0.17[a]
hCG day endometrial thickness (mm)	10.0 ± 2.2	9.3 ± 1.8	0.06[a]
Clinical pregnancy rate, *n* (%)	15 (39.5)	14 (18.7)	0.017*
Abortion rate, *n* (%)	3 (20)	3 (21.4)	0.41[a]

*$p < 0.05$.
BMI = body mass index; E2 = estradiol; FSH = follicle stimulating hormone; hCG = human chorionic gonadotropin; LH = luteinizing hormone; IUI = intrauterine insemination; SD = standard deviation.
[a] Independent samples *t* test.
[b] Mann–Whitney *U* test.

Table 2
Basic characteristics of patients according to the infertility etiology.

Parameter (mean ± SD)	PCOS (mean ± SD) $n = 35$	Unexplained infertility (mean ± SD) $n = 78$	p
Age (y)	28.7 ± 4.6	29.8 ± 5.4	0.29[a]
BMI (ratio)	25.4 ± 3.8	24.1 ± 2.9	0.56[b]
Infertility duration (y)	4.8 ± 3.4	3.6 ± 2.5	0.04[a,*]
Day 3 FSH (mIU/mL)	6.4 ± 1.4	7.6 ± 5.9	0.24[a]
LH (mIU/mL)	7.6 ± 3.7	7.1 ± 5.8	0.52[a]
E2 (pg/mL)	40.0 ± 12.9	41.1 ± 15.6	0.70[a]
Cycle day of gonadotropin commencement (d)	2.7 ± 0.5	2.7 ± 0.5	0.75[b]
hCG trigger day of cycle (d)	12.7 ± 3.3	11.9 ± 3.0	0.21[b]
>17 mm follicle number (*n*)	1.6 ± 0.9	1.7 ± 0.9	0.55[b]
Largest diameter of leading follicle (mm)	20.0 ± 0.0	17.0 ± 1.8	0.10[a]
hCG-day endometrial thickness (mm)	9.7 ± 2.2	9.4 ± 1.9	0.48[a]
Clinical pregnancy rate, *n* (%)	8 (22.9)	21 (26.9)	0.64[c]
Abortion rate, *n* (%)	2 (25)	4 (19)	0.25[c]

*$p < 0.05$.
BMI = body mass index; E2 = estradiol; FSH = follicle stimulating hormone; hCG = human chorionic gonadotropin; LH = luteinizing hormone; PCOS = polycystic ovarian syndrome; SD = standard deviation.
[a] Independent samples *t* test.
[b] Mann–Whitney *U* test.
[c] Pearson Chi-square test.

Clinical pregnancy rates were found to be similar when a receiver operator characteristic (ROC) curve analysis was created according to the cycle day of initiating gonadotropin treatment [area under the curve (AUC) = 0.53; $p = 0.61$; 95% CI = 0.41–0.65]. Based on another ROC analysis of the whole group, the cycle day of hCG trigger was found to be significantly related to clinical pregnancy rate (AUC = 0.62; $p = 0.04$; 95% CI = 0.50–0.74; $n = 113$; Fig. 1). Utilizing a later hCG trigger day appeared to positively affect the odds of clinical pregnancy establishment. An hCG trigger day cut-off value of 11.5 days was detected with sensitivity and specificity values of 65% and 50%, respectively. When a ROC analysis was performed to determine leading follicle diameter and clinical pregnancy rate, no statistically significant relationship was found (AUC = 0.41; $p = 0.18$; 95% CI = 0.29–0.53). However, a statistically significant relationship was found between high endometrial thickness values on hCG trigger day and clinical pregnancy rate (AUC = 0.66; $p = 0.007$; 95% CI = 0.55–0.77; Fig. 2). An hCG day endometrial thickness value cut-off value of 9.5 mm was

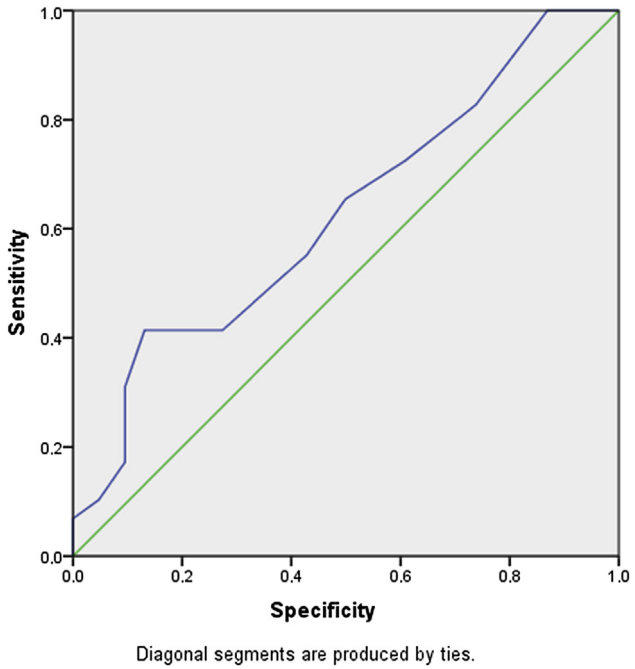

Fig. 1. ROC analysis of cycle day for hCG utilization and clinical pregnancy establishment following gonadotropin treatment for ovulation induction which demonstrates that a later ovulation trigger with hCG during the ovarian stimulation cycle results in higher clinical pregnancy rates (AUC = 0.62; $p = 0.04$; 95% CI = 0.50–0.74). AUC = area under the curve; CI = confidence interval; hCG = human chorionic gonadotropin; ROC = receiver operating curve.

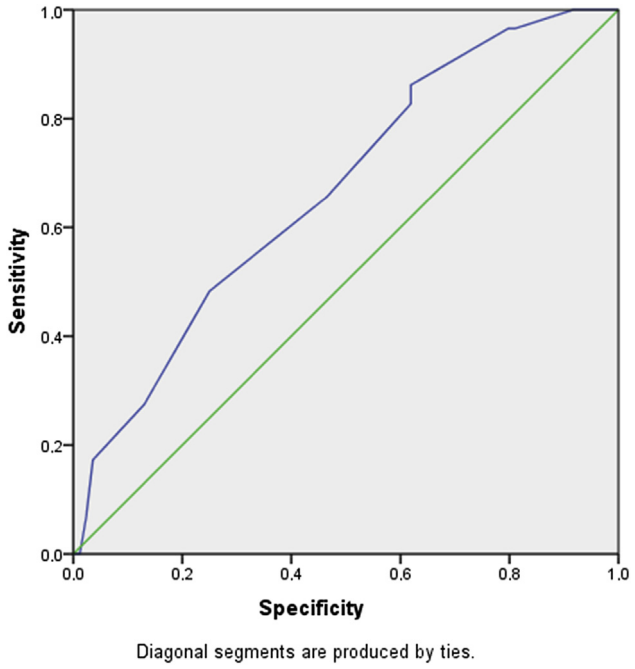

Fig. 2. ROC analysis of hCG day endometrial thickness and clinical pregnancy establishment following gonadotropin treatment for ovulation induction which demonstrates that increased endometrial thickness on hCG day of the treatment cycle results in higher clinical pregnancy rates (AUC = 0.66; $p = 0.007$; 95% CI = 0.55–0.77). AUC = area under the curve; CI = confidence interval; hCG = human chorionic gonadotropin; ROC = receiver operating curve.

detected with sensitivity and specificity values of 65% and 54%, respectively.

4. Discussion

IUI with controlled ovarian hyperstimulation has been used over the years as a treatment for mild male factor, anovulation, and unexplained infertility.[9,10] It is less expensive and less invasive than other assisted reproductive techniques. Therefore, these advantages have made the technique an attractive option for infertile couples.

Age, indications of IUI, sperm preparation, and insemination methods are several important factors affecting the outcome of controlled ovarian hyperstimulation-IUI.[8,11–13] However, the timing of administration of IUI seems to be the most critical factor among them. It should be noted that medical regimens vary between centers and also between clinicians. Hence, the correct timing of insemination to improve pregnancy has been the subject of recent debate.

Huang et al[14] compared 210 IUIs performed at 24 hours and 36 hours with different diagnostic and etiological categories including endometriosis, ovulation dysfunction, and unexplained infertility. The patients were divided into three subgroups who received FSH, hMG, and clomiphen citrate (CC)+hMG. Spermiogram parameters were all normal. Additionally, no significant difference in pregnancy outcomes was found between the two groups. Wang et al[15] demonstrated the effects of different timings (24 hours and 36 hours) of IUI after hCG injection in the subgroups of patients who received clomiphene citrate, clomiphene citrate plus gonadotropin, and gonadotropin alone. The pregnancy rates were found to be similar between two groups. Similarly, Osuna et al[16] performed a systematic review of the literature and they concluded that no significant differences were observed when two inseminations per cycle were performed, compared with one insemination. They also found great heterogeneity concerning ovarian management and insemination timing. The same group detected an improved pregnancy rate with two inseminations compared with one insemination when clomiphene citrate with or without gonadotropins and 5000 IU of HCG were used. In another study, Ragni et al[17] detected significant increases in pregnancy rates when the IUI procedure was performed during the preovulatory and periovulatory periods, but not the postovulatory period. According to another study, Kucuk[18] suggested that IUI should be withheld until follicular rupture is detected. He also claimed that monitoring of follicular rupture prior to IUI provides a pregnancy rate similar to natural fecundity.

In a Cochrane meta-analysis evaluating the effectiveness of different synchronization methods in natural and stimulated cycles for IUI in subfertile couples, the authors concluded that insufficient evidence exists to determine whether there is any difference in safety and effectiveness between different methods of synchronization of ovulation and insemination among subfertile patients.[5]

In our study, we compared the clinical pregnancy rates of patients with PCOS and unexplained infertility according to the

timing of single IUI procedures. To homogenize the study groups, we excluded other possible causes of infertility. Clinical pregnancy rates per cycle were 22.9% in the PCOS group and 26.9% in the unexplained group. However, IUI procedures performed 24 hours following hCG trigger day were found to be related to better cycle outcomes among patients with unexplained infertility, unlike PCOS patients. This result can be related to the sperm capacitating process within the woman's genital tract. Intercourse performed before ovulation has been related to an increase in the fertilization potential and pregnancy establishment. Primarily, the leading defect in pregnancy establishment for patients with unexplained infertility is fertilization defects.[8] This statement explains the importance of IUI procedure timing, and the technique used for this group of patients who regularly menstruate and ovulate preceding the ovulation induction treatment cycle. Spermatozoa and oocytes have only a limited survival time (around 72 hours and 24 hours, respectively); therefore correct timing of insemination is essential. Delaying the IUI procedure in couples with unexplained infertility theoretically decreases the fertilization potential of the inseminated sperm due to the short viability time of the oocyte. Also, in a prospective randomized controlled study, Blockeel et al[19] demonstrated that significantly higher clinical pregnancy rates per IUI cycle were observed in patients undergoing IUI 1 day after the LH rise, when compared with patients undergoing IUI 2 days after the LH rise in natural cycles. This proves the clinical importance of IUI timing on pregnancy rates among subfertile patients.[19] The main problem for PCOS patients is anovulation. Accordingly, for PCOS patients, IUI timing is not as important as for patients with unexplained infertility. We also found a significant relationship between the hCG trigger day of cycle and clinical pregnancy establishment. This result can be a reflection of higher quality of oocytes in the later hCG day trigger cycles than in earlier hCG day trigger cycles. Perhaps clinicians trigger the preovulatory follicles earlier than physiologically needed, which decreases the fertility potential of an originally competent oocyte. In our study, we also found a significant relationship between hCG day endometrial thickness and clinical pregnancy establishment, which is consistent with the previous literature.

In conclusion, IUI performed at either 24 hours or 36 hours after ovulation triggered by hCG injection does not change the clinical pregnancy rates for PCOS patients. Contrarily, patients with unexplained infertility seem to benefit from earlier IUI procedures, which increases their fertility potential during ovulation-induction with gonadotropins. However, avoiding artificial hCG triggering before IUI procedures earlier than physiologically needed results in improved pregnancy rates. Utilization of clinical interventions such as IUI during the treatment of infertile women necessitates rational applications, which increases the clinical usefulness of the procedure. Ultimately, large multicenter trials with increased patient numbers are necessary to elucidate the optimal timing of insemination among different infertile patient groups.

References

1. ESHRE Capri Workshop Group. Intrauterine insemination. *Hum Reprod Update* 2009;**15**:265−77.
2. Dodson WC, Haney AF. Controlled ovarian hyperstimulation and intrauterine insemination for treatment of infertility. *Fertil Steril* 1991;**55**:457−67.
3. Veltman-Verhulst SM, Cohlen BJ, Hughes E, Heineman MJ. Intra-uterine insemination for unexplained subfertility. *Cochrane Database Syst Rev* 2012;**9**:CD001838.
4. Matorras R, Osuna C, Exposito A, Crisol L, Pijoan JI. Recombinant FSH versus highly purified FSH in intrauterine insemination: systematic review and metaanalysis. *Fertil Steril* 2011;**95**:1937−42.
5. Cantineau AE, Janssen MJ, Cohlen BJ, Allersma T. Synchronised approach for intrauterine insemination in subfertile couples. *Cochrane Database Syst Rev* 2014;**12**:CD006942.
6. Luciano AA, Peluso J, Koch EI, Maier D, Kuslis S, Davison E. Temporal relationship and reliability of the clinical, hormonal, and ultrasonographic indices of ovulation in infertile women. *Obstet Gynecol* 1990;**75**:412−6.
7. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril* 2004;**81**:19−25.
8. Duran H, Mahmood M, Kruger T, Oehninger S. Intrauterine insemination: a systematic review on determinants of success. *Hum Reprod Update* 2002;**8**:373−84.
9. Goverde AJ, McDonnell J, Vermeiden JP, Schats R, Rutten FF, Schoemaker J. Intrauterine insemination or in vitro fertilisation in idiopathic subfertility and male subfertility: a randomised trial and cost-effectiveness analysis. *Lancet* 2000;**355**:13−8.
10. 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**:177−83.
11. Khalil MR, Rasmussen PE, Erb K, Laursen SB, Rex S, Westergaard LG. Homologous intrauterine insemination: an evaluation of prognostic factors based on a review of 2473 cycles. *Acta Obstet Gynecol Scand* 2001;**80**:74−81.
12. Kamath MS, Bhave P, Aleyamma T, Nair R, Chandy A, Mangalaraj AM, et al. Predictive factors for pregnancy after intrauterine insemination: a prospective study of factors affecting outcome. *J Hum Reprod Sci* 2010;**3**:129−34.
13. Demir B, Dilbaz B, Cinar O, Karadag B, Tasci Y, Kocak M, et al. Factors affecting pregnancy outcome of intrauterine insemination cycles in couples with favourable female characteristics. *J Obstet Gynaecol* 2011;**31**:420−3.
14. Huang FJ, Chang SY, Lu YJ, Kung FT, Tsai MY, Wu JF. Two different timings of intrauterine insemination for non-male infertility. *J Assist Reprod Genet* 2000;**17**:213−7.
15. Wang YC, Chang YC, Chen IC, Cnien HH, Wu GJ. Comparison of timing of IUI in ovarian stimulated cycles. *Arch Androl* 2006;**52**:371−4.
16. 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 Jul;**82**:17−24.
17. Ragni G, Somigliana E, Vegetti W. Timing of intrauterine insemination: where are we? *Fertil Steril* 2004;**82**:25−6.
18. Kucuk T. Intrauterine insemination: is the timing correct? *J Assist Reprod Genet* 2008;**25**:427−30.
19. Blockeel C, Knez J, Polyzos NP, De Vos M, Camus M, Tournaye H. Should an intrauterine insemination with donor semen be performed 1 or 2 days after the spontaneous LH rise? A prospective RCT. *Hum Reprod* 2014;**29**:697−703.