FERTILITY AND STERILITY®
VOL. 81, NO. 5, MAY 2004

Published by Elsevier Inc.
Printed on acid-free paper in U.S.A.

# Analysis of factors influencing pregnancy rates in homologous intrauterine insemination

*Gilberto Ibérico, M.D.,*[a] *Jesús Vioque, M.D., Ph.D.,*[b] *Nuria Ariza, M.D.,*[a] *Jose Manuel Lozano, M.D.,*[a] *Manuela Roca, M.D.,*[a] *Joaquín Llácer, M.D.,*[a] *and Rafael Bernabeu, M.D.*[a]

*Instituto Bernabeu, Alicante, Spain*

**Objective:** To identify predictors of pregnancy rate (PR) among women undergoing homologous IUI.

**Design:** Cross-sectional analysis of IUI cycles carried out from January 2000 to September 2002.

**Setting:** Private infertility center in Alicante, Spain.

**Patient(s):** Four hundred seventy women undergoing 1,010 cycles of IUI.

**Intervention(s):** Single IUI with ovarian stimulation using hMG.

**Main Outcome Measure(s):** Preovulatory follicles (>15 mm), motile spermatozoa count, type and duration of infertility, female age, insemination timing, and cycle number.

**Result(s):** Overall PR per cycle and multiple pregnancy and miscarriage rates were 9.2%, 8.6%, and 11.8%, respectively. Three significant predictors of pregnancy were identified by multiple logistic regression analysis: preovulatory follicles, spermatozoa count, and infertility duration. Interuterine insemination with three follicles almost tripled the PR with respect to only one, odds ratio (OR) = 2.89 (95% confidence interval [CI], 1.54–5.41). Compared with insemination with a motile sperm count >30 ×, 20.1–30, 10.1–20, 5.1–10, and ≤5 $\times 10^6$, insemination progressively decreased the PR, from 15.3% in the highest category to 3.6% in the lowest (OR lowest/highest = 0.20 [95% CI: 0.09–0.45]), with a statistically significant dose-response trend. Infertility duration ≥3 years was marginally associated with a lower PR, OR = 0.65 (95% CI, 0.40–1.04). Overall, female age was not a significant predictor of pregnancy, and although PR slightly decreased beyond two IUI cycles and when a single IUI was performed 36–40 hours after hCG administration, results were not statistically significant.

**Conclusion(s):** Homologous IUI achieves the best results with two or three induced follicles, a high motile spermatozoa count, and infertility duration <3 years, irrespective of female age and fertility history. (Fertil Steril® 2004;81:1308–13. ©2004 by American Society for Reproductive Medicine.)

**Key Words:** Homologous intrauterine insemination, human menopausal gonadotropin, pregnancy rate, prognostic factors, motile spermatozoa count

Received January 21, 2003; revised and accepted September 17, 2003.

Reprint requests: Rafael Bernabeu, M.D., Instituto Bernabeu, Avda de la Albufereta, 31, 03016-Alicante, Spain (FAX: 0034-96-515-13-28; E-mail: rbernabeu@institutobernabeu.com).

[a] Infertility Center, Instituto Bernabeu.

[b] Departamento Salud Publica, Universidad Miguel Hernández, San Juan de Alicante, Alicante, Spain.

0015-0282/04/$30.00
doi:10.1016/j.fertnstert.2003.09.062

Homologous IUI using different methods of semen preparation is a less expensive and invasive treatment than other assisted reproductive techniques. It is usually selected as a first option treatment for infertile couples with patent tubes, cervical factor, mild endometriosis, or mild or moderate male factor or as empirical treatment in unexplained infertility (1). Controlled ovarian hyperstimulation (COH) using gonadotropins with IUI has been shown to be a most effective treatment of infertility compared with timed vaginal intercourse (2, 3), intracervical insemination (4), or with IUI in natural cycles (5), presumably because it increases the number of available oocytes for fertilization and the number of spermatozoa that reach the oocyte.

In a recent review of the efficacy of treatment for unexplained infertility, hyperstimulation with clomiphene citrate (CC) was shown to be a cost-effective treatment, although the use of gonadotropin seemed to be a more efficacious option in IUI treatment (6). Since there was no clear evidence for a superior effect according to the type of gonadotropin used in IUI treatment, we routinely started with hMG because it was the least expensive medication and significantly decreased the final cost cycle (7).

The important differences observed in predictors of pregnancy rates (PRs), which usually range between 8% and 26% (8), may be mainly due to the influence of different factors on cycle outcome (9, 10). In this sense, some factors such as sperm count (11) and follicle development (12) have been positively related to PRs, whereas others like a high cycle number and higher female age have been negatively associated (8, 13). Although results may appear concordant for some of these factors, a lack of consistency is still evident for some of them, such as female age (14), addition of COH (15), or the optimal insemination timing (16).

To improve subfertility treatment and achieve the best PR in individual couples, we attempt to identify which factors may contribute to the success of COH/hMG/IUI cycles with the male partner's sperm.

## MATERIALS AND METHODS

### Subjects

This study was based on data collected from the records of 470 consecutive infertile couples who were referred for 1,010 male partner IUI cycles to our center in the period 2000–2002. Institutional Review Board approval was not required for this observational study because patients were treated according to standard and customary clinical practice. Couples were studied by means of several tests that included a postcoital test, midcycle P level, tubal patency assessment either by hysterosalpingogram or by laparoscopy, and two seminograms, with at least one of them improved by the swim-up technique.

Criteria for subjects' inclusion were [1] $\geq$1 year of primary or secondary infertility; [2]) female partner $<$45 years of age at the time of treatment with a normal ovulation history or ovulate response to medication; [3] female partner with bilateral patent fallopian tubes demonstrated within past 2 years; and [4] male partner with at least two semen analyses to confirm diagnosis and at least one trial sperm washing with a quantity of $\geq 5 \times 10^6$ of motile spermatozoa. In spite of this last general requirement, which is aimed at obtaining the highest success rate in IUI cycles, those patients with a lower sperm count after preparation on the day of IUI performance were finally included.

### Sperm Preparation

Couples were requested not to have intercourse for 3–5 days before the day of semen collection. Semen samples were produced by masturbation and collected in sterile containers. After complete liquefaction for 30 minutes at room temperature, each sample was analyzed using World Health Organization/Kruger guidelines. Semen for IUI was prepared by selecting the motile sperm fraction for all samples, performing one or more swim-up trials with Sperm Preparation Medium (Medi-Cult, Jyllinge, Denmark) to improve sample quality. The isolated fraction of motile sperm was diluted in 0.5–1 mL of the same preparation medium and incubated at 37°C for 40–45 minutes until IUI.

### Ovarian Stimulation and Timing of Insemination

HMG (hMG-Lepori; Farma-Lepori, Barcelona, Spain) combined with hCG (Profasi HP 2500, Serono, Madrid, Spain) were used to induce ovulation. Administration of hMG was usually started on day 3 of the patient's cycle. The routine commencement dose was 150 IU for 3 days in a step-down process. However, patients with polycystic ovary disease or young women with a high risk of multiple pregnancy used a low-dose regimen starting with 75 IU for five consecutive days until the first transvaginal ultrasound test. In addition, in older patients and/or those with a probable or proven decrease of ovary reserve, the initial COH dose began with 225 IU hMG. Although the hMG dose was decreased according to the circumstances, in a few cases it was increased in response to a low follicle development or blood $E_2$ level.

Follicular development was monitored by transvaginal ultrasound on alternate days, starting on days 6–8 of the cycle, and eventually a blood $E_2$ level according to physician criteria. If more than five follicles $>$15 mm diameter in both ovaries or an $E_2$ level $>$1,500 pg/mL were documented, the treatment was cancelled to avoid the high-risk multiple pregnancy. As an alternative, couples were asked to consider timed intercourse or an IVF procedure.

Patients were asked to abstain from intercourse when the follicle diameter exceeded 15 mm. When the leading follicle reached 18–20 mm and, preferably, when two to four follicles with a diameter $>$15 mm were observed, 5,000 IU of hCG were given and a single IUI was randomly performed 24–28 or 36–40 hours after hCG administration. Four or more cycles per couple were rare (8.5%). Treatment reevaluation was performed when one patient failed to conceive after 3–4 cycles. Cancelled cycles, mainly due to ovarian hyperstimulation or absence of ovarian response, were not included in the analysis since they did not progress to IUI. In addition, 10 cycles were excluded from final analysis because of missing data.

### Insemination Procedure and Detection of Pregnancy

The cervix was exposed with a bivalve speculum and cervical mucus cleaned with a cotton dressing. Hard (Gynetic, Gynetics Medical products; Hamont-Achel, Belgium) or soft (Embryon, Embryo Transfer Set; Rocketmedical PLC, Whashington, England) catheters were allocated without distinction to slowly inject 0.5–1 mL of prepared semen with motile spermatozoa into the uterine cavity, approximately 0.5 cm below the fundus. Qualitative hCG urine tests were performed 15 days after insemination to determine the establishment of the biochemical pregnancy. Clinical preg-

nancy was defined as one with presence of an embryonic sac confirmed by ultrasound scanning. Luteal support was not given because we determined that there was no physiological demand for its application.

## Data Collection and Statistical Analysis

Data from all consecutive patients who were referred for IUI cycles at the Infertility Center between 2000 and 2002 were included in this study. During this period, 1,010 IUI cycles were performed on 470 women. Information concerning pregnancy, multiple pregnancy, or abortion was recorded from the patients' files.

The variables selected for the analysis were female age, number of preovulatory follicles, sperm count, type, and duration of infertility, cycle number, dominant follicle diameter, ovulatory ovarian side, insemination timing, and catheter type (Tables 1 and 2). Female age and follicle number were categorized as follows: <30, 30–34, 35–39, or ≥40 years, and 1, 2, 3, or ≥4 follicles, respectively. Categories for total motile sperm count inseminated were <5 ×, 5.1–10 ×, 10.1–20 ×, 20.1–30 ×, and >30 × $10^6$ spermatozoa, and categories for cycles were 1, 2, 3, and ≥4 treatment cycles. Infertility type, duration of infertility, and timing of IUI were also treated as categorical variables: primary or secondary infertility, <3 or ≥3 years and 24–28 or 36–40 hours after hCG day, respectively.

Estimates of PR per cycle are presented in Table 1. To explore the association between PR (dependent variable) and the independent variables (e.g., sperm count, female age), odds ratios (OR) were calculated by unconditional logistic regression analysis (Table 2). Odds ratios refer to amount of times that pregnancy risk increases/decreases for each category of the variable using the first category as the reference (OR = 1). Thus, indicator variables for each category of the independent variables were automatically established. Odds ratios with 95% confidence intervals (95% CI) and *P*-values were estimated for the variables included in Table 2 using the statistical program STATA (17). The likelihood ratio statistic was used to evaluate the overall significance for each variable and the presence of linear trends.

Tests for trends were performed for each ordinal variable after unfactorizing and adding it to a previous model, including potential confounders. The statistical tests were two-sided. To allow for comparisons with other studies, all variables of Table 2 were included in the final model.

## RESULTS

Female age ranged from 18 to 43 years (mean ± SD: 32.6 ± 3.8). The overall PR per cycle was 9.2%. The multiple PR was 8.6%, all of them twins. Miscarriage, ectopic, and stillbirth rates were 11.8%, 5.4%, and 1.1%, respectively. The highest PRs per cycle were observed among those couples with a sperm count after preparation of >30 × $10^6$ (15.3%), three preovulatory follicles of >15 mm on the day of hCG administration (14.9%), and infertility duration of <3 years (10.6%) (Table 1).

**TABLE 1**

Pregnancy rates in patients undergoing homologous intrauterine insemination (IUI) according to different variables.

| | Cycles (n) | Pregnancy (n) | Pregnancy rate (%) |
|---|---|---|---|
| Women's age (y) | | | |
| <30 | 189 | 22 | 11.6 |
| 30–34 | 537 | 41 | 7.6 |
| 35–39 | 235 | 24 | 10.2 |
| 40–43 | 49 | 6 | 12.2 |
| Follicle number (≥16 mm) | | | |
| 1 | 446 | 25 | 5.6 |
| 2 | 355 | 39 | 11.0 |
| 3 | 154 | 23 | 14.9 |
| ≥4 | 55 | 6 | 10.9 |
| Total motile sperm count (×$10^6$) | | | |
| >30 | 333 | 51 | 15.3 |
| 20.1–30 | 157 | 13 | 8.3 |
| 10.1–20 | 183 | 15 | 8.2 |
| 5.1–10 | 116 | 6 | 5.2 |
| ≤5 | 221 | 8 | 3.6 |
| Infertility duration (y) | | | |
| <3 | 604 | 64 | 10.6 |
| ≥3 | 406 | 29 | 7.1 |
| Type of infertility | | | |
| Primary | 836 | 76 | 9.1 |
| Secondary | 174 | 17 | 9.8 |
| Cycle no. | | | |
| 1 | 402 | 40 | 10.0 |
| 2 | 302 | 29 | 9.6 |
| 3 | 220 | 15 | 6.8 |
| ≥4 | 86 | 9 | 10.5 |
| Size of dominant follicle (mm) | | | |
| 16–19 | 593 | 48 | 8.1 |
| ≥20 | 417 | 45 | 10.8 |
| Ovulatory ovarian side | | | |
| Left ovary | 506 | 48 | 9.5 |
| Right ovary | 504 | 45 | 8.9 |
| Insemination timing (hours) | | | |
| 36–40 | 519 | 41 | 7.9 |
| 24–28 | 491 | 52 | 10.6 |
| Catheter type | | | |
| Gynetics | 690 | 64 | 9.3 |
| Rocket | 320 | 29 | 9.1 |

*Ibérico. Predictors of pregnancy in homologous IUI. Fertil Steril 2004.*

In a final multivariate analysis and after controlling for the number of cycles and women's age (Table 2), the three predictors of PR were the number of preovulatory follicles ($P<.02$), the motile sperm count ($P<.01$), and the infertility duration ($P=.06$). Ovarian response with two or more preovulatory follicles produced better PRs than a monofollicular response (Table 1). Although a positive linear trend was observed with increasing ORs for IUI with two and three follicles (2.01 and 2.89, respectively) with respect to IUI

**TABLE 2**

Adjusted odds ratios[a] in patients undergoing homologous intrauterine insemination according to different variables.

| | Adjusted odds ratio[a] | 95% Confidence interval | | $P$[b] |
|---|---|---|---|---|
| Women's age (y) | | | | |
| <30 | 1.00 | | | |
| 30–34 | 0.55 | 0.31 | 0.97 | .039 |
| 35–39 | 0.68 | 0.35 | 1.32 | .252 |
| 40–43 | 0.97 | 0.35 | 2.71 | .953 |
| Follicle no. (≥16 mm) | | | | |
| 1 | 1.00 | | | |
| 2 | 2.01 | 1.17 | 3.45 | .011 |
| 3 | 2.89 | 1.54 | 5.41 | .001 |
| ≥4 | 1.93 | 0.72 | 5.13 | .190 |
| ($P$ trend) | *<.001* | | | |
| Total motile sperm count ($\times 10^6$) | | | | |
| >30 | 1.00 | | | |
| 20.1–30 | 0.50 | 0.26 | 0.96 | .038 |
| 10.1–20 | 0.47 | 0.25 | 0.87 | .016 |
| 5.1–10 | 0.33 | 0.14 | 0.81 | .015 |
| ≤5 | 0.20 | 0.09 | 0.45 | .001 |
| ($P$ trend) | *<.001* | | | |
| Infertility duration (y) | | | | |
| <3 | 1.00 | | | |
| ≥3 | 0.65 | 0.40 | 1.04 | .073 |
| Type of infertility | | | | |
| Primary | 1.00 | | | |
| Secondary | 1.01 | 0.55 | 1.85 | .967 |
| Cycle no. | | | | |
| 1 | 1.00 | | | |
| 2 | 0.99 | 0.59 | 1.68 | .984 |
| 3 | 0.68 | 0.36 | 1.29 | .236 |
| ≥4 | 0.85 | 0.38 | 1.91 | .700 |
| Size of dominant follicle (mm) | | | | |
| 16–19 | 1.00 | | | |
| ≥20 | 1.22 | 0.78 | 1.90 | .395 |
| Ovulatory ovarian side | | | | |
| Left ovary | 1.00 | | | |
| Right ovary | 0.99 | 0.64 | 1.54 | .961 |
| Insemination timing (hours) | | | | |
| 36–40 | 1.00 | | | |
| 24–28 | 1.28 | 0.81 | 2.00 | .286 |
| Catheter type | | | | |
| Gynetics | 1.00 | | | |
| Rocket | 1.04 | 0.65 | 1.68 | .863 |

[a] Odds ratios for pregnancy were adjusted by including all variables of the table. They refer to times that pregnancy risk increases/decreases for each category of the variable using the first category as the reference (OR = 1).
[b] $P$-value from the Wald test.

*Ibérico. Predictors of pregnancy in homologous IUI. Fertil Steril 2004.*

with one follicle ($P$-trend <.001), the OR for IUI with ≥ four follicles leveled off.

Compared with the insemination with a sperm count >30 $\times 10^6$, insemination with 20.1–30, 10.1–20, 5.1–10, and ≤5 $\times 10^6$ sperm progressively decreased the PR, from 15.3% in the highest category to 3.6% in the lowest one. The decreasing linear trend observed for sperm count was statistically significant ($P$-trend <.001). The OR decreased when infertility duration was ≥3 years ($P$=.07, OR = 0.65, 95% CI, 0.40–1.04).

Overall, female age was not significantly associated with PR in multivariate analysis ($P$=.18). The highest OR for PRs was observed among the youngest women, and the lowest, among women between 30 and 34 years of age (Table 2) although no linear decreasing trend in ORs was apparent by increasing age category. Women 40 years and older presented slightly lower ORs than the youngest women but higher than the women 30–34 years old although estimates did not reach statistical significance and were based on only a few observations.

Most pregnancies occurred within the two first IUI cycles (69 out of 93, i.e., 74.2% of pregnancies), with a PR close to 10%. Although lower ORs for PRs were observed on and after the third cycle, no statistically significant association was evident.

Timing of single insemination was not associated with pregnancy, although the OR for PR was 28% higher when insemination was performed 24–28 hours after the day of hCG administration rather than 36–40 hours. Type of infertility, dominant follicle diameter, ovulatory ovarian side, and catheter type were not associated to PR.

## DISCUSSION

In this study, a multifollicular ovarian response to hMG, a high motile spermatozoa count inseminated, and a short infertility duration were the variables associated with the highest PR after controlling for other variables, including the number of cycles and female age. The positive association between PR and the number of preovulatory follicles (>15 mm) on hCG day is in accordance with that reported in other studies (12, 18). In this sense, the higher PR observed among women with a dominant follicle ≥20 mm, although nonsignificant, could be along the lines of previous findings and due in part to a more intense ovarian stimulation. However, contrary to other studies (19), we found no association between PR and ovulatory ovarian side.

With respect to the sperm characteristics, higher concentration and better quality after sperm preparation were consistently related to improved PRs after IUI (10, 14). In this sense, the PR observed among those with sperm count higher than 30 $\times 10^6$ was on average double that of the middle categories (5.1–30 $\times 10^6$) and almost five times higher than in the lowest category (≤5 $\times 10^6$). Therefore, our results would not support the suggested sperm count of <10 $\times 10^6$ as the threshold value for IUI treatment of infertile couples (11, 20), since still acceptable PRs may be observed with sperm count between 5.1 and 10 $\times 10^6$. However, the considerable decrease in PR with ≤5 $\times 10^6$ would be very difficult to counterbalance by the presence of other favorable

factors such as a multifollicular response or a short duration of infertility.

As in other studies, we observed that a decreased PR was associated with longer infertility duration (12). Although the precise limits of infertility duration for recommending IUI have not been clearly established, according to our data, PR may be seriously compromised when it is ≥3 years unless a multifollicular ovarian response and a high sperm concentration are obtained.

Cycle fecundity has been reported to be relatively constant for the first three to six cycles in accordance with infertility etiology (21, 22), although decreasing PRs with an increased number of treatment cycles have also been shown (12). Accordingly, most of our pregnancies (74.2%) were obtained within the first two treatment cycles, and the possibility of achieving a pregnancy beyond the second one was lower, regardless of any other factors, although not statistically significant. Taking into account also that we found no correlation between potential IUI success and past fertility (infertility type), we have no data to support withholding IUI after three cycles, as suggested by others (23).

The incidence of high-order multiple pregnancies, defined as a pregnancy involving three or more fetuses, is a known adverse effect of the induction of ovulation with gonadotropin, and it has been correlated with the number of growing follicles on the day of hCG administration (18, 24). The proportion of multiple pregnancies in our study was low (8.6%), all of them twins. We reported no high-order multiple pregnancies, which could be in part related to the low proportion of cycles (5.4%) with four or more induced follicles >15 mm. In this sense, if we applied the data reported by Dickey et al. (22), with seven high-risk multiple pregnancies among 299 cycles with four or more induced follicles (37.2% of total hMG cycles), we should expect about one high-risk multiple pregnancy. However, since we have a low number of observations we cannot make definitive conclusions on this question.

Several published trials have underlined the importance of age in every aspect of natural and artificial reproduction techniques, and an age-related decline in female fecundity has been well documented, particularly in women undergoing IUI (8, 13). Although we found lower PRs among women 30–39 years old than in those younger than 30 years of age, no decline was found among women 40–43 years old, and overall, age was not significantly associated with IUI success. In this sense, some studies have found that advanced female age had no negative effect on IUI success (10, 25), and satisfactory PRs have been obtained among women 40–42 years old (26), similar to those found in our study.

Timing of insemination around ovulation has been suggested to be the most important variable affecting the success of IUI treatment. The optimal timing and number of inseminations in relation to hCG day needed to optimize the IUI success are important issues and are yet to be determined (27). In a recent review of randomized studies comparing double versus single IUI regimens, a beneficial effect of double insemination regimen with respect to single insemination was observed in two studies, although the overall effect measure was not statistically significant. In accordance with this review and one additional study showing no beneficial effect of double versus single insemination (16), we must conclude that the data are not conclusive enough to enable us to offer advice regarding clinical practice yet. In this sense, we used only one single insemination per cycle indistinctly within the 24–28 or 36–40 hours after hCG day, and although we found a better PR among those patients inseminated in the first 24–28 hours after hCG administration, results were not statistically significant and no definitive conclusion can be drawn.

Finally, we must mention the importance of counseling patients about the cost-benefit ratio of assisted reproductive techniques, particularly for making decisions about the different treatment options. To minimize the psychological distress associated with less effective procedures, some patients and centers opt for more sophisticated and expensive procedures such as IVF before considering IUI (28), even though IUI cycles are much less expensive than IVF cycles. If the average cost per pregnancy were to be estimated according to our PR (9.2%), assuming a €500 average cost per treatment cycle of hMG + IUI, then 10.8 cycles should be needed to get a pregnancy, and some €5.400 would be the average cost for a pregnancy. A much higher average cost per pregnancy should be expected if our patients were referred for IVF treatment as a result of its higher cost per treatment cycle (about €3,000/cycle). In addition, the higher risk of multiple pregnancies with the added costs during pregnancy, delivery, and the neonatal period of the IVF treatment would further favor the cost-effectiveness of IUI treatment in our setting.

In conclusion, our results suggest that hMG/hCG/IUI may be a useful treatment for infertile couples even in the presence of some unfavorable circumstances such as monofollicular ovarian response and long infertility duration, although it should be probably reconsidered when the sperm count is $\leq 5 \times 10^6$. As expected, a multifollicular ovarian response (up to three follicles) produced a better treatment outcome than monofollicular response, with no apparent increased risk of multiple pregnancies; increasing PRs were also observed for higher sperm count, with satisfactory PRs only above $5 \times 10^6$, and a lower although nonsignificant PR was observed with longer infertility duration (≥3 years). Contrary to other studies, we did not find female age to be a major determinant of PRs, although this result may need further research. Thus, we believe that our results may be helpful for better counselling and selection of couples undertaking infertility treatment, thereby increasing the success

of IUI therapy before opting for much more expensive and invasive assisted reproductive treatments.

*Acknowledgments:* The authors thank the nursing staff for their participation in the ovulation induction, Mr. Sergio Ribes for help in semen preparation, Jonathan Whitehead for help in editing the manuscript, and Maria Luisa Rebagliato for reading and commenting.

## References

1. Zayed F, Lenton EA, Cooke ID. Comparison between stimulated in vitro fertilization and stimulated intrauterine insemination for the treatment of unexplained and mild male factor infertility. Hum Reprod 1997;12:2408–13.
2. Melis GB, Paoletti AM, Ajossa S, Guerriero S, Depau GF, Mais V. Ovulation induction with gonadotropins as sole treatment in infertile couples with open tubes: a randomized prospective comparison between intrauterine insemination and timed vaginal intercourse. Fertil Steril 1995;64:1088–93.
3. Zeyneloglu HB, Arici A, Olive DL, Duleba AJ. Comparison of intrauterine insemination with timed intercourse in superovulated cycles with gonadotropins: a meta-analysis. Fertil Steril 1998;69:486–91.
4. Carroll N, Palmer JR. A comparison of intrauterine versus intracervical insemination in fertile single women. Fertil Steril 2001;75:656–60.
5. Hughes EG. The effectiveness of ovulation induction and intrauterine insemination in the treatment of persistent infertility: a meta-analysis. Hum Reprod 1997;12:1865–72.
6. Guzick DS, Sullivan MW, Adamson GD, Cedars MI, Falk RJ, Peterson EP, et al. Efficacy of treatment for unexplained infertility. Fertil Steril 1998;70:207–13.
7. Van Wely M, Westergaard LG, Bossuyt PMM, Van der Veen F. Human menopausal gonadotropin versus recombinant follicle stimulation hormone for ovarian stimulation in assisted reproductive cycles (Cochrane Review). The Cochrane Library 2003;2. Oxford: Update Software.
8. Tomlinson MJ, Amissah-Arthur JB, Thompson KA, Kasraie JL, Bentick B. Prognostic indicators for intrauterine insemination (IUI): statistical model for IUI success. Hum Reprod 1996;11:1892–6.
9. Stone BA, Vargyas JM, Ringler GE, Stein AL, Marrs RP. Determinants of outcome of intrauterine insemination: analysis of outcomes of 9,963 consecutive cycles. Am J Obstet Gynecol 1999;180:1522–34.
10. Khalil MR, Rasmussen PE, Erg K, Larsen 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.
11. Van Voorhis BJ, Barnett M, Sparks AE, Syrop CH, Rosenthal G, Dawson J. Effect of total motile sperm count on the efficacy and cost effectiveness of intrauterine insemination and in vitro fertilization. Fertil Steril 2001;75:661–8.
12. Nuojua-Huttunen S, Tomas C, Bloigu R, Tuomivaara L, Martikainen H. Intrauterine insemination treatment in subfertility: an analysis of factors affecting outcome. Hum Reprod 1999;14:698–703.
13. Frederick JL, Denker MS, Rojas A, Horta I, Stone SC, Asch RH, et al. Is there a role for ovarian stimulation and intra-uterine insemination after age 40? Hum Reprod 1994;9:2284–96.
14. van der Westerlaken LA, Naaktgeboren N, Helmerhorst FM. Evaluation of pregnancy rates after intrauterine insemination according to indication, age, and sperm parameters. J Assist Reprod Genet 1998;15: 359–64.
15. Cohlen BJ, te Velde ER, van Kooij RJ, Looman CW, Habbema JD. Controlled ovarian hyperstimulation and intrauterine insemination for treating male subfertility: a controlled study. Hum Reprod 1998;13: 1553–8.
16. Ransom MX, Blotner MB, Boher M, Corsan G, Kemmann E. Does increasing frequency of intrauterine insemination improve pregnancy rates significantly during superovulation cycles? Fertil Steril 1994;61: 303–7.
17. STATA Statistical Software. STATA/SE 7.0 for Windows. College Station, TX: STATA Corporation, 2002.
18. Dickey RP, Taylor SN, Lu PY, Sartor BM, Rye PH, Pyrzak R. Relationship of follicle numbers and estradiol levels to multiple implantation in 3608 intrauterine insemination cycles. Fertil Steril 2001;75:69–77.
19. Fukuda M, Fukuda K, Andersen CY, Byskov AG. Right-sided ovulation favours pregnancy more than left-sided ovulation. Hum Reprod 2000;15:1921–6.
20. Miller DC, Hollenbeck BK, Smith GD, Randolph JF, Christman GM, Smith YR, et al. Processed total motile sperm count correlates with pregnancy outcome after intrauterine insemination. Urology 2002;60: 497–501.
21. Sahakyan M, Harlow BL, Hornstein MD. Influence of age, diagnosis and cycle number on pregnancy rates with gonadotropin-induced controlled ovarian hyperstimulation and intrauterine insemination. Fertil Steril 1999;72:500–4.
22. Dickey RP, Taylor SN, Lu PY, Sartor BM, Rye PH, Pyrzak R. Effect of diagnosis, age, sperm quality and number of preovulatory follicle on the outcome of multiple cycles of clomiphene citrate–intrauterine insemination. Fertil Steril 2002;78:1088–95.
23. Yang JH, Wu MY, Chao KH, Chen SU, Ho HN, Yang YS. Controlled ovarian hyperstimulation and intrauterine insemination in subfertility. How many treatment cycles are sufficient? J Reprod Med 1998;43: 903–8.
24. Gleicher N, Oleske DM, Tur-Kaspa I, Vidali A, Karande V. Reducing the risk of high-order multiple pregnancy after ovarian stimulation with gonadotropins. N Engl J Med 2000;343:2–7.
25. Mathieu C, Ecochard R, Bied V, Lornage J, Czyba JC. Cumulative conception rate following intrauterine artificial insemination with husband's spermatozoa: influence of husband's age. Hum Reprod 1995; 10:1090–7.
26. Haebe J, Martin J, Tekepety F, Tummon I, Shepherd K. Success of intrauterine insemination in women aged 40–42 years. Fertil Steril 2002;78:29–33.
27. Cantineau AEP, Heineman MJ, Cohlen BJ. Single versus double intrauterine insemination (IUI) in stimulated cycles for subfertile couples (Cochrane Review). The Cochrane Library 2003;1. Oxford: Update Software.
28. Miskry T, Chapman M. The use of intrauterine insemination in Australia and New Zealand. Hum Reprod 2002;17:956–9.