Date of Search: 20/06/2016
Sources Searched: Medline, Embase, Cochrane Library

Search History:
1. Medline; Superovulation.ti; 642 results.
2. Medline; exp SUPEROVULATION/; 1792 results.
3. Medline; 1 OR 2; 1940 results.
4. Medline; (IUI OR "intrauterine insemination").ti,ab,ti; 2296 results.
5. Medline; exp INSEMINATION, ARTIFICIAL/; 10528 results.
6. Medline; 4 OR 5; 11484 results.
7. Medline; 3 AND 6; 290 results.
8. Medline; 7 [Limit to: Publication Year 2011-2016 and (Language English)]; 43 results.
9. Medline; INSEMINATION/; 925 results.
10. Medline; 3 AND 9; 10 results.
11. Medline; "so iui".ti,ab [Limit to: Publication Year 2011-2016 and (Language English)]; 5 results.
12. Medline; "Superovulation-intrauterine insemination".ti,ab [Limit to: Publication Year 2011-2016 and (Language English)]; 3 results.
13. Medline; "Superovulation-intra uterine insemination".ti,ab [Limit to: Publication Year 2011-2016 and (Language English)]; 0 results.
14. Medline; "intra uterine insemination".ti [Limit to: Publication Year 2011-2016 and (Language English)]; 16 results.
15. Medline; 3 AND 14 [Limit to: Publication Year 2011-2016 and (Language English)]; 0 results.
17. Medline; 3 AND 15 [Limit to: Publication Year 2011-2016 and (Language English)]; 0 results.
18. EMBASE; Superovulation.ti; 664 results.
19. EMBASE; exp SUPEROVULATION/; 2356 results.
20. EMBASE; 18 OR 19; 2476 results.
21. EMBASE; (IUI OR "intrauterine insemination" OR "intra uterine insemination").ti; 1704 results.
22. EMBASE; exp INTRAUTERINE INSEMINATION/; 3471 results.
24. EMBASE; 21 OR 22; 3858 results.
25. EMBASE; 20 AND 24; 198 results.
26. EMBASE; 25 [Limit to: English Language and Publication Year 2011-2016]; 49 results.
27. EMBASE; "Superovulation-intrauterine insemination".ti,ab [Limit to: Publication Year 2011-2016 and (Language English)]; 4 results.
28. EMBASE; "Superovulation-intra uterine insemination".ti,ab [Limit to: Publication Year 2011-2016 and (Language English)]; 0 results.
Title: The role of GnRH analogues in improving outcome at superovulation and intra-uterine insemination (IUI) after surgical correction of mild endometriosis-a randomized controlled trial

Citation: International Journal of Gynecology and Obstetrics, October 2015, vol./is. 131/(E126) (October 2015)

Author(s): Malhotra N., Bansal P., Dadhwal V., Deka D., Sharma A.

Language: English

Abstract: Objectives: The etiology of infertility in mild endometriosis is an enigma. Surgical correction followed by superovulation (SO) and IUI improves pregnancy outcome. While GnRH analogues prior to invitro- fertilization (IVF) improves pregnancy outcome, their benefit in IUI is controversial. The objective of this study was to assess the benefit of GnRH analogue (Luprolide 3.75 mg) given post surgically in women with mild endometriosis undergoing superovulation and IUI. Method: Ninety women were randomized to receive GnRH-a, luprolide acetate, 3.75 mg (study group I, n=45) or no treatment (control group II, n=45) after surgical correction of mild endometriosis (r- ASRM). Superovulation with urinary hMG was followed by IUI in the next cycle in both groups. Women with PCOS, recurrent endometriosis, male factor infertility were excluded. Couples were offered up to three cycles, but analysis was done after one cycle to see benefit of GnRH-a. The primary outcome was clinical pregnancy rate (PR), and secondary outcome was doses and days of gonadotropins, number of follicles >18 mm, endometrial thickness and miscarriage rate. Results: Both groups were comparable in age, BMI, duration of infertility and surgical treatment at laparoscopy. Clinical pregnancy rate was 15.5% in group I and 17.7% in group II with difference in proportion of 2.2%, 95% CI of 13.2 to 17.6% (p=0.7). Overall PR was 21.9% in GnRH-a (group I) treated and 23.8% in non treated (group II), (p=0.8). The doses (1102.7 vs 802.5 IU; p=0.5) and duration (12.0 vs 11.2 days; p=1.0) of gonadotropins were comparable in both groups. The number of follicles >18 mm and endometrial thickness
showed no variation between groups. There was no miscarriage in either group. Conclusions: GnRH analogue addition showed no improvement over surgical management in women with mild endometriosis undergoing SO and IUI.

**Publication Type:** Journal: Conference Abstract

**Source:** EMBASE

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**Title:** The effect of luteal progesterone support in women undergoing superovulation with gonadotropins followed by intrauterine insemination

**Citation:** Fertility and Sterility, September 2015, vol./is. 104/3 SUPPL. 1(e345), 0015-0282 (September 2015)

**Author(s):** Ilnitsky S., Motan T.

**Language:** English

**Abstract:** OBJECTIVE: Our objective was to determine if luteal phase support with progesterone increases pregnancy rates over no luteal phase support in women with any diagnosis of infertility undergoing superovulation with gonadotropins and intrauterine insemination (IUI). DESIGN: We performed a retrospective cohort study of 300 women with any diagnosis of infertility undergoing superovulation with gonadotropins followed by IUI from 1 January 2010 to 30 December 2013. Patients were excluded if data was incomplete, the treatment cycle was cancelled, or if IUI was not performed. MATERIALS AND METHODS: Patients who received luteal phase support (micronized progesterone 100 mg PV bid for up to 16 days beginning day 1 after IUI) were analyzed as the study group. Patients who did not receive luteal phase support were analyzed as the control group. The primary outcome was pregnancy rate. The secondary outcome was live birth rate. RESULTS: The control and study groups differed significantly in age and infertility duration. The study group was older (34.1 vs. 33.0 years, P=0.04) while the control group had a longer cycle length (45.84 vs. 33.67 days, P=0.0001) and duration of infertility (3.2 vs. 2.6 years, P=0.006). The pregnancy rate was not significantly different between the control and study groups (17.1% vs. 9.45% respectively, p=0.062). The live birth rate was also not significantly different (50% vs. 64%, p=0.51). Subgroup analyses showed no difference in pregnancy rates when the sample was analyzed based on age, BMI, or infertility diagnosis. CONCLUSIONS: In our study luteal phase support with progesterone did not have a significant effect on pregnancy or live birth rates in women undergoing superovulation with gonadotropins and IUI. These findings could deter the use of a potentially unnecessary medication that increases the cost of fertility treatments and has possible side effects. Further study in a larger sample size is required to determine if a true effect or possible detriment exists.

**Publication Type:** Journal: Conference Abstract

**Source:** EMBASE
OBJECTIVE: Letrozole (LET), an aromatase inhibitor, is an effective ovulation induction agent for ovulation induction (OI) and controlled ovarian stimulation (COS). Total dosage administration is generally limited to 5 days at 2.5 to 7.5 mg daily, albeit no studies have determined an optimal starting amount. We sought to compare the efficacy in achieving a pregnancy within different LET starting doses. DESIGN: Retrospective
MATERIALS AND METHODS: All patients who underwent COS with LET with or without intrauterine insemination (IUI) from January 2001 to December 2015 were included. Patients were administered a fixed dose of LET for 5 days beginning on cycle day 3 and segregated based on starting dosage (A: 2.5 mg; B: 5 mg; C: 7.5 mg). Main outcome measures included pregnancy rate (PR), clinical PR and multiple PR. Secondary outcomes involved age, day 3 follicle stimulating hormone (FSH), basal antral follicle count (BAFC), BMI, endometrial thickness at surge and number of follicles >14 mm in diameter. Categorical variables were assessed by chi-square or Fisher’s exact test for small frequencies, with significance at a p-value of <0.05. For comparison of all three groups together, significant differences were compared by ANOVA. RESULTS: A total of 4251 cycles were identified (A: n=68; B: n=2604; C: n=1579). We observed an increased number of follicles >14mm (p5mg>2.5mg). Because the small number of cases in Group A, statistical comparison was only carried out between Group B and Group C. Both the biochemical (15.5% vs. 11.6%) and the clinical (12.8% vs. 9.9%) PRs were statistically significant increase in Group B when compared to Group C. The multiple PR and the miscarriage rate were similar between groups. CONCLUSIONS: Letrozole has been shown to be an efficient and effective agent in inducing both ovulation and superovulation. There has been debate as to the optimal starting dose of letrozole. The 5mg-daily yields higher clinical PRs (p<0.05) than 7.5mg. In addition, this group had a lower prevalence of multiple PR and miscarriage rates (p=NS). To strengthen these findings, a randomized trial in cohorts of patients of diverse diagnoses that investigates a range of LET start and total dosages would enhance individualized clinical application. (Table presented).

Publication Type: Journal: Conference Abstract
Source: EMBASE
OBJECTIVE: To identify baseline characteristics of women associated with conception, clinical pregnancy, and live-birth following up to four cycles of superovulation (SO) with Letrozole, Clomiphene Citrate (CC), or gonadotropins plus intrauterine insemination (IUI) in couples with unexplained infertility. DESIGN: Secondary analyses of data from a prospective, randomized, multicenter clinical trial investigating pregnancy, live-birth, and multiple pregnancy rates following superovulation-intrauterine insemination treatments. MATERIALS AND METHODS: This secondary analysis included all 900 participants from The Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation (AMIGOS) clinical trial. Briefly, this trial enrolled women age 18-40 with at least one patent fallopian tube and regular menses to undergo SO-IUI with Letrozole, CC or gonadotropins for up to four treatment cycles. Male partners were required to have a semen analysis with at least 5 million motile sperm in the ejaculate. Baseline demographic and biochemical parameters were evaluated as predictors of the outcomes of conception, pregnancy, and live-birth with bivariate and multivariable analyses. An alpha value of \(< 0.05\) was considered statistically significant. RESULTS: In a multivariable logistic regression analysis, age, waist circumference, income, duration of infertility, and a history of prior pregnancy loss were significantly associated with at least one pregnancy outcome. Age (OR=0.93, CI=0.90-0.97 per year), an income of \(> 50,000\) USD (OR=2.07, CI=1.27-3.38), duration of infertility of \(> 24\) months (OR=0.65, CI=0.47-0.89), and history of a prior pregnancy loss (OR=1.59, CI=1.12-2.27) were significantly associated with the probability of live-birth. Other baseline demographic, biochemical, and lifestyle characteristics were not associated with outcomes. CONCLUSIONS: While age and duration of infertility were significant predictors of all pregnancy outcomes, most other baseline characteristics were not. The identification of income as a predictor of outcomes independent of race and education may be reflective of differences in the underlying etiologies of infertility between the groups as well as disparities in access to fertility and/or obstetrical care.
Abstract: INTRODUCTION: Superovulation-intrauterine insemination (SO-IUI) is the most common assisted reproductive technique (ART) in the world, with good evidence of efficacy and cost-effectiveness. However, parameters affecting its success have not been consistently reported. So in this study, we aim at determining the parameters influencing the success rate of SO-IUI. MATERIALS AND METHODS: We conducted a retrospective cohort study of 797 SO-IUI cycles from 606 patients, performed between 2007 and 2009 in a single centre. These women received clomiphene citrate (CC), recombinant FSH (rFSH) or both. RESULTS: There were 127 clinical pregnancies with a pregnancy rate (PR) of 15.9% (127/797) per treatment cycle. Factors associated with higher PR included maternal age <38 (P = 0.02), subfertility diagnoses of ovulatory disorders, unexplained infertility, sexual dysfunction and unilateral tubal obstruction (P = 0.02), an endometrial thickness >8 mm (P = 0.03), total number motile spermatozoa (TNMS) of >1 million (P = 0.03), and spermatozoa normal forms (NF) >4% (P <0.01) on bivariate analysis. When CC is used, the endometrial thickness is more likely to be suboptimal (<8 mm). All the above parameters remained significant except the subfertility diagnoses on multivariate analysis. CONCLUSION: Patients' selection with women <38 years old and preferably with ovulation disorders and unexplained infertility is associated with the highest PR in SO-IUI. Cycle parameters such as the use of rFSH alone, with the avoidance of CC, TNMS >1 million and NF >4% is likely to result in the best outcomes and reduce the high order multiple pregnancy risk.

Publication Type: Journal: Article

Source: EMBASE

Full Text: Available from Free Access Content in Annals of the Academy of Medicine - Singapore

Title: Does optimal follicular size in IUI cycles vary between clomiphene citrate and gonadotrophins treatments?

Citation: Gynecological Endocrinology, February 2014, vol./is. 30/2(107-110), 0951-3590;1473-0766 (February 2014)

Author(s): Shalom-Paz E., Marzal A., Wiser A., Hyman J., Tulandi T.

Language: English

Abstract: Objective: To evaluate pregnancy-related leading follicles during ovulation induction and superovulation with clomiphene citrate (CC) or gonadotropin. Design: Retrospective cohort. Patients: Five hundred and forty-two women who underwent a total of 615 treatment cycles with CC or gonadotropin. Intervention: We evaluated the effects of CC and gonadotropin on the leading follicles, clinical pregnancy rates and miscarriage rate. Results: The number of follicles larger than 15mm in the different protocols was comparable. In those treated with CC, the diameter of the dominant follicles before human
chorionic gonadotropins (hCG) trigger in the conception cycles (20.4+/-1.2mm) was significantly larger than in the non-conception cycles (18.8+/-1.9mm). In women treated with gonadotropin, the diameter of the leading follicle in the conception cycles (18.5+/-1.7mm) was comparable to that in the non-conception cycles (18.2+/-1.7mm). The pregnancy-related diameter of the leading follicle in CC cycles (20.4+/-1.2mm) was significantly larger than that in gonadotropin cycles (18.8+/-1.9mm; p=0.001; 95% CI, -2.2 to -0.9). Conclusion: Pregnancy-related diameter of the leading follicle in CC cycles is significantly larger than that in gonadotropin cycles and the best time for hCG trigger in the CC cycle is when the leading follicle reaches 20mm. © 2014 Informa UK Ltd.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Title:** Factors predictive of clinical pregnancy in the first intrauterine insemination cycle of 306 couples with favourable female patient characteristics.

**Citation:** Human fertility (Cambridge, England), Dec 2013, vol. 16, no. 4, p. 286-290, 1742-8149 (December 2013)

**Author(s):** Aydin, Yunus, Hassa, Hikmet, Oge, Tufan, Tokgoz, Vehbi Yavuz

**Abstract:** The objective of this study was to evaluate the factors predictive of clinical pregnancy in the first superovulation/intrauterine insemination (SO/IUI) cycle of couples with favourable female characteristics. We analyzed retrospectively the first SO/IUI cycle of 306 infertile couples with mild male factor infertility and unexplained infertility. The women had a favourable prognosis in terms of ovarian reserve. Univariate logistic regression analyses identified body mass index (BMI) [odds ratio (OR) = 0.9, P = 0.014], sperm concentration [OR = 1.007, P = 0.007] and inseminating motile sperm count (IMC) [OR = 1.007, P = 0.032] as significant predictive factors of clinical pregnancy. Multivariate logistic regression analysis identified BMI [OR = 0.87, P = 0.008] and sperm concentration [OR = 1.008, P = 0.011] as significant factors. Pregnant and non-pregnant groups did not differ significantly in terms of the age and smoking status of the woman, duration and type of infertility, length of the stimulation, total gonadotropin dosage or antral follicle count. Of the female characteristics investigated, BMI was the most significant predictive factor of clinical pregnancy in the first SO/IUI cycle of couples with unexplained or mild male factor infertility and favourable female characteristics. In overweight women, weight loss should be advised before starting SO/IUI. Sperm concentration and IMC were significant male predictive factors for clinical pregnancy in the first SO/IUI.

**Source:** Medline

**Full Text:** Available from Taylor & Francis in Human Fertility

**Title:** The efficacy of insemination in letrozole versus clomiphene citrate treatment cycles
OBJECTIVE: Letrozole usage for the treatment of idiopathic infertility couples has been increasing. Data suggest Letrozole is associated with a favorable side effect profile, and does not appear to affect endometrial or cervical gland function. Conversely, Clomiphene Citrate (CC) is associated with anti-estrogenic effects on the endometrium and cervical mucous production. Our study compares the efficacy of Letrozole versus CC in both intercourse (IC) and intrauterine insemination (IUI) cycles. DESIGN: Retrospective cohort study. MATERIALS AND METHODS: Clinical pregnancy rates (PR) -sac at first ultrasound (US) - were analyzed in all patients <40 years of age with normal ovarian reserve and semen parameters undergoing Letrozole or CC treatment (January 2012-February 2013). Letrozole or CC was administered days 3-7 with US monitoring initiated on day 12 until a follicle >20mm was observed. IUI or IC was recommended 24-36 hours after hCG trigger. Categorical variables were assessed by Chi-square or Fisher's exact test for small frequencies with significant at a P-value of <0.05. RESULTS: 1071 patients were identified and were treated with Letrozole or CC with IUI. 616 patients used Letrozole or CC with IC. No differences in age (36+/-1.2, 37+/-0.9) or baseline FSH (7.8+/-0.8, 7.2+/-0.7) was noted between groups. CONCLUSION: Our study demonstrated higher PR trends in Letrozole IUI cycles (18%) than CC IUI cycles (13%), albeit not statistically significant. No significant difference was observed in Letrozole PR with IUI (18%) or IC (14%); and there was no difference between success rates in cycles of Letrozole IC (14%) and CC IUI (13%). Routine insemination in cycles of ovulation induction or superovulation with Letrozole may not confer improved pregnancy rates. (Table Presented).
Abstract: Objective: The main objective of this pilot study was to determine whether a progesterone-releasing vaginal ring is a good alternative for luteal phase support for patients undergoing intrauterine insemination after ovulation induction with sc gonadotrophins. Material and methods: We performed a multi-center study involving three different reproductive medicine units. Patients included were diagnosed with unexplained infertility and this was their first IUI cycle after ovulation induction with rFSH (Puregon) and ovulation induction with urinary HCG (Pregnyl). The day of insemination patients were randomized to receive luteal phase supplementation with progesterone vaginal ring (Fertiring) or no supplementation. Results: One hundred patients were invited to participate, and completed the study. Forty seven received luteal phase support with Fertiring. Overall the pregnancy rate was 15%. It was higher, although without reaching statistical significance, in the group receiving luteal phase support Fertiring (19.1%) than in the group without supplementation (11.3%). Conclusions: In this study, patients undergoing ovulation induction with Puregon and received luteal phase support with Fertiring showed a higher pregnancy rate than those who received no luteal phase support, although statistical significance was not achieved.

Publication Type: Journal: Article

Source: EMBASE

Title: Comparison of Letrozole and Clomiphene Citrate efficacy along with gonadotrophins in controlled ovarian hyperstimulation for Intrauterine Insemination cycles

Citation: Journal of Reproduction and Infertility, July 2013, vol./is. 14/3(138-142), 2228-5482;2251-676X (July-September 2013)

Author(s): HaqNawaz F., Virk S., Qadir T., Imam S., Rizvi J.

Language: English

Abstract: Background: We performed this study to investigate and compare the effects of Letrozole and gonadotrophins versus Clomiphene Citrate and gonadotrophins in women undergoing superovulation for Intrauterine Insemination (IUI). Methods: We performed this prospective cohort study at Australian Concept and Fertility centre, Karachi Pakistan. Women younger than 40 years of age with patent fallopian tubes and infertility of more than 2 years in duration who were undergoing IUI and gonadotrophins therapy were divided into two groups, one received Letrozole for 5 days and another received Clomiphene Citrate for 5 days. Results: All 500 IUI treatment cycles conducted from March 2008 to March 2010 were included. Patients co-treated with Letrozole required fewer gonadotrophins administrations (median difference, 300 IU (95% confidence interval (CI), 225–375 IU), developed more follicles larger than 14 mm (median difference, 1 follicle, 95% CI, 1-2 follicles), and had a thicker endometrium (median difference, 1 mm, 95% CI, 0.4-1.6 mm). The pregnancy rate was not significantly different between two groups (11% vs. 12.6%). Conclusion: The addition of Letrozole to gonadotrophins decreases gonadotrophins requirements and improves endometrial thickness, without a significant effect on pregnancy
rates. An improved pregnancy rate has been observed in older age group, >35 years with Letrozole.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**
Available from *ProQuest* in *Journal of Reproduction and Infertility*
Available from *National Library of Medicine* in *Journal of Reproduction and Infertility*

**Title:** Cerebral venous sinus thrombosis during the first trimester after superovulation and intrauterine insemination with recombinant follicle-stimulating hormone: a case report.

**Citation:** European journal of obstetrics, gynecology, and reproductive biology, May 2013, vol. 168, no. 1, p. 118-119, 1872-7654 (May 2013)

**Author(s):** Oktem, M, Erdem, A, Demirdag, E, Cenksoy, C, Erdem, M, Bozkurt, N

**Source:** Medline

**Title:** Impact of superovulation for women with endometriosis.

**Citation:** Seminars in reproductive medicine, Mar 2013, vol. 31, no. 2, p. 150-153, 1526-4564 (March 2013)

**Author(s):** Kavoussi, Shahryar K

**Abstract:** Superovulation (SO)/Intrauterine insemination (IUI) has been used as a treatment approach for endometriosis-associated infertility. The existing medical literature regarding SO in endometriosis patients is composed of heterogeneous studies that differ in terms of study design, SO protocols, the addition of IUI, and comparison groups. There is a need for more well-designed studies to further investigate the efficacy of SO in women with endometriosis-associated infertility. Although in vitro fertilization (IVF) is most effective and is significantly superior to other treatments in endometriosis patients, most of the existing studies suggest some benefit of SO/IUI in infertility patients with early-stage disease. Therefore, SO/IUI is a reasonable early fertility treatment option for women with endometriosis who desire a short trial of potentially more cost-effective treatment options prior to pursuing an IVF cycle and those for whom IVF is not a feasible or desirable option. It appears that gonadotropins are most effective for SO in this patient population even though more head-to-head comparisons are needed. Thieme Medical Publishers 333 Seventh Avenue, New York, NY 10001, USA.

**Source:** Medline
Evidence-based therapy for infertility associated with early stage endometriosis

Abstract: Objectives: To demonstrate the usefulness of evidence based therapy in the management of infertile women with minimal or mild endometriosis. Setting: Gynecology Endoscopic Units in El Menoufia University Hospital and Infertility clinic at a private hospital. Design: A randomized prospective clinical trial. The study included 41 infertile women with laparoscopically confirmed endometriosis, stage I or II of the revised AFS classification. Twenty women were randomly allocated to resection or ablation of visible endometriosis during laparoscopy (Group I), and Twenty-one Women to diagnostic laparoscopy only (Group II). The base line distribution of subjects was similar in the two groups. Follow-up data were collected for 18 months after laparoscopy or up to 20 weeks of pregnancy. If pregnancy did not occur within 18 months of randomization in both groups, 3 cycles of superovulation with intrauterine insemination (IUI) were done as a co-treatment. Methods: Twenty women were randomly allocated to resection or ablation of visible endometriosis during laparoscopy (Group I), and Twenty-one Women to diagnostic laparoscopy only (Group II). The base line distribution of subjects was similar in the two groups. Follow-up data were collected for 18 months after laparoscopy or up to 20 weeks of pregnancy. If pregnancy did not occur within 18 months of randomization in both groups, 3 cycles of superovulation with intrauterine insemination (IUI) were done as a co-treatment. Results: By the end of the study, a total of 19/41 women (46.3%) conceived and no abortion occurred. Pregnancies occurred in 7/25 women (28%) in-group I and in 5/21 women (23.8%) in-group II by the end of 18 months follow up. The 3 cycles of superovulation and IUI resulted in an additional 9 pregnancies in both groups, 5/13 in group I (38.5%) and 4/11 in-group II (36.4%). Conclusions: Therapy for endometriosis associated infertility is currently in transition from experience-oriented practice to an evidence based one. RCTs are considered the 'gold standard for judging whether a new intervention does more good than harm. Compared with laparoscopy alone, resection or ablation of early stage endometriosis increases the likelihood of pregnancy in infertile women. As superior results occurred from superovulation and IUI, it should be the initial therapy or at least a co-treatment for laparoscopic surgery in women with early stage endometriosis that does not involve oviducts.

Publication Type: Journal: Conference Abstract

Source: EMBASE
Objective: Letrozole alone or in combination with gonadotropins might offer an alternative to clomiphene citrate as a first line regimen in women with unexplained infertility. The objective of this study was to compare the efficacy of letrozole and letrozole combined with gonadotropins as first line for superovulation in women with unexplained infertility undergoing IUI. Design: Prospective randomized trial. Materials and Methods: Sixty eight women with unexplained infertility undergoing superovulation and IUI for the first time were randomized into 2 groups. Group A (n=37) received letrozole (2.5mg/day from day 3-7) and Group B (n=31) received letrozole (2.5mg/day from day 3-7) plus urinary gonadotropins (HMG 150IU) alternate day from day 7 until the day of ovulation trigger. Trigger was given with injection hCG (5,000 IU) in both groups. Primary outcome assessed was pregnancy rate while secondary outcome included number of follicles, days of stimulation, endometrial thickness (ET), cancellation rate, multiple pregnancy and miscarriage rate between the 2 groups. Results: The pregnancy rate in letrozole -HMG combination was significantly higher (35.48%) than letrozole alone group (10.81%), (P=0.013). Mean number of dominant follicles was higher in letrozole-HMG group (3.22+/-.0.33) in comparison to letrozole group (2.89+/-.0.23) (P=0.0016) The mean ET was significantly higher in letrozole -HMG combination (7.93+/-.2.34 mm) versus letrozole group (7.12+/-.1.11 mm) (P=0.023).The cycle cancellation rate, miscarriage rate and multiple pregnancy were comparable in both groups. Conclusion: Better number of follicles and improved ET result in higher pregnancy rate in Letrozole- HMG protocol when compared to letrozole alone protocol. Letrozole -HMG should be preffered over latrozole as first line for superovulation in unexplained infertility.
Abstract: Unexplained infertility is a diagnosis of exclusion when systemic evaluation fails to identify a cause. It may be truly no abnormality (lower end of couples natural fertility) or there is a specific cause but cant revealed by available diagnostic test. This study aims to evaluate a simple strategy for improving endometrial receptivity and the result of pregnancy in unexplained infertile patients undergoing IUI. Materials and Methods: This is a randomized casecontrol study on 139 unexplained infertile women who were divided into two groups. After superovulation by clomiphen-citrate and gonadotropins and when the dominant follicles reached 18-20 mm, 10000 UI hCG was injected. Endometrial local injury was performed in the posterior wall of the uterus by Novak curette (in the same day of hCG injection) just in the experimental group. All the patients underwent single IUI after 36 hours. Results: There were 16 pregnancies in 65 cycle of IUI group comparing to 11 pregnancies in 74 cycle of case group (endometrial injury+ IUI group). Clinical and ongoing pregnancy rate were significantly higher in the endometrial injury group as compared to the control group (24.6% vs 14.9%) (p-value=0.108). Conclusion: As revealed by this study, local mechanical injury of the endometrium can increase uterine receptivity probably by provoking the production of molecules which improving the implantation of the embryo and in combination with IUI will increase ongoing pregnancy. This may help many couples to avoid the stress and cost of more invasive technologies.

Publication Type: Journal: Conference Abstract

Source: EMBASE


Title: Predictors of pregnancy and live birth after insemination in couples with unexplained or male-factor infertility

Citation: Fertility and Sterility, April 2012, vol./is. 97/4(959-967.e5), 0015-0282;1556-5653 (April 2012)


Language: English

Abstract: Objective: To identify risk factors for pregnancy outcomes in couples treated with intracervical or intrauterine insemination, with or without superovulation for unexplained or male-factor infertility. Design: Secondary analysis of data from a randomized superovulation and intrauterine insemination trial. Setting: Academic medical centers. Intervention(s): Treatment continued for four cycles unless pregnancy was achieved. Patient(s): Out of 932 couples randomized to four treatment groups, 664 couples who had completed the lifestyle questionnaires were assessed for occurrence of pregnancy and live birth. Main Outcome Measure(s): Pregnancy and live birth. Result(s): The pregnancy and live birth rates were
significantly higher in couples in which the female partners reported that they had consumed coffee or tea in the past or drank alcoholic beverages in the past (past users) compared with those who had never consumed coffee, tea, or alcoholic beverages. Past users also had significantly higher pregnancy and live birth rates than those currently consuming coffee or tea or alcoholic beverages. Demographic, occupational exposure, and other lifestyle factors were not significant. Conclusion(s): Couples in which the female partners drank coffee, tea, or alcoholic beverages in the past had higher pregnancy and live birth rates compared with never or current users. When discontinuing these habits, they might have made other lifestyle changes to improve the pregnancy outcome. © 2012 by American Society for Reproductive Medicine.

Publication Type: Journal: Article

Source: EMBASE

Title: Randomized comparison of superovulation with letrozole vs. clomiphene citrate in an IUI program for women with recently surgically treated minimal to mild endometriosis

Citation: Acta Obstetricia et Gynecologica Scandinavica, March 2012, vol./is. 91/3(338-345), 0001-6349;1600-0412 (March 2012)

Author(s): Hashim H.A., Rakhawy M.E., Elaal I.A.

Language: English

Abstract: Objective. To evaluate pregnancy rates with letrozole and clomiphene citrate (CC) alone for superovulation in an intrauterine insemination program for women with recently surgically treated minimal to mild endometriosis. Design. A randomized controlled trial following the CONSORT criteria. Setting. University teaching hospital and a private practice setting. Patients. 136 women with primary infertility due to minimal to mild endometriosis who did not achieve pregnancy after six to 12 months following laparoscopic treatment. Interventions: Superovulation using 5mg letrozole/day (69 women, 220 cycles) or 100mg CC/day (67 women, 213 cycles) for five days combined with intrauterine insemination up to four cycles. Main outcome measures. Clinical pregnancy rate per cycle, cumulative pregnancy rate after four cycles, number of follicles, serum estradiol, endometrial thickness on the day of human chorionic gonadotropin administration, serum progesterone, miscarriage and live birth rates. Results. The clinical pregnancy rate per cycle, cumulative pregnancy rate after four cycles, number of follicles, serum estradiol, endometrial thickness on the day of human chorionic gonadotropin administration, serum progesterone, miscarriage and live birth rates. Results. The clinical pregnancy rate per cycle, cumulative pregnancy rate after four cycles were comparable (15.9 vs. 14.5% and 64.7 vs. 57.2%; p=0.82, p=0.71 in letrozole and CC groups, respectively). Two twin pregnancies occurred in the CC/intrauterine insemination group. Miscarriage and live birth rates were comparable (11.4 vs. 12.9% and 44.9 vs. 40.3%; p=0.47, p=0.62 in letrozole and CC groups, respectively). The total number of follicles and serum estradiol on the day of human chorionic gonadotropin administration were significantly increased in the CC group. Conclusions. Superovulation with letrozole is not more effective than clomiphene citrate alone in an intrauterine insemination program for women with minimal to mild
endometriosis who did not achieve pregnancy after six to 12 months following laparoscopic treatment. ClinicalTrials.gov ID: NCT01334762. © 2011 The Authors.

**Publication Type:** Journal: Article

**Source:** EMBASE

**Full Text:**
Available from Wiley in *Acta Obstetricia et Gynecologica Scandinavica*
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**Title:** Significance of moderately abnormal basal FSH and/or estradiol-17beta in subfertile women undergoing complete justifiable treatment with IUI or IVF: Results of fastt and fort-t

**Citation:** Reproductive Sciences, March 2012, vol./is. 19/3 SUPPL. 1(98A), 1933-7191 (March 2012)

**Author(s):** Kaser D.J., Goldman M.B., Fung J.L., Alper M.M., Reindollar R.H.

**Language:** English

**Abstract:** Objective: To determine if moderately abnormal FSH and/or estradiol-17beta (E2) levels affect pregnancy outcomes in subfertile women undergoing IUI or IVF with mandated insurance coverage

Design: Secondary analysis of two prospective randomized trials

Methods: Cycle demographics, variables and outcomes were pooled from the Fast Track and Standard Treatment Trial (FASTT) and Forty and Over Infertility Treatment Trial (FORT-T). FASTT (n=503) randomized women ages 21-39 to traditional or accelerated treatment with clomiphene citrate IUI (CC-IUI), gonadotropin IUI (FSH-IUI), and IVF; FORT-T (n=154) randomized women ages 38-43 to superovulation IUI (SO-IUI: CC or FSH) then IVF or immediate IVF. Patients were treated until they no longer demonstrated a reasonable chance for success.

Four groups were identified according to day 3 FSH and E2 values (Table 1). Live birth rates were calculated for each group and treatment modality. Data were analyzed by ANOVA for continuous variables and Fisher’s exact for categorical variables.

Results: Patients with FSH > 10 were older than those with FSH < 10 (p=0.01). No live births occurred in Group 2B during SO-IUI (0/21) (p=0.02). When age was examined, no live births (0/28) occurred during SO-IUI among women > 40 years with FSH > 10 (n=19), regardless of E2 concentration. Discussion: Patients with FSH > 10 and E2 > 50 are unlikely to achieve live birth with CC-IUI or FSH-IUI, even if afforded complete treatment. In women > 40 years with FSH > 10, SO-IUI may not be an effective treatment option. This provides further support for beginning therapy with immediate IVF in women of advanced reproductive age. (Table Presented).

**Publication Type:** Journal: Conference Abstract

**Source:** EMBASE
Title: Psychological and physical symptoms in women undergoing superovulation with clomiphene citrate: A double-blind, placebo-controlled, crossover study

Citation: Fertility and Sterility, September 2011, vol./is. 96/3 SUPPL. 1(S153), 0015-0282 (September 2011)

Author(s): Pittman J.H., Hammoud A., Keye W.R., Gurtcheff S.E., Czajkowski L., Gibson M.

Language: English

Abstract: OBJECTIVE: To identify psychological and physical symptoms experienced by women taking clomiphene citrate for superovulation in a prospective setting. DESIGN: Randomized, double-blind, placebo-controlled, crossover study. MATERIALS AND METHODS: After initial screening, twenty women with unexplained infertility seeking treatment with clomiphene citrate for superovulation participated in a two month double blind, placebo-controlled crossover study that included treatment with clomiphene citrate 50mg or placebo during menstrual cycle days 3-7, administered in a randomized order. Clinical care for infertility treatment in each cycle of the study conformed to standard care for women undergoing superovulation with clomiphene citrate and intrauterine insemination. If pregnancy did not occur in the initial study cycle, participants then crossed-over to the second cycle of the study. Symptoms were recorded daily using the Calendar of Premenstrual Experiences (COPE), a 22-item survey including 12 behavioral and 10 physical symptoms. Mean follicular and luteal phase scores were determined for each study phase and analyzed using a paired t-test. RESULTS: Of the twenty subjects enrolled, 16 women completed both cycles. Three women had positive pregnancy test results after cycle 1 and one woman was anovulatory. Symptoms most frequently reported during the follicular phase were headache and fatigue, while bloatedness and irritability were more commonly reported in the luteal phase. CONCLUSION: Clomiphene citrate is well tolerated as treatment for superovulation, without significant increase in side effects compared to placebo.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: Extended letrozole regimen versus clomiphene citrate for superovulation in patients with unexplained infertility undergoing intrauterine insemination: A randomized controlled trial

Citation: Reproductive Biology and Endocrinology, June 2011, vol./is. 9/(no pagination), 1477-7827 (21 Jun 2011)

Author(s): Fouda U.M., Sayed A.M.

Language: English
Abstract: Background: The aim of this randomized controlled trial was to compare the efficacy of extended letrozole regimen with clomiphene citrate in women with unexplained infertility undergoing superovulation and intrauterine insemination (IUI). Methods: Two hundred and fourteen patients with unexplained infertility were randomized into two equal groups using computer generated list and were treated by either letrozole 2.5 mg/day from cycle day 1 to 9 (extended letrozole group, 211 cycles) or clomiphene citrate 100 mg/day from cycle day 3 to 7 (clomiphene citrate group, 210 cycles). Intrauterine insemination was performed 36 to 40 hours after HCG administration. Results: Both groups were comparable with regard to number of mature follicles (2.24 +/- 0.80 Vs 2.13 +/- 0.76) and the day of HCG administration. Serum estradiol was significantly greater in clomiphene citrate group (356 +/- 151 Vs 822 +/- 302 pg/ml, P = < 0.001) and the endometrial thickness was significantly greater in extended letrozole group (9.10 +/- 1.84 Vs 8.18 +/- 1.93 mm, P = < 0.001). The pregnancy rate per cycle and cumulative pregnancy rate were significantly greater in extended letrozole group (18.96% Vs 11.43% and 37.73% Vs 22.86%, respectively). Conclusion: The extended letrozole regimen had a superior efficacy as compared with clomiphene citrate in patients of unexplained infertility undergoing superovulation and IUI. Trial registration: ClinicalTrials.gov, NCT01232075. © 2011 Fouda and Sayed; licensee BioMed Central Ltd.
regarding the following: gonadotropin dose, duration of treatment, peak E<inf>2</inf>, number of follicles (total, large, and medium size), E<inf>2</inf>/follicle, endometrial thickness, spontaneous abortion, and clinical and multiple pregnancy rates. Result(s): There was a significant trend toward higher medication requirements and lower E<inf>2</inf> levels with increasing BMI. BMI was inversely associated with [1] the E<inf>2</inf> level per produced preovulatory follicle and [2] the number of medium-size follicles. Furthermore, BMI was inversely associated with the number of medium, large, and total follicles divided by total FSH dose, suggesting that women with a higher BMI develop a lower number of medium and/or large follicles at a given total FSH dose. BMI was positively associated with endometrial thickness, and endometrial thickness was positively associated with pregnancy. Mean number of cycles required to conceive, clinical pregnancy, and spontaneous abortion rates did not differ significantly among the different BMI categories. Conclusion(s): Obese women require higher doses of medication and produce fewer follicles for a given dose, but once medication and response are adjusted to overcome the weight effect, the success of the treatment cycle is comparable to that of normal weight women. ©2011 by American Society for Reproductive Medicine.

**Publication Type:** Journal: Article

**Source:** EMBASE
could have predictive value for pregnancy outcome after intrauterine insemination with superovulation in couples with unexplained infertility, and would be helpful when counseling patients before they make the decision to proceed with IVF/ICSI-ET.

**Source:** Medline

**Full Text:**

Available from *National Library of Medicine* in *Clinical and Experimental Reproductive Medicine*

**Title:** The effects of timing of intrauterine insemination in relation to ovulation and the number of inseminations on cycle pregnancy rate in common infertility etiologies.

**Citation:** Human reproduction (Oxford, England), Mar 2011, vol. 26, no. 3, p. 576-583, 1460-2350 (March 2011)

**Author(s):** Ghanem, Mohamad E, Bakre, Nagwa I, Emam, Mohamad A, Al Boghdady, Laila A, Helal, Adel S, Elmetwally, Abdel Gawad, Hassan, Mohamad, Albahlol, Ibrahim A, Elzayat, Mostafa M

**Abstract:** Controlled ovarian hyperstimulation with intrauterine insemination (COH/IUI) is an established tool in medically assisted conception for many infertility factors. However, the proper timing of IUI after hCG trigger and the frequency of IUI are still debated. We aimed to examine the association between the cycle pregnancy rate (CPR) and (i) single IUI timed at 36 ± 2 h post-hCG (pre- or post-ovulation) (ii) the number of IUI (single or double) for pre-ovulatory cases both aims in male, anovulatory and unexplained infertility. The study included a total 1146 first-stimulated cycles in infertile couples due to male factor, anovulation or unexplained infertility. Cycles were stimulated by clomiphine citrate (CC) or sequential CC-hMG or hMG and monitored by transvaginal ultrasound. When the leading follicle reached ≥ 18 mm mean diameter, 10000 IU hCG was given to trigger ovulation and IUI was timed for 36 ± 2 h later. Semen was processed and ovulation was checked at the time of IUI. Post-ovulatory cases received single IUI, while pre-ovulatory cases were sequentially randomized to receive either single or double IUI. The end-point of the cycle was CPR. Overall CPR in the whole cohort was 10.1%. When ovulation was present before IUI, CPR was 11.7% compared with 6.7% when ovulation was absent [OR (95% CI): 1.85 (1.12-3.06), P = 0.015]. When this OR was computed according to infertility etiology, it was 1.26 (0.52-2.95) (P = 0.82) for male factor infertility and 2.24 (1.23-4.08) (P = 0.007) for non-male factor infertility. Comparing the CPR for double versus single IUI in pre-ovulatory cases, the OR for all cycles was 1.9 (0.76-4.7) (P = 0.22), but according to etiology, it was 4.667 (0.9-24.13) (P = 0.06) in male factor and 1.2 (0.43-3.33) (P = 0.779) for non-male factors. Single IUI timed post-ovulation gives a better CPR when compared with single pre-ovulation IUI for non-male infertility, whereas for male factors, pre-ovulation, double IUI gives a better CPR when compared with single IUI.

**Source:** Medline

**Full Text:**
**Title:** Clomiphene citrate or aromatase inhibitors for superovulation in women with unexplained infertility undergoing intrauterine insemination: A prospective randomized trial

**Citation:** Human Reproduction, 2011, vol./is. 26/(i240), 0268-1161 (2011)

**Author(s):** Elnashar A., Badawy A., Totongy M.

**Language:** English

**Abstract:** Objective: To compare clomiphene citrate (CC) and letrozole used for superovulation before intrauterine insemination (IUI) in unexplained infertility. Design: Prospective randomized trial. Setting: A university teaching hospital and a private practice setting. Patient(s): Four hundred and twelve infertile women with unexplained infertility. Intervention(s): Patients were randomized to treatment with 100 mg of CC daily (207 patients, 404 cycles) or 5 mg of letrozole daily (205 patients, 400 cycles) for 5 days starting on day 3 of menses. The IUI was done 36 4 hours after human chorionic gonadotropin (hCG) injection. Main Outcome Measure(s): Number of follicles, serum estradiol level, serum progesterone level, endometrial thickness, and pregnancy and miscarriage rates. Result(s): The total number of follicles during stimulation was statistically significantly greater in the CC group (3.1+/-.36 vs. 1.6 +/- 0.41). There was no statistically significant difference in pretreatment endometrial thickness between the two groups or endometrial thickness at the time of hCG administration. Serum E2 and progesterone concentrations were statistically significantly higher in the CC group. The days to hCG injection were similar in both groups. Pregnancy occurred in 73 out of 205 patients (400 cycles) in the letrozole group (35.6% and 18.2%, respectively) and 78 out of 207 patients (404 cycles) (37.6% and 19.3%, respectively) in the CC group; the differences were not statistically significant. Two twin pregnancies occurred in the CC group. Conclusion(s): This study found no superiority between letrozole and CC for inducing ovulation in women with unexplained infertility before IUI.

**Publication Type:** Journal: Conference Abstract

**Source:** EMBASE
Abstract: Introduction: Intra-Uterine Insemination (IUI) with or without stimulation is the most common assisted reproductive technique (ART) in the world. There is good evidence of the efficacy and cost-effectiveness of stimulated IUI (SO-IUI). However, parameters affecting its success have not been consistently reported. Here, we aimed to conduct a retrospective study in a cohort of patients undergoing SO-IUI in KKIVF Centre (Singapore) on the factors influencing pregnancy rates (PR). Material and Methods: We retrospectively analysed 851 SO-IUI cycles from 640 patients over a period of three years. These women underwent ovarian stimulation with either clomiphene citrate alone, a combination of clomiphene citrate and recombinant FSH (rFSH) or rFSH alone. An hCG injection was administered when at least 1 follicle was > 16 mm, followed by IUI 36h later. Results: The overall PR was 16%. Factors associated with the highest PR were maternal age < 35 y.o. (17.8% vs 11.8% for patient > 35 y. o), where indication for IUI was sexual dysfunction, ovulation disorders or unexplained infertility (PR = 35.3%, 23.9% and 24.4% respectively), when more than 1 mature follicle was achieved (PR = 15.0% with 1, 19.0% with 2 and 20.3% with > 3 follicles), where inseminated motile sperm was > 1 million (16.7% vs 2.3% if less than 1 million) and when the sperm morphology was > 1% (17% vs 5.4%)(Kruger Criteria). Conclusion: Despite the tremendous increase in demand for IVF, SO-IUI still has an important role to play in ART with success rates of over 20% in certain groups of patients such as sexual dysfunction, ovulation disorders, unexplained infertility, mild male factor and when stimulation allows the maturation of more than 1 follicle.