RANDOMIZED CONTROLLED TRIAL COMPARING HIGHLY PURIFIED (HP-HCG) AND RECOMBINANT HCG (R-HCG) FOR TRIGGERING OVULATION IN ART. D. De Ziegler,[a,b,d] M. Bellavia,[b] C. De Geyter,[c] I. M. Streuli,[a,d] V. Ibecheole,[d] M. H. Birkhäuser.[e] [a]Dept of Ob Gyn II, Reproductive Endocr. and Infertility, Université Paris Descartes – Hôpital Cochin, Paris, France; [b]Maternity, CHUV (Centre Hospitalier Universitaire Vaudois), Lausanne, Vd, Switzerland; [c]Frauenklinik, Universitätsspital Basel, Basel, BS, Switzerland; [d]Hôpital Cantonal Universitaire, Geneva, GE, Switzerland; [e]Frauenklinik Inselspital, Bern, Switzerland.

OBJECTIVE: To compare the safety and efficacy of triggering ovulation in ART with hCG of highly purified (HP-hCG) or recombinant origin (r-hCG).

DESIGN: Multi-centre (n=4), prospective, controlled, randomized, non-inferiority, parallel group, investigator blind study.

MATERIALS AND METHODS: ART patients, 18 to 39 years, BMI between 18 and 30 kg/m2, normal hormonal profile (FSH<10 IU/L), regular menstrual cycles, infertility attributable to a tubal factor, grade I or II endometriosis, male factor or unexplained infertility and with no more than 3 prior ART attempts were included in the study. All patients underwent COS using HP-FSH (Fostimon, IBSA SA, Switzerland) in a long-GnRH-a protocol. Ovulation was triggered, using either 10,000 IU of HP-hCG (Choriomon/GonasiHP, IBSA SA, Switzerland), or 0.250mg of r-hCG alpha (Ovitrelle, Merck Serono, Switzerland). The primary efficacy criterion was the total number of oocytes retrieved. The secondary criteria included oocyte quality – notably, the fertilization rate – or that of the embryo, as implantation rate (IR) and clinical pregnancy rate (cPR).

RESULTS: 72 and 75 women got included in the HP-hCG and r-hCG groups, respectively. There were no relevant differences at baseline between the 2 populations. Results show no differences in ART outcome between women receiving HP-hCG or r-hCG. But, with 13.3±6.8 vs 12.5±5.8 (NS) oocytes retrieved, IR of 22.5% *vs* 17.2% (NS), cPR of 31.9 % *vs* 26.7% (NS) and live birth rates of 27.8% *vs* 22.7% (NS) in HP-hCG vs. r-hCG there was a persistent trend toward better outcome in the HP-hCG group. There were no differences in term of tolerability between the 2 populations.

CONCLUSION: This 1st RCT on HP-hCG and r-hCG concludes that these are equally effective and safe. A trend toward obtaining more oocytes and higher cPR and live birth rates in the HP-hCG group suggests that hCG of human origin may provide subtle practical benefit on oocyte quality and ART outcome.

Supported by: This study was sponsored by IBSA Institut Biochimique SA, Lugano Switzerland.

DOES METHOTREXATE ADMINISTRATION FOR ECTOPIC PREGNANCY FOLLOWING IN-VITRO FERTILIZATION IMPACT OVARIAN RESERVE OR OVARIAN RESPONSIVENESS?. C. E. Boots,[a] R. L. Gustofson,[b] E. C. Feinberg.[c] [a]Obstetrics & Gynecology, University of Chicago, Chicago, IL; [b]Colorado Center for Reproductive Medicine, Lone Tree, CO; [c]Fertility Centers of Illinois, Chicago, IL.

OBJECTIVE: Ectopic pregnancy accounts for 1.5-2% of all pregnancies and causes significant morbidity and mortality. Methotrexate (MTX) has replaced surgical management for asymptomatic ectopic pregnancy. Little is known of the impact of MTX on subsequent fertility and IVF outcomes. This study evaluates the effects of methotrexate by comparing ovarian reserve and ovarian responsiveness before and after an ectopic pregnancy treated with MTX.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients who had an ectopic from an IVF cycle who were treated with MTX were identified. Women who did not undergo a subsequent IVF cycle after MTX administration were excluded. Age, day 3 FSH, antral follicle count (AFC), IVF stimulation parameters and time from MTX administration to subsequent IVF cycle were compared between cycles. Paired t-test and ANOVA were used for analysis.

RESULTS: 157 ectopic pregnancies were identified. 66 women underwent IVF both before and after MTX and were included. 47/66 (71%) patients received a single dose of MTX and 19 (29%) required a second dose. There were no significant differences with regard to day 3 FSH, AFC, duration of stimulation, or peak estradiol. The post-MTX cycle required higher doses of gonadotropins but resulted in the same number of oocytes retrieved. There was no impact of time from MTX administration with regard to these parameters.

Patient Characteristics	Pre- Methotrexate (n=66)	Post- Methotrexate (n=66)	*P*
Antral follicle count	15.3±7.5	15.2±6.6	0.89
Max FSH (mIU/mL)	8.8±3.0	8.0±3.1	0.11
Duration of stimulation (days)	11.0±1.4	11.0±1.6	0.80
Serum E2 (pg/ml) on day of HCG	2,563±971	2,471±987	0.49
Total gonadotropin dose (IU)	3,678±1,701	4,217±1,861	<0.01
Number of oocytes retrieved	13.0±6.3	13.7±6.5	0.35

Mean±SD.

CONCLUSION: Methotrexate remains first-line therapy for medical management of ectopic pregnancy. There appears to be no adverse impact on ovarian reserve or ovarian responsiveness in subsequent IVF cycles after administration.

DRAMATIC PROGRAM-WIDE REDUCTION IN THE INCIDENCE OF SEVERE OVARIAN HYPERSTIMULATION SYNDROME (OHSS) REQUIRING PARACENTESIS WITH SELECTIVE USE OF GONADOTROPIN-RELEASING HORMONE (GNRH) AGONIST TRIGGER. S. Beall,[a] G. Betz,[b] J. Segars,[a] F. Chang,[a] K. Richter.[a] [a]Program in Reproductive and Adult Endocrinology, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD; [b]Shady Grove Fertility Reproductive Science Center, Rockville, MD.

OBJECTIVE: To compare rates of severe OHSS requiring paracentesis before and after the use of a GnRH agonist trigger protocol in high risk in vitro fertilization (IVF) patients.

DESIGN: Retrospective historical comparison.

MATERIALS AND METHODS: All patients undergoing oocyte retrieval (OR) for IVF from January 2008 through December 2011 were analyzed. Pituitary suppression was by either GnRH agonist (leuprolide acetate (LA)) or antagonist (ganirelix acetate (GA)). Before 2010 oocyte maturation was induced with human chorionic gonadotropin (hCG). Beginning in 2010 patients at high risk for OHSS (defined by a diagnosis of polycystic ovary syndrome, high antral follicle count, or prior history of OHSS) were offered GA pituitary suppression and LA trigger. All patients underwent a standard protocol of ovarian stimulation with gonadotropins. Patients successfully triggered with LA received hCG 1500IU at OR. The frequency of OHSS requiring paracentesis was evaluated. Statistical analysis was by Chi-Square or Mann-Whitney U test as appropriate.

RESULTS: In 2008 and 2009, 9277 OR procedures, all using hCG trigger, were performed. Paracentesis for OHSS was required after 181 of these (1.95%). In 2010 and 2011, 10,381 OR procedures were performed (2,499 of which were triggered with LA), with 86 subsequently requiring paracentesis (0.83%). This represented a statistically significant relative reduction in the frequency of severe OHSS requiring paracentesis of 57.7% ($P<0.0001$).

CONCLUSION: Selective use of LA to stimulate oocyte maturation before OR in high risk patients (approximately one quarter of the entire patient population) resulted in a dramatic program-wide decline in the incidence of severe OHSS requiring paracentesis. Leuprolide is a safer alternative to hCG in patients at high risk for OHSS.

Supported by: This work was supported in part by the Program in Reproductive and Adult Endocrinology, NICHD, NIH, Bethesda MD, USA.

HIGH OVARIAN STIMULATION DOESN'T IMPAIR EMBRYO QUALITY. CLINICAL EVIDENCE USING COMPARATIVE MODEL WITH SHARED EGG DONORS. J. Llacer,[a] B. Moliner,[a] A. Rodriguez,[a] J. Guerrero,[a] J. Ten,[a] R. Bernabeu.1 [a]Reproductive Medicine, Instituto Bernabeu, Alicante, Spain, [b]IB Biotech, Instituto Bernabeu, Alicante, Spain.

OBJECTIVE: To investigate the clinical relevance of the overstimulation in the oocyte quality in terms of embryo implantation using an egg donor shared model in order to avoid biass number of oocytes and endometrial receptivity.

DESIGN: Observational case-control study.

MATERIALS AND METHODS: A retrospective analysis was performed with data from 1535 oocyte donation cycles collected during the years 2006-2009. Only 553 recipients who received 7 to 10 oocytes were included in the analysis. We established 2 groups according to the number of oocytes obtained from the donor: "Normal Stimulation Group" when the recipient did not share the donor and therefore the stimulation resulted in the collection of 7-10 oocytes and "High Stimulation Group" when the recipient shared the donor and therefore, 15 o more oocytes were collected. We compare clinical outcomes: clinical pregnancy rate, implantation rate, biochemical pregnancy rate, miscarriage rate, maturation rate, and embryo quality. Univariate comparisons were performed using Pearson's chi-square test for categorical data and the T-student test for continuous measures. Multivariate analysis was performed using logistic regression for categoricals dependent variables and linear regression for continuous dependent variables. All of the multivariate analysis were adjusted by probably confusions factors, like was donor's age. ROC curve was performed to add predictor factor to analysis.

RESULTS: Both groups were comparable according to clinical outcomes. ROC curve showed all the variables analized witharea under curve less than 0,5 without statistical differences.

Results

	High Stimulation	Normal Stimulation	
Implantation Rate (%)	31,82	30,82	P=0,765
Clinical Pregnancy Rate (%)	50,12	47,72	P=0,324
Miscarriage Rate	14,64	17,71	P=0,327
Live Birth Rate	44,85	41,18	P=0,236

CONCLUSION: Oocytes obtained under high levels of estradiol retain the ability to generate normal embryos. The oocyte quality impairment in overstimulated cycles doesn't exist or is not clinical relevant.

Supported by: Instituto Bernabeu.

P-206 Tuesday, October 23, 2012

EFFECT OF PERTUBATION ON PREGNANCY RATES BEFORE INTRAUTERINE INSEMINATION TREATMENT IN UNEXPLAINED INFERTILE PATIENTS. F. Yildiz, N. Bozkurt, A. Erdem, M. Erdem, M. Oktem, O. Karabacak. Gazi Üniversity, Ankara, Turkey.

OBJECTIVE: In this prospective randomized study, patients diagnosed with unexplained infertility underwent pertubation* prior a controlled ovarian stimulation and intrauterine insemination protocol. The effects of pertubation on their successive pregnancy rates were evaluated.

* Pertubation: lavage procedure of intrauterine cavity and bilateral fallopian tubes

DESIGN: This was a single-center, prospective, randomized, blinded control trial undertaken at a tertiary care university fertility center between January 2010- March 2011.

MATERIALS AND METHODS: A total of 180 patients were included in the study, and amongst these pertubation of the uterine cavity was carried out in 79 patients before insemination. One patient in the pertubation group was later excluded since insemination could not be done due to reasons in follow up.

RESULTS: There were no significant differences between the demographic characteristics of both the study and control groups. When the pregnancy rates of both groups were evaluated, 14 patients (%17. 8) in the study group achieved pregancy. Three patients (3. 8%) had a biochemical pregnancy, 1 (1. 3%)patient miscarried and 10 patients(12. 7%) had live births. In the control group, a total of 24 pregnancies (23. 8%) were achieved, amongst which one patient had a biochemical pregnancy (1%), 3 (3%) miscarried and 20 (19. 8%) resulted in live births. There was no significant difference between both groups' total pregnancy rates and live birth rates (P>0. 05). When the rate of pregnancy loss was investigated, a loss of 21% in total was discovered. There was no significant difference between the control and study groups when pregnancy loss rates were considered (P>0. 05).

CONCLUSION: We conclude that, this study on a homogenous group of unexplained infertile patients, the addition of pertubation to a controlled ovarian hyperstimulation and intrauterine insemination treatment protocol does not affect pregnancy rates.

Supported by: Any institution or organization supported this project. The required materials were provided by us.

P-207 Tuesday, October 23, 2012

CHARACTERISTICS PREDICTIVE OF FAILED LEUPROLIDE ACETATE (LA) TRIGGER AMONG PATIENTS UNDERGOING GONADOTROPIN-RELEASING HORMONE (GNRH) ANTAGONIST SUPPRESSION FOR VITRO FERTILIZATION (IVF). S. Beall,[a] K. Moon,[a] E. Widra,[b] A. DeCherney,[a] F. Chang,[b] K. Richter.[a] [a]Program in Reproductive and Adult Endocrinology, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD; [b]Shady Grove Fertility Reproductive Science Center, Rockville, MD.

OBJECTIVE: To characterize patient characteristics associated with failure to mount an adequate endogenous luteinizing hormone (LH) surge in response to LA trigger for IVF.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Autologous IVF cycles from 2010 were reviewed. 806 patients were triggered with LA following gonadotropin stimulation with GnRH antagonist suppression. Serum LH and progesterone (P) concentrations were obtained 8-14 hours (mean 11.1) following LA trigger. An inadequate response was defined as serum LH<15 IU/L and P<3 ng/mL, or no oocytes obtained after aspiration of the first several follicles at oocyte retrieval. These patients were re-triggered with hCG to salvage the cycle. Patient characteristics including age and BMI (available for all cycles) and baseline follicle-stimulating hormone (FSH) and LH measured on cycle day 3 (available for 797 and 759 cycles respectively) were compared between successful and failed LA triggers by t test or Fisher's exact test as appropriate.

RESULTS: Of 806 patients triggered with LA, 22 had an inadequate response and were re-triggered with hCG. Mean patient age (33.4 vs 34.1 years, P=0.48), BMI (25.1 vs 24.0, P=0.37), baseline FSH (6.4 vs 6.7 IU/L, P=0.63), and baseline LH (5.9 vs 5.2 IU/L, P=0.31) were all similar between successful and unsuccessful LA triggers. However, BMI<22 was significantly more common among failed vs successful LA triggers (63.6% vs 39.0%, P=0.026), and baseline LH<2 IU/L was significantly more common among failed vs successful LA triggers (20.0% vs 3.1%, P=0.004). Failure rates for BMI<22 vs higher BMI were 4.4% vs 1.6%, while failure rates for LH<2 IU/L vs higher LH were 14.8% vs 2.2%.

CONCLUSION: Low baseline LH is associated with a dramatic increase in LA trigger failure rates, and low BMI is associated with a more moderate increase in failure rates. Thus LA trigger may be less appropriate for such patients.

Supported by: This work was supported in part by the Program in Reproductive and Adult Endocrinology, NICHD, NIH, Bethesda MD, USA.

P-208 Tuesday, October 23, 2012

THE EFFECTS OF RESVERATROL ON AN OVARIAN HYPERSTIMULATION SYNDROME MODEL IN RATS. M. Oktem,[a] S. Ozgur,[a] O. Erdem,[b] S. Elbeg,[c] C. Cenksoy,[a] A. Helvaci.[b] [a]Obstetrics & Gynecology, Gazi University Faculty of Medicine, Ankara, Turkey; [b]Pathology, Gazi University Faculty of Medicine, Ankara, Turkey; [c]Biochemistry, Gazi University Faculty of Medicine, Ankara, Turkey.

OBJECTIVE: The effect of resveratrol on an ovarian hyperstimulation syndrome (OHSS) model in rats.

DESIGN: Randomized controlled, animal study.

MATERIALS AND METHODS: Female Wistar rats (22 days old) were divided into four groups: group 1 (control group; n :6) received 0.1 mL of intraperitoneal (IP) saline from days 22-26; group 2 (mild-stimulated group; n 6) received 10 IU of pregnant mare serum gonadotropin (PMSG) on day 24 and 10 IU of hCG 48 hours later (day 26); group 3 (OHSS group; n:6) was given 10 IU of PMSG for 4 consecutive days from day 22 and 30 IU hCG on the fifth day to induce OHSS; group 4 (resveratrol group; n:6) was treated the same as group 3, but received 60 mg/kg Resveratrol 2 hours before the