

in clinical pregnancies. Out of 744 embryos cleaving in the new media, 260 were transferred and 247 were cryopreserved; for the control media, from 640 cleaving embryos, 103 were transferred and 255 were cryopreserved.

Conclusions: This study represents one of the largest for culture media so far undertaken. Preliminary results indicate that the new sequential media series are as good as, if not better than, the current media being used in one facility. Based on these observations, it is unlikely that Phase II of the study will be conducted. PII S0015-0282(01)01737-X

## P-18

**Recombinant FSH Preparations for Controlled Ovarian Stimulation in Assisted Reproduction: A Comparison of Gonal F and Follistim.** C. Racowsky, B. W. Walsh, M. D. Hornstein, A. R. Garguilo, E. S. Ginsburg. Department of Obstetrics/Gynecology and Reproductive Biology, Center for Reproductive Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

Objective: To assess the relative efficacy of the two recombinant FSH (rFSH) preparations, Follistim and Gonal F, on outcome in assisted reproductive technology (ART) cycles.

Design: A retrospective analysis comparing outcomes after controlled ovarian stimulation (COS) using either Follistim or Gonal F in patients under 40 years of age.

Materials and Methods: 247 cycles with Follistim were compared with 647 cycles with Gonal F. All cycles involved luteal down regulation with leuprolide acetate in patients at their first or second IVF or ICSI attempt, who underwent either a day 3 or day 5 transfer. Choice of rFSH preparation was based on physician preference. The primary outcome measure was ongoing/delivered pregnancy rate; secondary outcomes included number of oocytes retrieved, fertilization rate, cryopreservation rate, and embryo quality as assessed by cell number and degree of fragmentation on day 3. Data were analyzed using Chi square and Fisher's exact tests, or the Mann Whitney U test, as appropriate.

Results: The two rFSH groups did not differ in terms of the use of ICSI, the proportion of cycles with day 5 transfer, age, ART attempt number, cancellation rate, number of ampoules of FSH used, number of mature oocytes, or number of embryos transferred. There was no significant difference between the Gonal F and Follistim groups for implantation rate (fetuses per embryos transferred: 23.7% vs. 23.6%), ongoing/delivered rate (44.3% vs. 43.7%), or the proportion of patients having at least one high quality embryo transferred (75.2% vs. 75.2%), or cryopreserved embryos (18.5% vs. 18.7%). However, the fertilization rate of mature oocytes was significantly higher in the Gonal F group (mean  $\pm$  SD: 70.8  $\pm$  21.0% vs. 67.4  $\pm$  24.8%,  $P < .05$ ). Furthermore, compared with day 3 embryos in the Follistim group ( $n = 2,071$ ), significantly more in the Gonal F group ( $n = 5,312$ ) had at least 8 cells (33.1% vs. 38.1%;  $P < .0006$ ), and significantly more exhibited  $< 10\%$  fragmentation (44.5% vs. 49.0%;  $P < .006$ ).

Conclusions: Comparable ongoing/delivered rates were achieved following controlled ovarian stimulation with either Gonal F or Follistim. Although fertilization rate and overall quality of the embryo cohort appear superior in the Gonal F group, these benefits did not translate to improved clinical outcome or an increased incidence of cryopreservation. A multi-center prospective randomized trial is warranted to determine the true efficacy of using these two rFSH preparations for controlled ovarian stimulation. PII S0015-0282(01)01738-1

## P-19

**Very High FSH Levels Do Not Result in Additional Follicular Development in Poor Responders to Ovarian Stimulation.** P. Saadat, C. C. Slater, S. Patel, J. K. Jain, F. Z. Stanczyk, R. J. Paulson. Department of Obstetrics and Gynecology, University of Southern California Keck School of Medicine, Los Angeles, CA.

Background: Patients who respond inadequately to standard regimens of controlled ovarian hyperstimulation (COH) are commonly treated with one of two regimens, including the micro-dose flare (MDF) and a combination of clomiphene citrate and human menopausal gonadotropin (CC/hMG). Both protocols stimulate folliculogenesis via endogenously produced as well as exogenously administered follicle-stimulating hormone (FSH), but whether higher FSH levels result in greater estradiol ( $E_2$ ) or number of oocytes has not been established.

Objective: To compare treatment-related FSH levels in patients undergoing COH with either MDF or CC/hMG and to correlate these with increases in serum  $E_2$  and the number of oocytes retrieved.

Materials and Methods: Treatment was begun either on day 2 of spontaneous menses or on the 4th day after the last oral contraceptive pill. Group 1 ( $n = 6$ ) received 100 mg of CC on cycle days 1-5 along with 8 amps of hMG daily given concurrently and continued until the day of hCG (dhCG). Group 2 ( $n = 5$ ) used the MDF protocol (40  $\mu$ g of leuprolide acetate b.i.d. starting on cycle day 1 and 8 amps of hMG daily starting on day 3). There was no statistically significant difference in average age or weight between the two groups. Serum FSH and  $E_2$  values were measured at baseline, day 5, and on dhCG administration. Data were analyzed by linear regression and Student's t-test.

Results:

Group	Baseline		Day 5		Day of hCG	
	$E_2$ (pg/ml)	FSH (mIU/ml)	$E_2$ (pg/ml)	FSH (mIU/ml)	$E_2$ (pg/ml)	FSH (mIU/ml)
CC/hMG	24.6 $\pm$ 7.7	9.95 $\pm$ 2.9	956 $\pm$ 1371	41.9 $\pm$ 12	1321 $\pm$ 614	45.0 $\pm$ 8.6
MDF	20.6 $\pm$ 19	9.54 $\pm$ 4.7	355.8 $\pm$ 215	25.2 $\pm$ 6	1202 $\pm$ 594	24.7 $\pm$ 8.1
P-value	.67	.87	.93	.02	.752	0.003

  

Group	Increase in value baseline—d5		Increase in values baseline—dhCG	
	$E_2$ (pg/ml)	FSH (mIU/ml)	$E_2$ (pg/ml)	FSH (mIU/ml)
CC/hMG	371 $\pm$ 178	32 $\pm$ 11.2	1297 $\pm$ 609	35.1 $\pm$ 7.4
MDF	335 $\pm$ 199	16.0 $\pm$ 9.9	1138 $\pm$ 592	15.4 $\pm$ 9.73
P-value	0.76	0.03	0.67	.007

Results reported as mean value  $\pm$  SEM.

Treatment associated FSH levels were consistently higher in the CC/hMG group than in the MDF group. Additionally, the increase in FSH levels from baseline to day 5 and dhCG was greater in the CC/hMG group. However, serum  $E_2$  levels were similar in the two groups as was the number of oocytes retrieved (7.8  $\pm$  2.3 in group 1 vs. 6.4  $\pm$  4.3 in group 2,  $P = NS$ ). Serum FSH levels on dhCG did not correlate with serum  $E_2$  nor with the number of oocytes retrieved. The mean endometrial echo complex (EEC) was also similar in both groups.

Conclusion: Since the amount of exogenous gonadotropins used was the same in both groups, the difference in the FSH levels reflects pituitary FSH production. In spite of a nearly two-fold greater increase in levels of FSH in the CC/hMG group, as compared with MDF group, there was no statistically significant difference in  $E_2$ , number of oocytes retrieved, or the EEC between the two groups. We conclude: 1) CC is a more potent stimulator of FSH production than micro-dose Lupron when administered in conjunction with exogenous hMG; and 2) elevation in FSH levels beyond a certain threshold value does not result in any additional follicular development in poor responders to ovarian stimulation. PII S0015-0282(01)01739-3

## P-20

**Recombinant FSH Provides More Efficient, Cost-Effective Stimulation for Ovulation Induction/Intrauterine Insemination (OI/IUI) Cycles Than Highly Purified Urinary FSH.** K. M. Silverberg, R. A. Ormand, L. J. Hansard, T. C. Vaughn. Texas Fertility Center, Austin, TX.

Introduction: Recent changes in manufacturing processes from urinary to recombinant follicle-stimulating hormone (FSH) have resulted in the production of pharmacologic preparations with enhanced purity. Although safety advantages of recombinant technology are obvious, published comparisons of efficacy in IUI cycles are needed. This prospective study was designed to compare the stimulation efficiency of highly purified and recombinant FSH preparations.

Materials and Methods: Patients undergoing OI with gonadotropins between January 1998 and June 1999 were prospectively evaluated to assess

their response to highly purified urinary (Fertinex) or recombinant (Gonal F) FSH. Ovarian function was monitored with serial transvaginal sonography and serum estradiol ( $E_2$ ) levels. Human chorionic gonadotropin (hCG) was administered when at least one follicle exceeded 19 mm in average dimension. IUI was performed on the two consecutive days following hCG administration. End points included days of stimulation, total ampules and dose of FSH, total number of follicles exceeding 14 and 18 mm, serum  $E_2$  on the day of hCG, and clinical pregnancy rate. Statistical analysis was performed using ANOVA, chi-square and t tests where appropriate.

Results: Of the 570 cycles performed during this study, 476 were included for analysis. Cycles in which Lupron or more than 1 type of gonadotropin were used were excluded. No demographic differences existed in terms of patient age, weight, or diagnosis between the two groups. Patients stimulated with Gonal F required significantly fewer ampules of medication and a significantly lower total dosage of medication to achieve follicular maturity ( $P < 0.01$ ). Clinical pregnancy rates were similar between both groups.

	N	Days of stim.	Total dose	No. amps	No. Foll >18	No. Foll >14	Clinical PR (%)
Fertinex	159	9.2	1,927.9	25.7	1.9	4.0	14.0
Gonal F	317	9.0	1,715.2	22.9	2.0	3.9	18.1
P value		.4	<.01	<.01	.7	.6	.3

Conclusion: Recombinant FSH provides a more efficient stimulation than highly purified urinary FSH. In addition to achieving similar cycle end points with greater safety and purity, the fewer ampules of recombinant FSH required translates into a significant cost saving for patients. PII S0015-0282(01)01740-X

#### P-21

##### Prognostic Significance of a Biochemical Pregnancy in IVF Cycles.

L. N. Weckstein, A. Jacobson, D. Galen, C. Smikle, S. Willman, W. Shen, D. Walker, K. Ivani. Reproductive Science Center of the San Francisco Bay Area, San Ramon, CA.

Objectives: To investigate the significance of a biochemical pregnancy in an IVF cycle in terms of its prognostic importance for a successful pregnancy in subsequent IVF cycles.

Design: A retrospective evaluation of biochemical pregnancies arising from IVF cycles, and pregnancy outcome in subsequent cycles.

Materials and Methods: Data were compiled from all IVF cycles between January 1998 and August 2000. Patients having a biochemical pregnancy during that time period were analyzed for cycle outcome in other IVF cycles. A biochemical pregnancy was defined as HCG levels  $>5$  on two occasions 15 days or greater after HCG injection, with no gestational sac ever visible with ultrasound.

Results: Sixty-seven patients had biochemical pregnancies during the study period. Thirty-three of these patients did not undergo any other IVF cycles. Thirty-four patients underwent one or more subsequent cycles. Twenty of these (59%) subsequently delivered or have an ongoing pregnancy beyond 12 weeks. In 17 patients the delivery resulted from the IVF cycle immediately following the biochemical pregnancy, and in three patients the delivery resulted from the second IVF cycle following the biochemical pregnancy.

Two patients (6%) had subsequent clinical pregnancy losses, and 12 (35%) had negative cycles after the biochemical pregnancy (two of these had more than one subsequent biochemical pregnancy).

Thirteen patients had IVF cycles prior to the biochemical pregnancy cycle. Eleven had one or more negative cycles (none of whom had a successful pregnancy after the biochemical pregnancy), and two patients had an IVF cycle resulting in a delivery prior to the biochemical pregnancy (both of these patients also had a delivery following the biochemical pregnancy).

Conclusions: From our preliminary data a biochemical pregnancy is not indicative of a poor prognosis for future IVF cycles. Patients who have a biochemical pregnancy should be encouraged to go through another IVF cycle. PII S0015-0282(01)01741-1

#### P-22

##### Androgen Levels Prior to, and Following Prophylactic Oophorectomy.

C. C. Slater, K. S. Parks, F. Z. Stanczyk, C. Zhang, R. J. Paulson, D. R. Mishell, Jr. Department of Obstetrics and Gynecology, University of Southern California Keck School of Medicine, Los Angeles, CA.

Background: Testosterone in the female is important for bone mass, muscle mass, energy levels, and possibly libido. Bilateral oophorectomy is commonly recommended in selected women who are undergoing hysterectomy.

Purpose: To measure androgen levels pre- and post-oophorectomy in both premenopausal and postmenopausal women.

Materials and Methods: Eleven women between the ages of 42 and 70 (premenopausal and postmenopausal) underwent hysterectomy for benign disease with concomitant elective oophorectomy. Serum reproductive hormone levels were measured prior to, and two weeks after oophorectomy. Total testosterone (T), total estradiol ( $E_2$ ), estrone ( $E_1$ ), androstenedione (A), dihydrotestosterone (DHT),  $3\alpha$ -androstenediol glucuronide ( $3\alpha$ -diol G, a marker of peripheral androgen action), dehydroepiandrosterone sulfate (DHEAS), and sex hormone-binding globulin (SHBG) levels were measured by specific radioimmunoassays. Free T and  $E_2$  were calculated.

Results: In women who were premenopausal prior to surgery, mean T levels fell from 20.2 ng/dL to 13.4 ng/dL ( $P = .01$ ), mean A levels fell from 68.8 pg/mL to 50.1 pg/mL, mean DHT levels fell from 99.5 pg/mL to 72.5 pg/mL. In women who were postmenopausal prior to surgery, mean T levels fell from 29.8 ng/dL to 17.5 ng/dL ( $P = .02$ ), mean A levels rose slightly but insignificantly, mean DHT levels fell from 95.7 pg/mL to 68.1 pg/mL.  $3\alpha$ -Diol G, DHEAS and SHBG levels did not significantly change in either group.

Conclusion: Oophorectomized patients should be counseled that T levels decline by approximately 35% two weeks after oophorectomy, and that estrogen replacement without T replacement may be inadequate hormone replacement. PII S0015-0282(01)01742-3

#### P-23

##### Evaluation of Baseline Carotid Artery Intima-Media Thickness and Its Progression Over Two Years in Postmenopausal Women With and Without Intact Ovaries.

C. C. Slater, D. Shoupe, W. J. Mack, F. Z. Stanczyk, H. N. Hodis. Departments of Obstetrics and Gynecology, Preventive Medicine, Atherosclerosis Research Unit, University of Southern California Keck School of Medicine, Los Angeles, CA.

Background: Cardiovascular disease is the leading cause of morbidity and mortality in postmenopausal women. Prior studies have shown that bilateral oophorectomy is associated with earlier onset of subclinical atherosclerosis than natural menopause. Estrogen replacement therapy (ERT), however, has been found to decrease progression of atherosclerosis.

Purpose: To determine if postmenopausal ovarian estrogen levels ( $<20$  pg/mL) affects progression rate of atherosclerosis.

Materials and Methods: A cohort of postmenopausal women were studied prospectively. Carotid artery intima-media thickness (IMT) was measured with B-mode ultrasonography at baseline and 2 years later. All patients were screened for cardiovascular risk factors and placed on a cardiovascular diet. None of the patients were taking ERT. Statistical analysis was done with t-test with unequal variance.

Results: Baseline IMTs were  $0.78 \pm 0.02$  mm and  $0.86 \pm 0.04$  mm for the no oophorectomy ( $n = 58$ ) and oophorectomy groups ( $n = 11$ ), respectively. IMT progression rate over 2 years were  $0.02 \pm 0.03$  mm/year and  $0.002 \pm 0.001$  mm/year for the no oophorectomy ( $n = 27$ ) and oophorectomy groups ( $n = 8$ ), respectively ( $P = NS$ ).

Conclusion: Perimenopausal and early menopausal ovarian hormone levels provide protection against atherosclerosis progression. Carotid artery IMT progression rate does not differ between natural menopause and surgical menopause when remote from time of menopause. PII S0015-0282(01)01743-5

#### P-24

##### Outcome of Repeated Cycles of In Vitro Fertilization With Blastocyst Stage Embryo Transfer.

B. S. Shapiro, K. S. Richter, D. C. Harris,