treatment usually includes gonadotropin ovulation induction. This study evaluates whether the addition of metformin, an insulin sensitizer, to the gonadotropin regimen improves laboratory values (including insulin-like growth factor binding protein (IGF-1BP), testosterone (T), insulin, sex hormone binding globulin) or the ovulation rate in patients with PCOS.

Design: Prospective, randomized, placebo-controlled double-blind study.

Materials and Methods: Ten women with PCOS as defined by clinical oligomenorrhea and hyperandrogenism (NICHD 1990 definition of PCOS) were randomized to receive either metformin or placebo treatment. All of these women had similar baseline characteristics and had previously failed clomiphene citrate induction. A two month wash out period occurred prior to starting either treatment. Patients were administered metformin (1000 mg BID) or placebo medication in a double-blind fashion for a total of 6 weeks, and laboratory values were compared. If patients had a spontaneous bleed between days 28-42, they were started on a low dose ovulation induction protocol (Hamilton-Fairley et al., 1991). If no bleed had occurred yet by day 42, it was induced with IM progesterone. Medication adjustments were made at the discretion of the reproductive endocrinologist (VSR) based on baseline and routine monitoring. HCG was administered when the estradiol level was between 350-2200 pg/ml, and $\geq$ 1 follicle ($>$ 16 mm) was present on u/s. If the patient did not conceive, a break cycle would occur prior to starting the next regimen. This was continued for up to 3 gonadotropin stimulation cycles. Endpoints included ovulation which was detected by a progesterone level $\geq$ 8.0 ng/ml, changes in laboratory values at the different points in fasting insulin levels, SHBG, total and free T, and IGF-1 BP.

Results: The laboratory values were compared at baseline and after 6 weeks of drug (metformin vs. placebo) administration. A student's t-test was utilized for comparison. There was no significant difference in either the metformin (n = 5) or the placebo (n = 5) group when examining the IGF-1BP, SHBG, free and total T levels. There was a statistically significant drop in the fasting insulin levels of the metformin-treated group (p value = .0435) after 6 weeks of treatment, starting with an insulin level of 27.98 $\pm$ 27.74 and dropping to 20.1 $\pm$ 22.84. Four of the five (80%) women on metformin and gonadotropins successfully ovulated, but none of the five women on placebo and gonadotropins ovulated. Utilizing the Fisher's Exact test, this was a significant difference with a two-tailed p value of .04762.

Conclusions: The short term use of metformin does not appear to remarkably alter or improve the laboratory values in patients with PCOS. When metformin is used in conjunction with gonadotropin stimulation, there is a significant increase in ovulation in PCOS patients. For PCOS patients undergoing gonadotropin therapy, metformin supplementation could lead to higher ovulatory rates and thus higher pregnancy rates.

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Wednesday, October 15, 2003
4:30 P.M.

O-288

Effect of metformin on subgroups of patients with polycystic ovaries undergoing controlled ovarian hyperstimulation for assisted reproductive techniques. Faruk Vanlioglu, Semra Kahraman, Guvenc Karlikaya, Hale Karagozoglu, Melih Aygun. Istanbul Memorial Hosp Assisted Reproductive Techniques & Reproductive Genetics Unit, Istanbul, Turkey.

Objective: To evaluate the effect of metformin on laboratory parameters and clinical results in patients with polycystic ovaries (PCO) undergoing assisted reproductive techniques (ART) as well as to define a subgroup of PCO patients who will benefit most from the use of metformin during controlled ovarian hyperstimulation (COH).

Design: Retrospective study.

Materials and Methods: This study involved women with PCO undergoing ICSI due to severe male factor infertility (n = 147) between April 2000 and November 2002. PCO patients were divided into four groups according to the presence of hirsutism and/or obesity: Group I (n = 29) had ultrasonically diagnosed typical morphological appearance of the ovaries (PCO ovaries), Group II (n = 36) patients with PCO ovaries and hirsutism, Group III (n = 38) patients with PCO ovaries and obesity, Group IV (n = 44) patients with PCO ovaries, hirsutismus and obesity. Body mass index (BMI), serum LH and androgen levels were compared before and after metformin therapy. The laboratory and clinical parameters were compared in four different groups undertaking metformin treatment.

Result(s): Metformin has led to significant decreases in LH and androgen levels but not in BMI. Addition of metformin in COH enables better control of estradiol levels.Group II and Group III patients with PCO ovaries and hirsutismus or obesity showed significant improvement in implantation and clinical pregnancy rates in comparison to Group I and Group IV patients with only PCO ovaries and PCO ovaries plus hirsutism and obesity. Pregnancy rates were 62.6 % in Group II and 61.5 % in Group III, these rates were significantly different than Group IV (59.8 %) and Group I (49.3 %) ($p < 0.05$). Abortion rate was found significantly higher in metformin Group IV (28.2 %) than the other Groups (in Group II 14.7 %, Group III 18.4 % and Group I 15.6 %) ($p < 0.01$). Implantation rates were 34.2 % in Group III and 36.8 % in Group II, these rates were significantly different than Group I (31.2 %) and Group IV (30.3) ($p < 0.01$).

Table I. Comparison of parameters among metformin subgroups.

	Group I	Group II	Group III	Group IV	p value
Implantation(%)	31.2	36.8*	34.2*	30.3	P< 0.01
Pregnancy(%)	64.3	79*	77.6*	69.8	P< 0.05
Clin/pregnancy	49.3	62.6*	61.5*	59.8	P< 0.05
Abortion rate(%	15.6	14.7	18.4	28.2*	P< 0.01

Conclusions: Use of metformin among subgroup of PCO patients during COH yields significantly different results in laboratory parameters, clinical pregnancy and implantation rates. However patients with PCO, hirsutismus and obesity still have a significantly higher abortion rate. The use of insulin sensitizing drugs to reduce miscarriage rates in PCO patients is also promising.

Wednesday, October 15, 2003
4:45 P.M.

O-289

Does dehidroepiandrosterone sulfate (Dheas) co-treatment improve art outcome? A prospective, randomized, double-blind placebo-controlled trial. Andrea E. Divita, Laura S. Kanzepolsky, Judith A. Notrica, Fernando D. Neuspiller, Ester Polak de Fried. CER Medical Institute, Buenos Aires, Argentina.

Objective: In the presence of adequate gonadotrophin concentrations, testosterone stimulates follicular development. In previous publications of Haning et al., it was proposed that DHEAS may act as a prehormone of ovarian testosterone. It has been suggested in other publications that co-treatment with DHEAS might be appropriate in poor responders patients to ART protocols.

The objective of this syudy was to evaluate if DHEAS co-treatment may improve ART outcomes.

Design: Prospective randomized double-blind placebo-controlled trial.

Materials and Methods: Thirty-one infertile couples who underwent consecutive ART cycles between July 2002 and December 2002 were randomly divided into treatment group (group I n = 16) and no treatment group (group II n = 15). Group I received a daily oral dose of 40 mg of micronized DHEAS, and group II received placebo. Both groups started co-treatment (DHEAS or placebo) and GnRha (leuprolide acetate 0,5 mg/day) in the midluteal phase of the previous cycle. Ovulation induction was started with rec-FSH 300 IU and continued on an individual basis. Monitoring and laboratory procedures were performed as usual. DHEAS and placebo were suspended after pregnancy test regardless of the result. IVF outcome variables analysed included: cancellation rate, number of oocytes retrieved, fertilization rate, number of embryos transferred, implantation and pregnancy rates. The data were analysed by X^2 and ANOVA. $p < 0, 05$ was considered statistically significant.

Results: The number of gonadotrophin ampoules used and the length of the treatment were similar in both groups. (see Table (values are expresed as mean $\pm$ SD).

Table I			
	Group I *n 16*	Group II *n 14*	P value
Age (years)*	31.13±4.62	35.50±3.88	NS
Cancellation rate (%)	-	6.66	
# oocytes*	8.0±3.67	8.71±4.16	NS
Fertilization rate (%)	83.71	78.74	NS
# Embryo transferred*	2.58±0.73	2.64±0.63	NS
Implantation rate (%)	31.25	23.81	NS
Pregnancy rate (%)	43.81	35.73	NS

Conclusion: Although in this preliminary trial we did not find statistically significant differences, it appears that the use of DHEAS shows a tendency towards improving fertilization, implantation and pregnancy rates. Furthermore, we did not observe cancellations due to failure in ovarian response in the treatment group. This encourages us to continue with this trial. A larger study is recommended.

Wednesday, October 15, 2003
5:00 P.M.

O-290

Bee venom treatment of refractory pregnancy. A modern trend. Ali Ali, M. Mostafa, W. Hamed, A. Mekled. Ain Shams Univ, Cairo, Egypt.

Objective: To determine the role of bee venom injection in women who previously failed to achieve a successful pregnancy following at least 3 IVF-ET cycles and if it would improve the chances of successful conception following another IVF-ET cycle.

Design: Pregnancy after failed repeated 3 successive in vitro fertilization and embryo transfer-IVF-ET trials is a striking subject and to the best of our knowledge, no report in the literature has dealt with this topic. It has been suggested that an increase in the Natural Killer cell percentage in the blood or increase in NK cell activity in the endometrium can cause embryo/fetal destruction. Trying to negate these adverse effects was warranted.

We have found that bee venom due to its peculiar chemical composition can offer a solution for this problem. Our own speculation is that immune rejection is more related, not to a cellular immune system that is always over-stimulated, but rather to a failure to secrete sufficient immuno-modulatory protein after trophoblast invasion which inhibits what should be a normal immune response to allograft.

Materials and Methods: Seven cases were enrolled in this study. Criteria for selection were previous failure to have a successful pregnancy after, at least, 3 or more attempts of IVF-ET. Patients were referred from different centers. Two cases had failed 5 attempts, 4 had failed 4 attempts and one case failed after 3 attempts. Mean age was 38.2+2.1.

Bee venom therapy was started for 2 weeks every other day (0.1 ml SC Farid ampoule-first author of this study). Following this, another IVF-ET attempt was done.

Results: Four cases got pregnant (57.1%): 2 from failed previous 4 attempts, one case from failed previous 5 attempts and one from failed previous 3 attempts. Live births rate was 3 cases (75%). One case aborted at 6 weeks of pregnancy.

Conclusion: These data revealed that bee venom therapy can stimulate post-implantation immuno-stimulatory protein, opening a new horizon in the field for improvement of results of IVF-ET. However, this should be confirmed by a randomized prospective trial.

ART: MALE FACTOR

Wednesday, October 15, 2003
2:00 P.M.

O-291

Pregnancy outcome of IVF/ICSI with profound teratospermia (Kruger strict criteria of zero). Laurie J. McKenzie, John E. Buster, Pauline Cisneros, Dolores Lamb, Larry Lipshultz, Sandra A. Carson. Baylor Coll of Medicine, Houston, TX.

Objective: To assess the pregnancy outcome of in vitro fertilization with intracytoplasmic sperm injection (IVF/ICSI) in couples with profound teratospermia (Kruger strict criteria of zero).

Design: Retrospective analysis of 545 consecutive cycles of IVF/ICSI at a university-based assisted reproductive technologies program from January, 2000 to January, 2003. All patients received Lupron(r)/human menopausal gonadotropins for stimulation and embryo transfer was performed on day 2 in all cycles.

Materials and Methods: Of 545 patients, each having a recent semen analysis and presenting for IVF to Baylor Assisted Reproductive Technology, 45 were identified with a semen strict morphology of 0 using Kruger's strict criteria. Cases in which sperm was obtained surgically were excluded. All strict morphology analyses were confirmed by a second blinded evaluator. The mean sperm concentration for all samples was 16.2 million/ml with an mean motility of 28.9%. The average age for all women undergoing IVF/ICSI with a strict morphology of 0 was 33.8 years. Ovarian downregulation (Lupron(r)) was followed by controlled ovarian stimulation exclusively with human menopausal gonadotropins. Embryo transfer was performed two days following transvaginal aspiration/ICSI. The mean number of embryos transferred per cycle was 3.7. Pregnancy outcomes and newborn/infant status were recorded. A positive pregnancy test was defined as a BHCG over 5 IU/L two weeks after embryo transfer.

Results: Of 45 patients undergoing 54 treatment cycles, 21 patients were positive for pregnancy (38.9% pregnancy/cycle). Of the 21 pregnancies, there were 3 biochemical pregnancies, 2 spontaneous abortions, 1 ectopic gestation, 12 live births, and three are ongoing. Average gestational age at delivery was 38.3 weeks. No birth defects were noted at time of delivery and all infants had obtained appropriate developmental milestones before one year of age. Mean infant follow up was 11 months, and infant outcomes were assessed via hospital records and patient telephone interview. 241 live births however, would be required to detect a two fold increase in birth defects above the background population baseline of 2-3% (power = 0.8).

Conclusions: Men with profound teratospermia (Kruger's strict criteria of zero) may still achieve acceptable pregnancy rates after IVF/ICSI thereby alleviating the use of donor sperm in this subgroup. Furthermore, no increased risk of birth defects is apparent in this small series. These data are helpful in counseling this subgroup of patients.

Wednesday, October 15, 2003
2:15 P.M.

O-292

Use of a novel technique for the conservative recovery of small quantities of cryopreserved nonrenewable sperm specimens for ICSI. Rachel K. Ashby, Katherine V. Jackson, Matthew G. Retzloff, Thomas F. O'Leary, Catherine Racowsky. Brigham and Women's Hosp, Harvard Medical Sch, Boston, MA.

Objective: To describe patient outcomes following ICSI after recovery of cryopreserved sperm using a novel technique designed to conserve nonrenewable male gametes obtained prior to chemotherapy or other procedures known to cause azoospermia.

Design: Retrospective case series from analysis of 2341 ICSI cycles from 1998 to 2002.

Materials and Methods: Charts were reviewed of all men who underwent ICSI. Eight patients were identified who had autologous cryopreserved sperm and subsequently underwent ICSI with the "shaving technique". The shaving technique entailed shaving off pieces of frozen specimen with a spatula during constant submersion of the vial under liquid nitrogen. Outcomes of those cycles in which banked sperm were subjected to conservative sperm recovery, using the shaving technique (n = 10), were compared with those cycles from the same patients where no shaving was performed (n = 15). Outcome variables included fertilization and pregnancy rates, in addition to identification of sperm availability for future cycles.

Results: Of the eight patients who had the shaving procedure performed, seven also had non-shaved ICSI cycles prior to the shaved cycle. The mean age of the male patients was 40.9y and the female partner mean age was 37.9. The mean cycle attempt was 3.1. Diagnoses of the 8 patients included: 6 men with cancer (75%), one with end stage renal disease and one with an autoimmune disease requiring chemotherapy. The incidence of coexisting female infertility was 75% (n = 6), with decreased ovarian reserve as the most common diagnosis. Pre-cycle sperm concentrations, as determined by a post-thaw semen analysis done at the time of banking, ranged from 0.55 million/ml to 76 million/ml with motilities ranging from 24% to 57%. Fertilization rates following use of sperm from shaved and non-shaved