

scheduling. 64 COH cycles were initiated with recFSH (Follistim™; Organon Inc. or Gonal F®; Serono, Norwell, NJ) at starting doses ranging from 150 to 450 IU on the fifth day after the last OC. Donors were randomly assigned to either no LH add-back or LH add-back with Repronex™ (Ferring Pharmaceuticals Inc., Suffern, NY) or dilute recombinant hCG (Ovidrel™; Serono). Antagon™ 250 µg per day was started when the lead follicle was 1.3 cm or estradiol was greater than 400 pg/ml, but no later than day 7. Estradiol and ultrasound monitoring were continued until 3 follicles reached 1.8 cm, at which point hCG was given (Pregnyl™; Organon Inc. or Ovidrel™). Egg retrieval was performed 37 hours later by ultrasound-guided transvaginal ovarian puncture. Insemination was performed by IVF or ICSI. Donor recipients were treated with agonist down regulation followed by sequential estradiol and progesterone for endometrial preparation. Two to three embryos were transferred to the recipient on day 3. Pregnancy was recorded if viability was seen past the 10th week.

Results: Pregnancy rates in donor recipients were similar with and without LH add-back (65% and 61% respectively). Pregnancy rates did not differ regardless of the type of LH add-back used (64.7% Ovidrel™ vs. 61.5% Repronex™; $p > 0.05$). There was a trend toward better embryo quality with LH add-back, however duration of stimulation was surprisingly longer in the LH add-back group (10.2 ± 1.0 versus 9.7 ± 1.1 days; $p < 0.05$). Though LH add-back appears to increase the number of embryos available for cryopreservation (9.6 ± 8.1 v. 6.6 ± 6.0 ; $p = 0.09$), this did not reach statistical significance. Estradiol levels were higher in the LH add-back group (2990 ± 1257 v. 2009 ± 875), though this did not translate into higher pregnancy rates. The total drug cost per cycle was similar with and without LH ($\$3835 \pm 906$ v. $\$3917 \pm 841$).

Conclusion: The routine use of LH add-back in COH for oocyte donation is not justified, as it does not improve pregnancy rates or reduce the length and cost of stimulation. Though LH add-back may increase the number of high quality embryos available for cryopreservation, more data will be required to determine if this finding is significant.

O-176 Assessment of the predictive value of LH levels in IVF cycles stimulated with GnRH antagonists and agonists

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Introduction: Increased LH levels are thought to be associated with negative outcome of IVF. LH is thought to trigger apoptosis in oocytes, leading to lower fertilization rates and poor embryo quality. LH release is not blocked until treatment either with GnRH antagonists or agonists is initiated. The aim of this study was to investigate the role of LH levels in IVF cycles stimulated with GnRH antagonists and agonists. Attention was paid to LH levels in the initial days of stimulation before GnRH antagonists were included into the stimulation protocol.

Material and methods: Prospective randomized study. A hundred and twenty women were allocated at random to stimulation protocols either with GnRH agonists or antagonists regardless the indications to IVF and prestimulatory LH levels (as checked on day 3 of the natural cycle). In 63 women triptorelin 3,75 (Diphereline SR 3,75; Beaufour Ipsen) was administered on day 20 of the preceding cycle and 14 days later if $E2 < 30 \text{ pg/mL}$, stimulation with recFSH (Gonal-F; Serono) was initiated. The remaining 57 patients received recFSH from day 2 of the cycle, and when the leading follicle reached 13

Variable	Cetrorelix cycles [n=57]	Triptorelin cycles [n=63]	P-value
Age [years]	32,5 (±4,8)	32,1 (±5,1)	NS
Number of FSH ampoules used	26,1 (±7,8)	28,4 (±10,1)	$P < 0,05$
Number of oocytes retrieved	8,9 (±3,6)	9,5 (±4,2)	NS
Fertilization rate [%] of all retrieved oocytes	64,2 (±21,9)	59,3 (±26,1)	NS
Early cleavage rate [%]	26,7 (±23,3)	27,2 (21,6)	NS
Grade A embryos rate [%]	62,4 (±30,9)	68,7 (±33,2)	NS
Number of embryos transferred	2,5 (±0,5)	2,6 (±0,8)	NS
Clinical pregnancy rate [%]	23,1	28,6	NS
LH1	1,83 (±1,43)	1,14 (±0,85)	$P < 0,05$
LH2	1,07 (±0,88)	0,90 (±0,79)	NS

mm cetrorelix 0,25 mg (Cetrotide; Serono) was started. The LH levels were checked on the day, when the leading follicle reached 13 mm (LH1) and 21 mm (LH2). In all cycles only ICSI with day 3 ET were performed.

Results: Both protocols differed in numbers of recFSH ampoules and LH1 levels. The remaining parameters did not differ significantly (see table). In all patients, logistic regression revealed no association between the LH1 levels and the IVF outcome. Such an association was found between the quality of embryos as measured by embryo early cleavage and grade.

Conclusion: Higher LH levels during stimulation with GnRH antagonist, when compared to stimulation with GnRH agonist seem to have no significant effect on the IVF outcome.

FREE COMMUNICATION

Session 43 – ART/IUI

Monday 28 June 2004

17:00–18:00

O-177 Results after homologous intrauterine insemination. The German Group for Conservative Infertility Treatment

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Introduction: The AKF intends to evaluate the results of conservative infertility treatment performed in hospitals and private practices (monitoring of the menstrual cycle, insemination (IUI) with and without ovarian stimulation). The group was founded in May 2001 and the presented data have been collected from 21 centres.

Material and methods: Data were extracted from the computer program RecDate which is commonly used in Germany for the documentation of IVF cycles. During the time period from 12/1996 until 9/2003, 12,008 patients and 28,402 treatment cycles were documented. These could be divided into 4,835 cycles with monitoring and sexual intercourse at the time of ovulation and 23,567 IUI cycles.

Results: In our data analysis we focused on data validity - which was 93% - and on the pregnancy rates in correlation with the following: 1.) number of cycles, 2.) female age, 3.) number of follicles and estrogen concentration, 4.) stimulation protocol, 5.) concentration and motility of sperm.

	Pregnancy rate in %		Pregnancy rate in %
IUI	9.4	IUI and number of follicles	
Cycle monitoring	8.8	1	9.8
IUI Cycles		2	9.3
First	7.8	3	13.9
Second	5.0	>4	33.3
Third	3.4	IUI and sperm count after purification	
Fourth	1.8	in Million	
IUI and age		≤5	5.7
≤29	11.4	5.1 - 10	49.3
30-34	9.3	10.1 - 25	10.7
35-39	8.0	25.1 - 100	13.0
>40	4.3	> 100	14.1
IUI and stimulation		IUI and sperm motility after purification	
No medical treatment	7.2	in %	
Clomifen	7.3	<20	4.6
HMG	8.9	21-40	7.9
FSH	10.1	41-60	9.6
FSH + GnRH Antagonist	11.7	61-80	6.7
FSH + GnRH Agonist	13.4		
IUI and estrogen in pg/ml			
< 100	2.9		
101 - 200	8.5		
201 - 300	9.3		
301 - 400	11.1		
401 - 500	13.1		
> 501	14.4		

Conclusion: Using RecDate, we were in the privileged position to evaluate the largest number of cycles published so far. We found pregnancy rates that correspond to published data. Our results suggest that unfavorable results of IUI are more frequent with the following factors: age over 40 years, more than 3 unsuccessful IUI cycles, no accompanying medical treatment, estrogen levels less than 200 pg/ml, sperm count less than 5 million/ml and less than 20% motility. Due to the limited number of documented cycles, it cannot be told from our data yet, if higher pregnancy rates could be achieved using modern medications (FSH with GnRH-Agonists or GnRH-Antagonists). Further collection and analysis of data is necessary. In the future it might be possible to develop guidelines for the improvement of IUI indications and implement routine examinations for the patients before the intended treatment.

O-178 Comparison of COH-IUI results with different gonadotrophin preparations

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Objective: To compare the efficacy of different gonadotropin preparations in COH-IUI cycles

Materials and methods: Two hundred forty-one patients with unexplained primary infertility were enrolled in this study (i- primary infertility of > 2 years, ii- woman's age between 20 and 40 years, iii-normo-ovulatory patients, iv- normal hysterosalpingography (HSG) or laparoscopy (L/S), v-normal sperm analysis). All groups were comparable with regard to the age and duration of infertility.

Two hundred forty-one couples were divided randomly into three groups: 81 in the follitropin-alpha; Group I (Gonal-F, Serono), 80 in the uFSH; Group II (Metrodin, Serono), 80 in the HMG; Group III (Pergonal, Serono). Ovarian cycle stimulation was started on the second or third day of menstruation with 75 IU of gonadotropins if the patient's body mass index (BMI) < 25 kg/m² and 150 IU if the patient's BMI ≥ 25 kg/m² with daily injections. Stimulation of the cycles was monitored by serum estradiol (E₂) level and transvaginal sonography and gonadotropin doses were adjusted individually. Human chorionic gonadotropin (hCG, 10,000IU) (Profasi, Serono) was given on the day which one or more follicles of ≥16mm diameter. The indications for cycle cancellation were: decreasing estradiol levels, more than four follicles of ≥16 mm on the day of HCG. A single insemination per cycle was performed after the 36 h of HCG administration.

Serum samples were obtained 7 days after hCG administration for progesterone levels and 14 days after hCG administration for progesterone and β hCG levels. Clinical pregnancy was shown by transvaginal USG 6 weeks after the IUI.

Results: With regard to the ovarian cycle parameters; there was no significant difference in terms of stimulation day. FSH dose consumed per cycle was significantly low in the rFSH group than uFSH and HMG groups (825 IU in follitropin-alpha, 1107 IU in uFSH and 1197 IU in HMG groups; p< 0.05). The number of follicles ≥ 16 mm diameter was significantly high in follitropin-alpha group with respect to the uFSH and HMG groups (2.6 in follitropin-alpha, 1.4 in uFSH and 1.6 in HMG groups; p< 0.05) and harmoniously E₂ concentration on the day of HCG was significantly high (644 pg/ml in follitropin-alpha, 395 pg/ml in uFSH and 455 pg/ml in HMG groups; p< 0.05). There was no difference between the groups with respect to the endometrial thickness on the HCG day.

With regard to the clinical pregnancy rates per cycle there was significant difference among the groups (25.9% in follitropin-alpha, 13.8% in uFSH and 12.5% in HMG groups; p < 0.05).

Conclusion: In this study, rFSH had a higher potency than uFSH and HMG in COH-IUI cycles with unexplained infertility.

O-179 Timing ovulation for intrauterine insemination with a GnRH antagonist increases pregnancy rates

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Introduction: The purpose of this study was to determine whether including a gonadotropin-releasing hormone antagonist in the controlled ovarian hyperstimulation intrauterine insemination (COH-IUI) cycles would increase pregnancy rates.

Material & Methods: A prospective, multicenter, randomised study was done. Patients were recruited following the guidelines set by the Spanish Committee of Assisted Reproductive Techniques and in accordance with the Helsinki Declaration of 1975 on human research. Women between 19 and 38 years old with primary or secondary infertility participated in this prospective randomized study. Polycystic ovary syndrome was excluded. 82 patients were randomly assigned to a controlled ovarian stimulation consisting of recombinant FSH + the GnRH antagonist (Ganirelix Acetate) initiated when the recruited follicles were ≥ 16mm (n=40) or rFSH alone (n=42). Ovulation was induced with HCG 5,000 IU/i.m. A single insemination was performed, 36-38 hours post-HCG, in both groups.

Results: One cycle was cancelled in each group due to excessive ovarian response (>4 follicles ≥ 16 mm). An increase in the total amount of rFSH was seen in the GnRH antagonist group (707±240 units) with respect to the control group (657±194 units). The number of mature follicles (≥ 16 mm) was significantly higher in patients treated with GnRH antagonist than in the control group (2.4±1.4 vs. 1.7±1.2, p<0.05). Pregnancy rates were significantly higher in the group of patients receiving the GnRH antagonist (38%) than in the control group (14%). The only none-single pregnancy (triplet) occurred in the antagonist group.

Conclusions: The addition of the GnRH antagonist to the controlled ovarian hyperstimulation protocol for intrauterine insemination cycles significantly increases pregnancy rates. Since this increase seems to be related with an increase in the number of follicles recruited, the risk for multiple gestations needs to be carefully evaluated.

O-180 Sperm-washing and intrauterine insemination in HIV positive men: are there any predictors of outcome?

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Introduction: We have treated HIV positive men with "sperm-washing" as part of a risk reduction program since 1999 and have performed the largest series of intrauterine inseminations (IUI) in such men in the UK. Previous studies have suggested that maternal age, stimulation regime and sperm parameters (particularly total motile count inseminated, TMC) can affect IUI outcome. The study aimed to analyse factors that may influence the outcome of IUI following sperm-washing in HIV-positive men for the first time.

Materials and methods: Seven (5%) of the 140 cycles commenced were cancelled due to a positive nucleic acid-based sequence amplification (NASBA) test for viral RNA following sperm washing. The remaining 133 cycles proceeded to insemination and we assessed the effect of age, stimulation regime, sperm parameters, markers of HIV-disease and the use of antiretrovirals on outcome.

Results: Pregnancy rates per insemination of 31.2%, 20.0%, 15.7% and 10.5% were achieved for maternal ages of <30, 30-34, 35-39 and >40 years (y) respectively. No significant difference in IUI outcome was seen according to paternal age (≥ 40y vs. <40y), stimulation regime (natural vs. stimulated), number of follicles (1 vs. >1), or time (≥ 8y vs. <8y) since HIV diagnosis (Fisher's exact test, all p>0.1). Similarly, no significant difference in outcome was demonstrated by pre-preparation sperm motility (≥ 50% vs. <50% and >70% vs. ≤ 70%) or pre-preparation sperm morphology (>70% vs. ≤ 70% and ≥ 85% vs. <85% abnormal: all p>0.10). Although a pre-preparation total sperm count had an effect of borderline statistical significance on IUI outcome (>100million vs. < 100million: p=0.10), there was no difference in outcome seen according to post-preparation TMC inseminated (<5million vs. >5million and >1million vs. <1million: p>0.1). The only factors that

significantly affected IUI outcome were viral load (VL) of the HIV-positive men and use of antiretrovirals, with a significantly higher IUI success in men with a VL <1000copies/ml (29.2% vs. 11.4%: $p=0.04$) and on treatment (27.4% vs. 9.1%: $p=0.02$). CD4 count did not significantly affect outcome ($>200\text{cells}/\text{mm}^3$ vs. $<200\text{cells}/\text{mm}^3$: $p=0.71$).

Conclusion: Undetectable viral load and the use of antiretrovirals improve the outcome of IUI/sperm-washing in HIV-positive men. Sperm parameters, after suitable choice of patient appear to have little impact on success.

FREE COMMUNICATION

Session 44 – Reproductive Surgery

Monday 28 June 2004

17:00–18:00

O-181 Robotic tubal reversal in a training program

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Introduction: Microsurgical tubal reversal of surgical sterilization is traditionally performed through a laparotomy incision; however, the decreases in morbidity and hospitalization associated with laparoscopy have led reproductive surgeons to explore minimally invasive techniques.

The laparoscopic approach has been hindered by the formidable learning curve associated with precise intracorporeal suturing. Robotic technology may bridge the gap by facilitating laparoscopic microsuturing, providing three-dimensional vision, and the fine motor precision of a wristed instrument. The objective of our study was to evaluate the feasibility of developing robotically assisted microsurgical tubal reanastomosis training in a reproductive endocrinology and infertility fellowship program.

Material and methods: We prospectively followed women who desired reversal of surgical sterilization. Our computer assisted surgical assistant was the daVinci surgical system (Intuitive Surgical, Sunnyvale, CA). From February 2003 until January 2004, one faculty mentor and the training fellow performed all robotic assisted procedures. Sixteen patients underwent an outpatient robotically assisted laparoscopic microsurgical tubal reanastomosis. After induction of general anesthesia, and port placement, the occluded segments were opened. The mesosalpinx was reapproximated with interrupted 6-0 delayed absorbable sutures. The mucosal and muscular layers of the tubal segments were sutured with four interrupted 7-0 PDS (Polydioxanone) sutures. The serosa was closed separately with interrupted 7-0 PDS suture and patency was determined by chromotubation. Main outcome measures included operative times, hospitalization, complications, postoperative patency and clinical outcomes.

Results: Of the 16 patients, the mean age was 33.1 years (range 27-38), and the average body mass index was $31.3\text{ kg}/\text{m}^2$ (range 20.8-39.8). Thirteen patients previously underwent a postpartum tubal ligation and three patients had laparoscopic placement of silastic bands. The average time from sterilization to reversal was 8.43 years (range 3-18). Fourteen patients underwent bilateral tubal reanastomoses and two had unilateral tubal reanastomoses. One patient had bleeding from a superficial epigastric vessel that was ligated with cautery. There were no other complications. The mean operative time was 201 minutes (range 140-263); mean time of cases #12-16 was 177.2 minutes (range 147-220). All patients were discharged to home within four hours after completion of the operation. Post-surgical tubal lengths on the right side were 5.8 centimeters (range 3.5-8) and the left side were 5.5 centimeters (range 4-8). In all patients, patency was established in at least one tube by hysterosalpingogram or subsequent pregnancy. The mean follow-up time was 7.9 months (range 0.25-11), and the pregnancy rate was 62.5% ($n=10$); 5 confirmed intrauterine pregnancies, 4 ectopic pregnancies, and 1 preclinical spontaneous pregnancy loss.

Conclusions: Robotically assisted laparoscopic microsurgical tubal reanastomosis is feasible in a fellowship training program. The high patency rates provide optimism. Whether robotically assisted laparoscopic microsurgi-

cal tubal reanastomosis provides success rates comparable to the standard technique in a training environment remains to be definitively established.

O-182 Unilateral ovarian diathermy is effective and longlasting in restoring spontaneous ovulation

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Background: As bilateral laparoscopic ovarian diathermy has replaced wedge resection of the ovaries, we have undertaken a prospective study to compare the efficacy and duration of unilateral (UOD) and bilateral (BOD) ovarian diathermy in the management of anovulatory infertility in women with Clomiphene Citrate resistant PCOS.

Methods: We have evaluated the clinical and hormonal response in 20 women aged 20 to 38 years with PCOS who consistently failed to ovulate with Clomiphene Citrate (CC) randomly allocated for unilateral or bilateral ovarian diathermy. Recall follow up took place once between 18 and 48 months after laparoscopic ovarian diathermy (LOD) for clinical review and early follicular phase hormonal tests and scan.

Results: Of ten patients who underwent UOD, seven clinical pregnancies were achieved in five women. Of the ten patients who underwent BOD, seven clinical pregnancies were achieved in six women. Postoperative endocrine profiles showed a statistically significant decrease in serum T, the downward trends in other hormone levels not being statistically significant in the UOD group. By contrast, in the BOD group, a statistically significant decrease in serum LH, A4, E₂ and inhibin B levels was seen.

Conclusion: UOD is as effective and long lasting as BOD in infertile women with PCOS resistant to Clomiphene Citrate in the relation to resumption of menstruation and pregnancy.

O-183 Preemptive subdiaphragmatic analgesia is not effective in gynecologic laparoscopies –prospective randomized double-blind study

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Introduction: Postoperative shoulder pain is a common postoperative sequel. Preemptive subdiaphragmatic analgesia was shown in some studies to reduce shoulder pain. Instillation of the analgesic at the beginning of laparoscopy may further ease pain due to inhibition of “neurogenic inflammation” and hypersensitivity reduction of posterior horns of the spinal cord. This study was designed to test the hypothesis that: (i) subdiaphragmatic instillation of local analgesic is efficacious in treatment of postoperative shoulder pain and (ii) application of analgesic at the beginning of laparoscopy is more effective.

Materials and methods: One hundred forty five infertile women (33.4 ± 1.7 yrs of age; mean duration of infertility 2.4 ± 0.6 yrs) with no cardio-respiratory problems, undergoing gynecologic laparoscopy were randomized to four treatment groups. Chronic pelvic pain, endometriosis stage III/IV, and allergy to medications were excluded. Patients and the operating surgeon were blinded to treatment solution. Patients received saline solution (15 ml) or bupivacaine (0.5%; 15ml), at (i) the beginning or (ii) the end of laparoscopy. Solutions were instilled under the direct vision to the right subdiaphragmatic area. Anesthesia was performed according to standard protocol. Pain was assessed with visual analog pain scale (VAPS) at 1, 4, 8, 24, and 48 hours postoperatively in the shoulder region. Mean durations of laparoscopies were not different in the studied groups. Statistical analysis was performed using Kruskal-Wallis ANOVA on ranks or ANOVA, with post hoc comparisons, as appropriate.

Results: Overall incidence of shoulder pain was at the level of 78%, with no significant differences between treatment and control groups. There was no significant difference in mean VAPS when placebo and bupivacaine groups were compared, at all study intervals. Significantly increased mean values of VAPS were observed at 24 hour interval for all four treatment groups. Also the timing of treatment application had no significant effect on mean values of VAPS in the studied groups.