

Results: The serum LH and FSH level increased rapidly after injection of first GnRHa. The FSH level reached peak (27.53 ± 6.34 IU/l) in 5 h while LH level reached peak (34.35 ± 7.18 IU/l) in 4 h. The flare of gonadotrophins persisted even after second and third day injection of GnRHa, although the peak levels were not as high as first injection (19.56 ± 3.74 IU/l in second day, 9.15 ± 1.29 IU/l in third day for FSH; 32.18 ± 8.12 IU/l in second day, 13.59 ± 1.04 IU/l in third day for LH). The down-regulation of gonadotrophin was established in 4 days. The oestradiol level increased for 3 days then decreased. When GnRHa was given for 7 days, the gonadotrophin levels began to rise 6 days after last injection; when given for 3 days, the gonadotrophin levels began to rise 3 days after last injection.

Conclusion: Even with ultra-low dose of GnRHa, the down-regulation of gonadotrophin could be achieved. The flare-up of gonadotrophin would persist for 3 days with this dose. The duration of down-regulation was influenced by the duration of GnRHa administration. In conclusion, 5 µg of triptorelin may be used as an ovarian stimulation protocol with adjustment of duration of administration.

10.15–10.30

O-111. A prospective randomized study comparing the use of HMG versus rec-FSH with the single dose GnRH antagonist (Cetrorelix) protocol in IVF–embryo transfer

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Introduction: This multicentric randomized prospective study was designed to compare in ovarian stimulation and in-vitro fertilization (IVF)–embryo transfer the use of human menopausal gonadotrophin (HMG) and recombinant follicle stimulating hormone (rec-FSH) in the single dose gonadotrophin releasing hormone (GnRH) antagonist (Cetrorelix) protocol.

Materials and methods: Sixty-two infertile patients between 23 and 39 years old, with normal menstrual cycle and no more than three previous IVF attempts, were included in the study. The single dose of 3 mg Cetrorelix was injected in the late follicular phase. HMG ($n = 31$) or rec-FSH ($n = 31$) were randomly attributed and started on cycle day 2 with 2 ampoules per day. Monitoring of the cycles was done with daily oestradiol and luteinizing hormone and ultrasounds.

Results: The IVF–embryo transfer results (mean values) are presented in Table I.

Conclusion: The majority of the studies published so far with GnRH antagonists have been performed using HMG for ovarian stimulation. In this study we compared, in the single dose antagonist administration protocol, the IVF–embryo trans-

fer results obtained with HMG and rec-FSH. No differences were observed in the two groups of patients.

Table I.

OR	Stimulation days	Ampoules	Oestradiol at HCG (pg/ml)	Oocytes total		Oocytes matured		Fertilization rate (%)		Embryos total	Embryos transferred	
				IVF	ICSI	IVF	ICSI	IVF	ICSI			
HMG	30	8.8	21	1241	8.3	10.3	7.0	7.0	69	69	5.3	2.4
rec-FSH	30	9.3	24	1541	8.8	11.7	7.1	7.8	57	56	5.3	2.7

No significant differences were observed between the two groups. OR = oocytes retrieved.

10.30–10.45

O-112. An open, randomized, group-comparative bi-centre study comparing recombinant FSH Follitropinum β 150 IU and highly purified urinary FSH 225 IU as a fixed dose regimen in IVF/ICSI treatment

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Introduction: The objective of the study was to assess the efficacy and efficiency of a fixed daily dose of recombinant follicle stimulating hormone, Follitropinum β (rFSH; 150 IU, 3 ampoules of 50 IU; Puregon®, NV Organon) and highly purified urinary FSH (uFSH HP; 225 IU, 3 ampoules of 75 IU; Metrodin HP®; Ares-Serono SA) in a fixed daily dose regimen in in-vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) patients based upon the assumption that the bioactivity of 50 IU of rFSH is in the range of the bioactivity of 75 IU of FSH HP.

Materials and methods: A total of 148 subjects were included in an open, randomized, group-comparative, bi-centre study. All women were between 18–39 years of age (rFSH mean 31.8 ± 3.6 and FSH HP 31.9 ± 3.4), had regular cycles and a BMI between 18–29 kg/m². Male factor infertility was not excluded. Prior to the start of FSH treatment the patients have been treated by a gonadotrophin releasing hormone agonist (s.c.) in a long down-regulation protocol. Stimulation with FSH was done in a fixed dose regimen of rFSH 150 IU or FSH HP 225 IU. Criterion for human chorionic gonadotrophin administration (5000 or 10 000 IU) was the presence of 2–3 follicles ≥ 17 mm according to hospital routine. All statistical analyses were done on an intent-to-treat basis using analysis of variance and testing for group differences adjusting for centres.

Results: Patients were comparable with respect to mean age, mean body mass index and duration and cause of infertility. A total of 165 cycles have been performed; rFSH: 89, FSH HP: 76. The incidence of cycle cancellations (42; rFSH: 19, FSH HP: 23) was comparable between the two treatment groups. The treatment outcome (mean adjusted for centre \pm

SD) showed no significant differences between the groups, e.g. treatment days: rFSH, 11.2 ± 2.3 ; FSH HP, 11.0 ± 1.8 ; no. of ampoules used: 33.0 ± 6.5 , 32.6 ± 5.4 ; oocytes retrieved: 9.1 ± 5.1 , 11.9 ± 7.3 ; mature oocytes: 7.7 ± 4.3 , 10.0 ± 6.5 ; embryos obtained: 5.6 ± 3.3 , 7.3 ± 5.3 ; type I/II embryos obtained: 5.4 ± 3.5 , 7.1 ± 5.4 ; embryos replaced: 2.0 ± 0.4 , 2.0 ± 0.5 ; pregnancy rate/started cycle: 23/80 (28.8%), 16/72 (22.2%); pregnancy rate/transfer: 23/70 (32.9%), 16/53 (30.2%); incidence of ovarian hyperstimulation syndrome: 3/85 (3.5%), 3/68 (4.4%) respectively. The dosage of FSH activity based upon the no. of ampoules used was 1650 IU (± 421 IU) rFSH and 2445 IU (± 477 IU) FSH HP. This difference is highly significant ($P < 0.0001$).

Conclusion: The clinical efficacy of the rFSH 150 IU equals the efficacy of FSH HP 225 IU. These results suggest that 1 IU of rFSH is not identical to 1 IU FSH HP as shown by the significant reduction of the total dosage per cycle of 795 IU in the rFSH group. With the introduction of recombinant hormones such as Follitropinum β , the classical standardization of 1 IU has become questionable.

10.45–11.00

O-113. Cessation of gonadotrophin-releasing hormone analogue (GnRHa) upon down-regulation versus conventional long GnRHa protocol in poor responders undergoing in-vitro fertilization

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Introduction: Our objective was to determine whether an ovarian stimulation regimen which involves gonadotrophin-releasing hormone analogue (GnRHa) discontinuation prior to administration of gonadotrophins would benefit poor responders to a conventional continuous down-regulation ovarian stimulation protocol.

Material and methods: Sixty-three patients with either previous poor response to ovarian stimulation and/or high basal follicle stimulation hormone (FSH) level (≥ 9 mIU/ml) undergoing 78 in-vitro fertilization (IVF)-embryo transfer cycles were randomly assigned to two groups. In all patients ovarian down-regulation by administration of GnRHa started in mid-luteal phase. Whereas in the study group (40 cycles) it ended before administration of gonadotropins (interrupted regimen), in controls (38 cycles) GnRHa treatment was continued throughout the follicular phase.

Results: Significantly higher cancellation rate was noted in the interrupted regimen group compared to controls (22.5% versus 5%, respectively; $P < 0.05$). Both interrupted and control regimens resulted in similar stimulation characteristics, and clinical pregnancy rates per embryo transfer (11% versus 10.3%, respectively, $P =$ non-significant). In 13 patients with basal follicle stimulating hormone (FSH) that was not persistently high, the interrupted regimen resulted in significantly

higher number of retrieved oocytes compared to standard 'long' protocol (7.6 ± 1.03 versus 4.0 ± 0.68 , respectively, $P < 0.05$).

Conclusions: Whereas for most low responders cessation of GnRHa treatment upon down-regulation offers no further advantage, by meticulous individualization of its application it may confer a benefit for a subset of patients with adequate ovarian reserve as evidenced by basal FSH level that is not persistently high.

11.00–11.15

O-114. Recombinant gonadotrophins: is there a difference in the tolerability of these products?

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Introduction: Since recombinant gonadotrophins are highly purified ($>99.9\%$) and can be administered subcutaneously, local tolerance to injections should be similar between the two available products: Gonal-F[®] and Puregon[®]. However, anecdotal reports at the time suggested that Puregon was less well tolerated by patients compared to Gonal-F. This study was designed to confirm or refute these reports.

Materials and methods: A total of 39 patients who had up to two previous cycles of in-vitro fertilization (IVF) were randomized into the study: Gonal-F 20 patients and Puregon 19 patients. Following long down-regulation (600 μ g intranasal nafarelin from day 21) 150 IU per day gonadotrophin was administered (2 ampoules of 75 IU Gonal-F or 1 ampoule each of 50 IU and 100 IU Puregon). Patients or their partners were shown how to administer their injections. Tolerability (pain, burning, itching redness and bruising) to each injection was recorded on a diary card. Ovarian response was assessed by ultrasound monitoring and human chorionic gonadotrophin (10 000 IU) was given with at least one follicle ≥ 20 mm and two others >16 mm

Results: Local reactions were compared between treatments from day 2 until the end of cycle. Two patients in the Gonal-F group did not return their diary cards, therefore data are presented on 18 patients. The day 1 injection was excluded from the analysis to remove any learning curve from the injection procedure. Interim data are shown and complete data will be presented with statistical comparisons. In the Gonal-F group the proportion of the treatment cycle which was symptom-free (all symptoms) was 40.7% compared to 8.8% for Puregon patients. Data also suggest that a greater proportion of injections led to moderate or severe reactions with Puregon than Gonal-F (Table I), most clearly demonstrated for pain and burning. Also, more patients in the Puregon group reported reactions with a maximum severity of moderate or severe than Gonal-F patients, with pain and burning being the most common (Table II).