P-274

Optimizing GnRH antagonist administration: A meta-analaysis of fixed vs flexible protocol. H. G. Al-Inany Jr., H. G. Al-Inany Jr., M. A. Aboulghar Sr., R. T. Mansour Sr., G. Serour Sr. Cairo University, Cairo, Egypt; Egyptian IVF-ET CENTER, Cairo, Egypt; Egyptian IVF-ET CENTER, Maadi, Cairo, Egypt.

OBJECTIVE: The most commonly used method for administration of the antagonist is on a daily dose of 0.25 mg starting on a fixed day (day 6 of gonadotrophin stimulation). As there are individual variations in patient response to ovarian stimulation, then a starting GnRH antagonist according to follicular size (flexible protocol) could be of value. The aim is to investigate whether flexible GnRH antagonist administration according to follicular size would be more beneficial than starting it in a fixed day.

DESIGN: Meta-analysis of randomized controlled trials

MATERIALS AND METHODS: A comprehensive search strategy was applied including searching Cochrane Menstrual Disorders and Subfertility Review Group specialized register, MEDLINE and EMBASE databases, Hand searching the reference lists of included studies, review and relevant textbooks and abstracts of major international meetings. Only randomised controlled trials in which subfertile couples undergoing ovulation induction using GnRH antagonist as part of an assisted reproductive cycle were included. The data combined for meta-analysis with RevMan software (using the Mantel-Haenszel method). **Outcomes:** Primary outcomes included pregnancy rate (per woman or per couple) and incidence of premature LH surge. Secondary outcomes included number of oocytes retrieved, amount of antagonist ampoules used, amount of gonadotrophins needed

RESULTS: Seven trials were identified (Ludwig et al, 2001, Mansour et al, 2002, Othman et al, 2003, Klipesten et al, 2003, Mochtaret al, 2003 and Escudero et al, 2004.) Only three RCT met out inclusion criteria (Ludwig et al, 2001, Mochtar et al, 2003 and Escudero et al, 2004) enrolling 373 participants. There was no statistically significant difference in pregnancy rate per woman randomized O.R 0.7 (95% CI 0.45–1.1). There was no premature LH surge in any participants in both protocols. However, there was statistically significant reduction both in number of antagonist ampoules and amount of gonadotrophins used in the flexible protocol (O.R -1.2 95% CI -1.26–-1.15). There was a trend to an increase in the number of oocytes retrieved with the flexible protocol (OR 1.28 95% CI 0.9–1.6).

CONCLUSION: The flexible protocol yields similar pregnancy rate as the fixed protocol but is more cost effective. However, further studies with large sample size and adequate power are needed.

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P-275

The thromboembolic disease (TED) during assisted reproductive technology (ART). Results of a french survey. R. Wainer, N. Trillot, J. Ninet, C. Lefebvre, P. Edelman, Club de Perifoetologic. Poissy Saint Germain Hospital, Poissy, France; Jeanne de Flandre CHU, Lille, France; Edouard Herriot CHU, Lyon, France; Club de Perifoetologic, Paris, France.

OBJECTIVE: The TED during ART are rare but serious complications occuring in young and healthy women involved in ART. The characteristics of these TED are unclear because the single publications are isolated "cases reports". The objective of this survey was to gather about fifty TED post-ART occured in France and to analyse their background and their issue.

DESIGN: Retrospective study.

MATERIALS AND METHODS: 45 TED after IVF or ICSI were gathered from 13 french ART centres from 1987 to 2003. We made inquiries about every case of these TED.

RESULTS: 1) Population: The mean age of the patients is 31.19 ± 3.67 years (from 25 to 41 years). The mean Body Mass Index is 22.68 ± 4.01 (from 16 to 34). Primary infertility represents 78% of the cases. 2) Criteria of these ART: The ranges n°1 and n°2 of ART represent 79% of the cases. The mean dose administered of gonadotropin is 2,297 ± 947 iu. The mean level of estradiol on DHCG is 2,698 ± 2,872 pg/ml. The mean number of oocytes picked up is 13.9 ± 7.3. A pregnancy occurs in 93% of the cases (70% of single pregnancy and 30% of multiple pregnancy). An Ovarian Hyperstimulation Syndrome (OHSS) occurs in 81% of the cases (mild 31%, moderate 45%, severe 24%). 3) Delay between HCG injection and TED: Table 1 4)Site of TED: venous thrombosis 82% and arterial thrombosis 18%. 10 pulmonary embolisms (1 fatal). 29 TED of the upper part of the body: internal jugular or subclavian (13), intracerebral (9), upper limb (6), coronary (1). 8 TED of the lower limb.

CONCLUSION: This study gathers the larger series of TED post ART ever published. The patients who present these TED are" good responders". 90% of these women begin a pregnancy during this treatment. 80% of these women present an ovarian hyperstimulation syndrome (OHSS) and the TED occurs during the 45 days following HCG injection. 80% of the TED are localized in the upper part of the body.

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<= 15 days	16 to 45 days	46 to 90 days	> 90 days
13	20	8	2
30.2%	46.5%	18.6%	4.6%

P-276

Comparing the effects of fixed (day 6 Start) and flexible start of GnRH antagonist on endometrial receptivity in PCOS. O. Taskin, G. Akkoyunlu, M. Akar, M. Simsek, R. Demir, S. Sadik. Akdeniz University School of Medicine, Antalya, Turkey; SSK Tepecik, Izmir, Turkey.

OBJECTIVE: To compare the effects of two GnRH antagonist protocols (Fixed and flexible) on endometrial receptivity using immunohistochemical criteria of epithelial integrin expression in PCOS patients.

DESIGN: Prospective randomized clinical study.

MATERIALS AND METHODS: Infertile PCOS women who were randomized to fixed (started on day 6, n:6), and flexible (started when the leading follicle >15 mm, n:5) regimens of GnRH antagonist (cetrorelix 0.25). All received rFSH (follitropin beta) 150 IU starting on menstrual day 2. Endometrial biopsy was obtained 3 days after oocyte retrieval. Immunohistochemical staining intensity and distribution (HSCORE) of $\alpha v\beta 3$ subunit integrins and traditional histologic endometrial dating were compared.

RESULTS: There were no significant differences among the groups with respect to baseline characteristics. Although both protocols produced better folliculogenesis, the changes in endometrial receptivity as determined by integrin positivity and HSCORE were better in the fixed protocol (integrin positivity 5 vs 3 respectively). The androgen levels and progesterone on HCG day and later were greater in the flexible protocol. Nine of the 11 endometrial samples were in-phase histologically, distributed similarly through the 2 patient groups (all advance 1–2 days). Integrin $\alpha v\beta 3$ expression was not predicted by in-phase histology, with integrin staining low in all three groups ($p< 0.32$). Just as, presence of integrin was not associated with in-phase histology, neither was intensity of integrin staining as measured by the mean HSCORE ($p < 0.73$).

CONCLUSION: Although both protocols were similar in follicular recruitment in PCOS, endometrial receptivity and luteal hormonal mileu were not similarly enhanced, and could explain the observation of reduced implantation or high miscarriage rates in PCOS patients who conceive. However, early start of GnRH antagonists may be preferable for optimal endometrial maturation in PCOS since it may suppress high LH levels and lead more favourable hormonal mileu for optimal endometrial receptivity compared to late start. Current studies are underway to further evaluate the role of endometrial receptivity in PCOS patients undergoing GnRH antagonists.

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P-277

Reproductive performance in second IVF cycles treated with the use of either GnRH anatgonists (-antag) vs GnRH agonists (-ag) after failure with long protocols with GnRH agonists: a prospective randomized trial. R. Inza, G. Van Thillo, E. Lombardi, C. Bisioli, M. Diradourian, A. Kenny. Instituto de Ginecología y Fertlidad (IFER), Buenos Aires, Argentina.

OBJECTIVE: To compare reproductive performance and pregnancy rates in patients undergoing their second COH-IVF cycle; with either the use of GnRH-antag or GnRH-ag, after having failed getting pregnant in their first IVF-ET attempt using a GnRH agonist long protocol.

DESIGN: Prospective randomized study.

MATERIALS AND METHODS: 45 patients who have failed a first IVF