

## INTRAUTERINE INSEMINATION IN MILDLY STIMULATED CYCLES

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### **Unexplained infertility**

Is diagnosed in 20% of the couples after the initial diagnostic workup. This number grows with the inclusion of couples with mild male infertility. This figure indicates that the clinical evaluation of infertility must be greatly improved and in particular that there is an urgent need of clinical tests looking at the quality of the oocyte and at the fertilizing ability of the semen. Due to these limitations, today there is a wide use of empirical treatments, in particular, intrauterine insemination (IUI).

It is well known that IUI carried out during natural menstrual cycles is associated with low pregnancy rates, this is why most of the clinics use IUI in controlled ovarian hyperstimulated (COH) cycles.

### **Intrauterine insemination in COH cycles**

According to the largest available clinical studies, IUI in cycles stimulated with conventional doses of gonadotropins induces a pregnancy in 10-15% of cases, with better results in couples with normal semen. Unfortunately about 15-20% of the achieved pregnancies were twins and 5-10% triplets or more. Since the reduction of iatrogenic multiple pregnancies is considered today the most important priority to prevent neonatal cerebral palsy, IUI in stimulated cycles has been marked as an unsafe technique and an appropriate trial for the use of uni- or bifollicular stimulated IUI cycles was called for.

### **Milder ovarian stimulation for IUI cycles**

Protocols of mild ovarian hyperstimulation are currently gaining consent, the effectiveness, safety profile and the best pharmacological and monitoring protocols of this approach remain however to be fully clarified. In particular a debated issue in this context is related to the usefulness of gonadotropin-releasing hormone (GnRH) antagonists. This drug may be of benefit since it has been demonstrated that it effectively prevents premature LH surge and theoretically, this may consent to more properly time the insemination thus increasing the chances of pregnancy. The role of GnRH antagonist in COH-IUI cycles has been previously investigated in randomised studies but results are conflicting.

### **The multicentric trial**

A large randomised trial was organized with the aim to clarify the role of the GnRH antagonist in mildly stimulated IUI cycles. 290 couples with unexplained infertility were received in 11 centres. Women allocated to the GnRH antagonist group received 50 IU recombinant FSH starting on day 3 of the menstrual cycle and Ganirelix 0.25 mg daily starting the day in which a follicle with a mean diameter of 13-14 mm was visualized at ultrasound. Women allocated to the control group were administered only 50 IU recombinant FSH starting on day 3 of the menstrual cycle. Clinical pregnancy rates per initiated cycle in women who did and did not receive GnRH antagonists were 12.2% and 12.6%, respectively. The relative risk of conception (95% Confidence Interval) for the use of GnRH antagonists was 1.0 (0.7-1.4). According to the results of the trial in mild controlled ovarian hyperstimulation and intrauterine insemination cycles, the use of GnRH antagonists does not improve the pregnancy rate.

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