

## **POOR OVARIAN RESPONDERS' BEST THERAPEUTIC OPTIONS: A CENTER'S EXPERIENCE**

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**Objective:** The aim of this study was to identify the IVF (in vitro fertilization) protocol(s) giving the best live-birth rate (LBR) for poor ovarian responders (POR) according to Bologna criteria.

**Design:** Retrospective study

**Setting:** Public hospital

**Patient(s):** 255 POR undergoing 306 fresh IVF/ICSI cycles between January 1<sup>st</sup>, 2011 and December 31<sup>st</sup>, 2013.

**Intervention(s):** GnRH agonist, antagonist and natural protocols were analyzed. The stimulation drug used in the GnRH agonist protocol was FSH (follicle stimulating hormone) alone. For the GnRH antagonist protocol, it consisted in a choice of three different regimens: (i) FSH alone, (ii) FSH and LH (luteinizing hormone) or (iii) FSH and GH (growth hormone), while natural protocol involved no treatment or Letrozole alone.

**Main Outcome Measure(s):** The primary outcome was the live birth rate (LBR) and the secondary outcomes were the number of oocytes collected, the number of usable embryos, the embryo transfer (ET) cancellation rate and the miscarriage rate.

**Result(s):** There were 45 natural, 48 agonist and 213 antagonist cycles. Overall, their mean age was 39.9 years (SD=3.5). The three groups had comparable demographics and clinical characteristics. Their LBR was significantly different with the natural cycle having the highest (respectively 26.7% and 11.4% vs 5.7%,  $p=0.017$ ). However, after adjustment for age and the number of years of infertility, only the LBR of the agonist protocol remained significantly higher than the antagonist while no significant difference was found between the LBR of the natural and antagonist protocol (respective adjusted OR=3.38; 95% CI 1.01 to 11.29;  $p=0.048$  and 3.02; 95% CI: 0.83 to 10.98;  $p=0.094$ ). When the treatment cycles were analyzed in sub-groups according to the type of stimulation received, the natural and agonist cycle with FSH showed significantly higher LBR than antagonist cycle (respective adjusted OR=11.44; 95% CI 1.14 to 114.46;  $p=0.038$  and 12.81; 95% CI: 1.34 to 122.15;  $p=0.027$ ). The antagonist group using FSH and LH achieved a reasonable LBR of 11.3% even though it didn't reach the level of significance when compared to FSH alone or FSH and GH with respective LBR of 1.8% and 2.6% ( $p=0.062$ ).

The number of oocytes collected in the agonist group was two times higher than in the antagonist group (9.8 (SD=6.7) vs 4.7 (SD=4.9),  $p<0.001$ ). Due to its non-stimulated nature, a lower number of eggs were collected from the natural cycle (0.6, (SD=0.7)) with a higher proportion of cancelled ET procedures (61.5% vs 21.1% and 6.4% in the natural, antagonist and agonist groups respectively,  $p<0.001$ ). No miscarriage was observed in the natural cycles while it was relatively high in the antagonist and agonist group (59.1% and 37.5% respectively,  $p=0.112$ ).

**Conclusion(s):** GnRH agonist protocol with high doses of FSH seems to be good first line therapy for POR. If the oocyte yield is low, natural cycle can be considered as a second therapeutic option, cost-effective and patient-friendly. However, patients should be aware that repeated cycle attempts are often required before achieving an ET in the latter. A randomized controlled trial is needed to confirm this.