

P99. GLP-1 Receptor Agonist Liraglutide increased IVF Pregnancy Rates in Obese Women with PCOS and previous poor response to first line reproductive treatments:: a Pilot Randomized Study

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Objective: GLP-1 has been investigated in regulation of reproductive system in animal models. Current observations suggest that it directly regulates kisspeptin and GnRH expression and that ovaries express GLP-1 mRNA. In obese PCOS, GLP-1 receptor agonist liraglutide provided positive effects on weight reduction and glucose homeostasis.

Aim: to evaluate the impact of low dose liraglutide in combination with metformin compared to metformin alone on IVF pregnancy rate (PR) and cumulatively PR (IVF and spontaneous) in infertile obese women with PCOS who had been previously poor responders regarding weight reduction with lifestyle modification and resistant to first line reproductive treatments.

Design/Participants/Methods: A prospective randomized open-label study was conducted with 28 infertile obese PCOS patients (aged 31,07±4,75 years, BMI 36,7±3,5 kg/m², mean ± SD). They were assigned to metformin (MET) 1000 mg BID or combined MET 1000 mg BID and low dose liraglutide 1.2 mg QD s.c. (COMBI) for 12 weeks. Ovarian stimulation protocol was started after 4-week medication free period. IVF PR was defined as number of clinical pregnancies confirmed with ultrasound visualization of a gestational sac, divided by the total number of cycles performed or embryo transfers (ET). The rate of spontaneous pregnancies was tracked for 12 months.

Results: Patients in MET lost on average 7,0±6,0 kg (P?0.001) compared with 7,5± 3,9 kg loss in COMBI group (P?0.001), with no significant between-treatment difference (P=0,103). After intervention, PR per ET was significantly higher in COMBI (85,7 %) compared with MET (28,6%) (P=0.03). Moreover, cumulatively PR in time frame of 12 months in COMBI was 69,2% (9/13) compared to 35,7% (5/14) in MET: one pregnancy occurred spontaneous immediately after the intervention in COMBI and MET, 6 pregnancies in COMBI and 2 in MET occurred with IVF and another 2 in COMBI and MET occurred spontaneously after the unsuccessful IVF. There were no between treatment differences in the dosage of stimulation, number of retrieved, mature, fertilized and degenerated oocytes, number of embryos and blastocysts at day 5.

Conclusion: Short-term preconception intervention with low dose liraglutide as an add on to metformin was superior to metformin alone in increasing PR per ET and cumulative PR in infertile obese PCOS, despite comparable weight reduction in both arms. Potential direct crosstalk between GLP-1 and reproductive system needs further exploration.

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