

Pituitary Suppression Protocol does affect clinical outcomes in egg donation cycles.

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Study question. To compare different pituitary suppression protocols in endometrial priming of egg donation cycles based on clinical outcomes and cancellation rates.

Summary answer. The use of depot GnRH agonist in midluteal phase in endometrial priming protocol is associated with better implantation rates in egg donation cycles.

What is known already?

In patients with ovarian function, it is possible that during endometrial priming for embryo transfer, occur spontaneous ovulation leading to desynchronization of implantation window. To avoid this phenomenon there are different pituitary suppression techniques as use of depot GnRH agonist or GnRH daily dose antagonist during first 5-7 days of estrogen supplement. Not administering any medication is considered a valid option if the initial dose of estrogen is maximum so suppression would be obtained by negative feedback.

Previously reported studies refer no difference in clinical outcomes using different protocols.

Study design, size, duration.

Retrospective analysis with common database from 11 private clinics of IVI group. We included 7690 women with preserved ovarian function who underwent egg donation cycle with endometrial priming for fresh embryo transfer from Jan 1st 2014 to Dec 31st 2015. Statistical analysis was performed by ANOVA and chi-square.

Participants/materials, setting, methods.

Participants received increasing dose of oral estradiol from 2 to 6 mg or transdermal estrogen 75 to 150 µg every 3 days. Subjects in the agonist group received GnRH agonist 3,75 mg in midluteal phase of previous cycle. The group with GnRH antagonist received 0,25mg daily during the first 7 days of estrogen supplementation. The third group received oral estradiol with initial dose of 6 mg. Cycles were supplemented with vaginal progesterone 400 mg twice/day.

Main results and the role of chance. Patients were distributed as follows: 47.9% (n=3684) were prepared with GnRH agonist; 35.2% (n=2706) were primed with GnRH antagonist; 16.9% (n=1300) did not receive any medication for pituitary suppression. According to analyzed clinical variables, we found statistical differences among the study groups. Data were as follows for agonist, antagonist and without suppressive therapy group respectively; age (41.1 ± 0.1 ; 41.3 ± 0.1 ; 40.8 ± 0.2 , $p < 0.001$); endometrial thickness (mm) (7.8 ± 1.5 ; 7.8 ± 1.3 ; 8.9 ± 0.3 , $p < 0.001$).

When we considered clinical outcomes, we found a significant increase in implantation rate in the agonist group (53.2%) compared with the antagonist group (50.8%) and the women without pituitary suppression (49, 2%), $p = 0.014$. Similar results were observed in pregnancy rate in favor of the agonist group (64.7%) in relation with the antagonist group (62.8%) and women without GnRH analogues (58.3%), $p = 0.001$. Finally, miscarriage rates were comparable among groups being 10.2%, 8.8% and 9.1% ($p = 0.346$) for agonist, antagonist and no analogue administration.

Concerning cancellation rate due to endometrial impairment, data were identical for the three treatments (2.0%)

Limitations. Despite the advantages that our data set confer the analysis, limitations still remain. One consequence of a retrospective study is that not all pertinent risk factors are likely to have been identified and subsequently recorded. So only association, and not causation, can be inferred from the results.

Wider implications of the findings.

In the endometrial preparation for egg donation cycles, there is a statistically significant advantage regarding clinical outcomes with the use of depot GnRH agonist for pituitary suppression when compared with antagonist protocol or no pituitary suppressive protocol.

Study finding/competing interest. None

Trial registration number. It does not apply