Can serve Medroxiprogesterone acetate (MPA) as pituitary suppressor instead of GnRH antagonist during ovarian stimulation (OS) in oocyte donation (OD) cycles trigger with GnRH agonist?

Study question:
Is ovarian response of oocytes donors when pituitary is suppressed with MPA comparable to the conventional treatment with GnRH antagonist cycles?

Summary answer:
MPA serve as pituitary suppressor during OS in OD since it does not present lower number of MII or worse reproductive outcome compared to antagonist.

What is known already:
Administering progestins orally in the follicular phase since the beginning of OS is an efficient alternative to prevent LH from peaking, related to its effect on LH pulse frequency and amplitude, with similar results to conventional protocols.

Progestins have been successfully used in normo-ovulating patients, Polycistic Ovarian Syndrome, endometriosis and low-responders.

A randomized controlled trial (RCT) in OD reported no differences with GnRH antagonist in OS parameters, mature oocytes and top quality embryos. However, pregnancy outcomes were lower.

In contrast, no differences were observed between the two groups in terms of reproductive outcomes in other recently published retrospective studies.

Study design, size, duration:
University-affiliated infertility clinic. Prospective RCT study, from October 2017 to June 2019, to evaluate ovarian response in terms of number of oocytes. We randomized 318 donors in two groups in a 1:1 ratio. A difference of ± 3 oocytes respect a mean of 21 in the reference group was considered as an equal response (NCT03300960).

Cycle outcome of the recipients were later analysed retrospectively. Oocytes obtained were assigned to 364 recipients (1910-VLC-091-JG).
Participants/materials, setting, methods:
In MPA group 161 participants received intervention (10 mg daily administered orally during OS) and 156 were treated with antagonist (started once the leading follicle reached 13 mm). Transvaginal ultrasound and serum estradiol (E2), LH, and progesterone (P) were performed during monitoring controls.

Other parameters that were analyzed: endocrine profile (in serum and follicular fluid), number of MII, pregnancy outcomes. For the latest, a questionnaire was offered to all participants after the oocyte retrieval.

Main results and the role of chance:
No significant differences were observed in donor demographic characteristics. The number of oocytes retrieved were 21.41±11.71 in the MPA group vs. 21.26±9.27 in the antagonist group (P=0.949) (Mean difference 0.14 [95%CI= -2.233, 2.517]).

The total dose of rFSH, length of OS and endocrine profile in follicular fluid in the oocyte pick-up procedure (FSH, estradiol, LH, progesterone) were comparable between groups. LH values on the day of trigger were significantly lower in study group (1.8±2.0 vs 0.9 ±1.1, p=<0.001), while no early luteinization was observed in either group.

No differences between groups were observed for implantation rate (78% vs. 73.9% p=0.441), clinical pregnancy rate (78.3% vs. 73.3, p=0.383), ongoing pregnancy rate (70.9 vs. 67%, p=0.592) and early pregnancy loss (9.7% vs. 8.0%, p=0.669). Live birth rate would be presented at the congress since there are still gestations in progress.

There is a significant difference in favor of the MPA group in questions related to ease of administration and number of injections. In donors with previous cycle with antagonists level of satisfaction has been very high / high with respect to the previous cycle in 92.74%.

Limitations, reasons for caution:
This is a non-inferiority study with number of retrieved oocytes as the primary outcome. The limitations of this RCT include that treatment could not be blinded, because of the different administration route of the medication in study. Another limitation to take into account is that oocyte recipients were not randomized.

Wider implications of the findings:
We observed comparable oocyte retrieval, endocrine profile, viable embryo numbers and similar pregnancy outcomes in the two groups. Therefore, MPA is useful for OS in OD and provides a more friendly approach.

Keywords:
oocyte donation
medroxyprogesterone acetate
progestin-primed ovarian stimulation
RCT
GnRH antagonist