Start of ovarian stimulation on day three versus luteal phase of the menstrual cycle in the same oocyte donor. A prospective observational study

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Study question:
Assess ovarian response (oocytes) after ovarian stimulation starting on day 3 or luteal phase of the menstrual cycle in the same oocyte donor.

Summary answer:
In the same oocyte donor, the ovarian response is similar when the stimulation is started on day 3 or on the luteal phase of cycle.

What is known already:
To optimize the IVF process and obtain sufficient mature oocytes, controlled ovarian hyperstimulation (COH) is needed. Usually, COH is performed from the beginning of the follicular phase on day 2 or 3 of the menstrual cycle. Current findings have described the presence of multiple waves of follicular recruitment within a single ovulatory period. There are publications describing that is possible to obtain mature oocytes starting the COH on luteal phase of cycle. This is an important tool to consider for oncologic patients who want to preserve their fertility and for the programs oocyte donors.

Study design, size, duration:
Prospective observational study on a group of 8 oocyte donors from our oocyte donation program between January 2015 and December 2015. Donors who meet the legal requirements and agreed to participate in the study were recruited. Donors were subjected to two cycles of COH, one cycle of conventional COH starting on day 3 (Classical COH) and another on luteal phase after confirming ovulation with ultrasound (Luteal COH), in a 3-5 month interval.

Participants/materials, setting, methods:
In the two cycles of stimulation, COH was performed with recombinant FSH at doses of 150-225 IU/day. Administration of GnRH antagonist was started whit a follicle measuring >14 mm. A GnRH agonist was used to trigger ovulation and oocyte retrieval was performed 36 hours later. We evaluated count of follicles >10 mm on day 5 of stimulation, follicles >15 mm and estradiol levels on day of agonist GnRH, oocytes and mature oocytes retrieved.

Main results and the role of chance:
A total of eight stimulation cycles on Classical COH and eight stimulation cycles on Luteal COH were performed on eight oocyte donors (age 23.38 ± 2.45 years) a 3-5 month interval. No statistically significant differences were found in the COH donors' responses **between the Classical COH and** Luteal COH starts. The count of follicles >10 mm on day 5 of stimulation was 9.50 ± 3.58 vs 10.13 ± 2.16, the follicles >15 mm on day agonist GnRH 17.13 ± 7.24

vs 16.63 ± 5.58, estradiol level (pg/mL) on day agonist GnRH 2,312 ± 1,081 vs 2,463 ± 954, total days of stimulation 10.25 ± 1.98 vs 10.25 ± 0.88, total doses of gonadotropin 1959.37 ± 442.38 vs 1950.00 ± 198.20, oocytes retrieved 23.00 ± 13.09 vs 19.38 ± 6.11, mature oocytes 21.50 ± 12.37 vs 17.00 ± 5.37

Limitations, reasons for caution:
The limitation of our study could be the small sample size. The study was performed on healthy young women (<35 years), so the results could not be extrapolated to other clinical conditions such as low ovarian reserve, older women, etc.

Wider implications of the findings:
The ovarian response in donors is similar when the COH start on early follicular phase or on luteal phase. These results demonstrate that the ovarian stimulation starting in the luteal phase could be useful in patients that want to preserve oocytes o preserve fertility for cancer o social reasons.