Abstract title: Retrospective analysis of DuoStim cycles shows similar overall performance and oocyte quality between follicular and luteal phase stimulation

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Study question:
Is there any difference in the overall performance of follicular and luteal phase stimulation among patients undergoing double ovarian stimulation (DuoStim)?

Summary answer:
DuoStim shows similar results with respect to the number of retrieved oocytes, fertilization and blastocyst formation rates in both the follicular and luteal phase stimulation.

What is known already:
Previous studies have demonstrated that several waves of cyclic development of antral follicles may coexist within the same menstrual cycle. Moreover, it has been shown that follicles formed during the luteal phase have a similar ovulation potential. Often, physicians are compelled to perform several stimulation cycles to obtain more eggs. Thus, the DuoStim protocol could be an attractive alternative to obtain a higher number of oocytes in a shorter period, declining the time-to-pregnancy. It also emerges as an interesting option for emergency fertility preservation in oncologic patients. However, more studies are needed to validate its feasibility.

Study design, size, duration:
Retrospective analysis of DuoStim cycles performed over the past year in IVI-RMA Global clinic, Madrid, Spain. We aimed to evaluate the potential usefulness of the DuoStim protocol by comparing oocyte quality and overall performance between follicular and luteal phase stimulation within the same menstrual cycle.

Participants/materials, setting, methods:
We included 25 women who underwent a total of 30 cycles using the DuoStim protocol in 2017 at IVI-RMA Global clinic, Madrid, Spain. Data containing baseline and demographic characteristics along with the variables of interest from both the follicular and the luteal stimulation were exported from our institutional repository software platform. Statistical analysis included ANOVA test for variables with normal distribution and Mann-Whitney U test whenever the distribution was not normal.

Main results and the role of chance:
Baseline characteristics revealed that the median values of age, AMH, AFC and IMC were 39.2 years, 1.34, 5.88 and 20.8 kg/m\(^2\), respectively. Thus, our study population was mainly composed of women with advanced age and low ovarian reserve. In fact, all patients presented with very poor reproductive prognosis and multiple IVF failures. Variables of interest presented a normal distribution, except for the blastocyst formation rate. ANOVA test demonstrated no significant differences between the follicular and luteal stimulation, respectively, regarding the median of: days of stimulation (10.53 vs. 11.83; \(p=0.077\)), amount of gonadotropin administered (2059.26 UI vs. 2603.45 UI; \(p=0.061\)), retrieved oocytes (4.83 vs. 5.17; \(p=0.737\)), MII oocytes (3.93 vs. 4.20; \(p=0.741\)) and fertilization rate (60.75% vs. 62.76%; \(p=0.830\)). Likewise, Mann-Whitney U test did not show any difference with respect to the blastocyst formation rate (20.78% vs. 26.62%; \(p=0.260\)). There was a trend to use greater amounts of gonadotropin during the luteal phase, although not statistically significant. In conclusion, the use of the DuoStim protocol exhibited encouraging results irrespective of age and ovarian reserve. Similar findings were reported by other few studies comprising patients with a distinct clinical profile. Randomized clinical trials are needed to legitimize its use in daily practice.
Limitations, reasons for caution:
Unequivocal limitations are essentially related to the retrospective design. Therefore, the study is prone to sources of error due to confounding factors. Nevertheless, considering the scarcity of prospective data in literature, our results provide important insights on the effectiveness of the DuoStim.

Wider implications of the findings:
This work contributes to confirm the efficiency of the DuoStim protocol. It may be especially convenient for oncologic patients or those with a poor reproductive prognosis pursuing infertility treatments. Not only it reduces the time to obtain a higher number of eggs, but it also attenuates the couple’s anxiety.

Trial registration number:
Not clinical trial.

Keywords:
ovarian stimulation
DuoStim
MII oocytes
ART therapies