LETTER

Triggering final follicular maturation—hCG, GnRH-agonist or both, when and to whom?

Raoul Orvieto^{1,2}

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Dear editor

We read with interest the study by O'Neill et al. [1], who retrospectively compared the rates of ovarian hyperstimulation syndrome (OHSS) after using gonadotropin-releasing hormone agonists (GnRHa) alone and GnRHa in combination with low-dose human chorionic gonadotropin (hCG, dual trigger) for final oocyte maturation in women undergoing controlled ovarian hyperstimulation (COH). In this study, they observed a significantly higher incidence of early OHSS after dual trigger than GnRHa trigger (8.6 vs 0 %), with increased number of total oocytes and percentage of mature oocytes obtained compared to GnRHa trigger alone.

While describing the methods that have been made to improve reproductive outcome following GnRH agonist trigger, they mentioned the options of low-dose hCG bolus given 35 h prior to oocyte retrieval and at the time of oocyte retrieval. Another method that was recently offered is one bolus of 1500 IU hCG 5 days after the triggering bolus of GnRHa [2–4]. Patients at risk to develop severe OHSS were re-evaluated 3 days after oocyte retrieval (on day of embryo transfer) for signs of early moderate OHSS. If no early signs of OHSS developed, one embryo was transferred, and the patients were instructed to inject 1500 IU of HCG. By deferring the hCG bolus by 3 days (5 days following GnRHa trigger), the corpus luteum was rescued, with an observed extremely high midluteal

progesterone levels [4], reasonable pregnancy rate, with no patient developing severe OHSS.

Regarding the association between high levels of E2 and the occurrence of OHSS, it is well established that the previously accepted high serum E2 levels, as a risk factor, are unreliable for the prediction of severe OHSS [5]. OHSS usually develops in patients having marked multiple follicular development, which is linked to increased E2 production and serum levels, while the hCG promotes the ovarian secretion of vasoactive substance/s causing OHSS. OHSS almost always develops after hCG or in early pregnancy and may even occur in patients who conceived spontaneously [6], and in those with low [7] or high [8] serum E2 levels on the day of hCG administration.

Regarding the role of dual or double triggers in improving oocyte yield and maturation, surprisingly, all of our recently published studies went unnoticed [2, 9–11]. In these studies, we offer standard hCG dose concomitant with GnRHa (dual trigger), 35–37 h before oocyte retrieval to normal responders patients, aiming to improve oocyte yield, number of matured oocytes, top quality, and cryopreserved embryos. GnRHa 40 h and standard hCG added 34 h prior to OPU (double trigger), respectively, are offered to two groups of patients demonstrating abnormal final follicular maturation despite normal response to COH, those with low (<50 %) number of oocytes retrieved per number of dominant follicles >14 mm in diameter on day of hCG administration [9] and those with low proportion of mature/metaphase-II (MII) oocytes (<66 %) per number oocytes retrieved [10]. Finally, standard hCG dose concomitant with GnRHa (dual trigger), 34 h before oocyte retrieval was offered to poor responders patients, aiming to improve oocyte yield, maturation, and prevent premature luteinization.

✉ Raoul Orvieto
raoul.orvieto@sheba.health.gov.il

¹ Infertility and IVF Unit, Department of Obstetrics and Gynecology, Sheba Medical Center, Ramat Gan, Israel

² Sackler Faculty of Medicine, Aviv University, Tel Aviv, Israel

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