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P-634 Safety of ART cycles with extremely high estradiol levels - A retrospective cohort study

A. Hourvitz1, A. Kedem1, S. Avraham1, Y. Gidoni1, J. Barkat1, G. Yerushalmi1, O. Baruchin1, I. Gat1, M. Baum1, E. Maman2, M. Youngster1

1Shamir Medical Center Assaf Harofeh, IVF Unit, Beer Yaakov, Israel
2Hertzelia Medical Center- Israel, IVF Unit, Hertzelia, Israel

Study question: Are IVF treatments with extremely high peak estradiol levels during ovarian hyperstimulation associated with higher complication rates?

Summary answer: Extremely high estradiol levels were not associated with higher major complication rates, but patients were more likely to seek medical care following retrieval.

What is known already: The freeze-all policy and the increasing popularity of social oocyte freezing, have led to an increase in gonadotropin doses and number of oocytes retrieved and, as a direct effect, higher estradiol levels. Studies reporting major ART complications (OHSS, bleeding, infection, torsion, thromboembolic events) are based on heterogeneous patient populations without stratification by oocyte number or estradiol levels, except for a single study reporting an association between peak estradiol levels and the risk of ovarian torsion. Extreme estradiol levels, are associated with larger ovaries, repeated ovarian punctures, and possibly a thrombogenic effect. Therefore, higher complication rates can be expected.

Study design, size, duration: A retrospective cohort study including patients from two large medical centers treated between 2019-2021.

Participants/materials, setting, methods: A study group (239 patients) with extremely high peak estradiol levels (>20,000 pmol/L on the day of ovulation induction, or >15,000 pmol/L on the previous day) and a control group (208 patients) with normal range estradiol levels (3000-12000pmol/L), treated at two large units were included. Patients were surveyed about complaints and medical care related to ovum pick up (OPU), and medical files were reviewed. Complication rates and the need for medical assistance were compared.

Main results and the role of chance: Several differences between the study and control group were observed as a consequence of the study design: Mean age was 33.01 ± 5.14 vs. 34.57 ± 4.52 (p = 0.01), Mean peak estradiol levels was 26645.34 ± 8592.56 vs. 7229.750 ± 2329.20 (p < 0.001), mean number of oocytes were 27.55 ± 13.46 vs. 11.63 ± 5.77 (p < 0.001) for the study and control group respectively. More patients in the control group underwent fertility preservation. Mean FSH levels and total gonadotropin dosage were higher in the control group. Major complications [3 (1.25%) in the study group vs. 1 (0.96%) in the control group] were similar between groups (p = 0.62). In the study group Two patients were diagnosed with ovarian torsion (0.83%), and one (0.41%) with early severe OHSS as a result of a positive hCG related to an undiagnosed pregnancy prior to OPU. All three were admitted (1.25%). In the control group one patient was diagnosed with PID requiring inpatient IV antibiotic treatment (0.48%). One more patient was admitted with severe abdominal pain following OPU, for a total of 2 admissions (0.96%) (p = 1). 33 patients (13.8%) in the study group and 10 (4.8%) in the control group sought medical care after OPU, mostly due to abdominal pain, without further workup or hospitalization (p = 0.001).

Limitations, reasons for caution: A retrospective study with possible recall bias. Major adverse events are rare in IVF and may not be fully captured in the study population.

Wider implications of the findings: Based on our results, extremely high estradiol levels during ovarian hyperstimulation were not associated with thromboembolic events, higher major complication or hospitalization rates, thus may be considered safe. Nevertheless, patients may be informed of possible higher rates of discomfort, mostly abdominal pain. Larger studies are warranted to confirm our results.

Trial registration number: 0090-21-ASF