

Abstract Details

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Abstract title:

Bone marrow derived stem cells restore ovarian function and fertility in premature ovarian insufficiency women. Interim report of a randomized trial: mobilization versus ovarian injection

Biography

Degree in Medicine "Universitat de València" Extraordinary Award of Medicine School 2015 .
Professional category: Resident in obstetrics and gynecology, from 2016-today. 4th year resident
R&D projects funded through competitive calls of public or private entities: 1 FIS, 5 running till today.

Publications and scientific documents(10): in Fertility and Sterility, American Journal Of Obstetrics and Gynecology, Biology of Reproduction, Reproductive Biology Endocrinology.

Works submitted to national or international conferences 14: ESHRE 2017,2018. ASRM2018 , 2019. SEGO. Dexeus forum, CROG,

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Study question:

Could reproductive outcomes and menopausal symptoms of POI women be improved by autologous stem cell ovarian transplant (ASCOT) or Granulocyte-colony stimulating factor (G-CSF) stem cell-mobilization?

Summary answer:

Both ASCOT and G-CSF mobilization promoted follicle growth and raised AFC in 60% POI women; obtaining after COS 4 MII-oocytes, 2 embryos, and 1 pregnancy.

What is known already:

Premature ovarian insufficiency (POI) is characterized by oligo-amenorrhea due to follicular depletion in young women, where the only practical option is egg/embryo donation, as their spontaneous pregnancy rate is very low(<4%). We recently described that bone marrow derived stem cell (BMDSC) infusion promotes follicular growth by increasing ovarian vascularization, stromal cell proliferation, and reducing cell death in POI mice models and xenografted human ovarian tissue. Based on this, ASCOT technique has been already tested in poor responders improving ovarian function biomarkers (AMH and AFC) in 81.3% of women and allowing a total of 6 pregnancies and 3 healthy babies

Study design, size, duration:

Randomized prospective pilot study started in 2018 at La Fe University Hospital, Valencia. The study involves 20 POI women, according to the following inclusion criteria: ≤38 years, ≥4months

oligo/amenorrhea, serum FSH>25IU/l.

Patients were randomized into two study arms: 1) Mobilization of bone marrow stem cells to peripheral blood by a 5-day treatment with G-CSF (10ug/kg/day subcutaneous injection), where cells remain circulating; 2) ASCOT: after G-CSF mobilization, stem cells were collected and transplanted into one ovary.

Participants/materials, setting, methods:

To date, 10 patients have been included, 4 of them were randomized to the G-CSF arm and 6 to the ASCOT. After intervention, patients were monitored during 6-month for endocrine function, serum levels of FSH, AMH and estradiol, antral follicle count (AFC) was assessed by ultrasound scan. Patients' basal levels were established before treatment.

When follicular growth was detected (AFC increased in at least 1 follicle) controlled ovarian stimulation was initiated following standard protocols.

Main results and the role of chance:

Preliminary results in 10 patients, showed follicular development in both arms when compared to basal levels; these follicular growth waves were detected 90-140 days after treatments.

In the G-CSF group, AFC increased in 50% of recruited patients (2/4) while in the ASCOT this improvement was detected in 66.6% of women (4/6).

Statistically significant decrease of FSH levels was not recorded, but two women in the G-CSF group(50%) and 1 in the ASCOT(16%) showed a two-fold decrease, concluding the follow-up period(82.7 ± 8.1 to 24.1 ± 17.4 and 34.9 to 18.1 ; respectively).

After G-CSF mobilization, 2/4 women, initiated COS, with a total of 4 punctured follicles, 2 MII obtained and 1 embryo vitrified. Embryo transfer was performed but pregnancy was not achieved; this patient currently has regular menses after the follow-up period. In the ASCOT group, 4 of 6 patients initiated COS cycles. Oocyte pick-up was performed in 70% of initiated COS; where 3 MII and 1 GV were retrieved. One 3-day embryo was vitrified and transferred, having an ongoing pregnancy(20 weeks). These women were unable to undergo COS/oocyte pick-up before treatments due to absence of antral follicles.

Within menopausal symptoms, hot flashes and vaginal dryness improved in 50% of women, while 40% recovered menses (spotting).

Limitations, reasons for caution:

These are descriptive preliminary results obtained in the first 10 recruited women that should be confirmed at the end of the trial. Our study lacks from a real control group, without treatment, though poor prognosis POI patients should not be left untreated, as their only reproductive option is egg donation.

Wider implications of the findings:

ASCOT in POI women can be a potential therapy for women with no option of having offspring with their own oocytes. This study has shown a future use of stem cells in POI women, even without direct ovarian infusion, which suggest potential development of less invasive procedures in the future.

Keywords:

Autologous stem cell ovarian transplant (ASCOT)
Premature Ovarian Insufficiency (POI)
Follicle stimulating hormone (FSH)
Controlled ovarian stimulation (COS)
Antral follicular count (AFC)