Successful preimplantation genetic diagnosis program in poor responder patients after consecutive ovarian stimulation cycles and embryo vitrification.

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Background:

Poor responder patients are known for their reduced potential to produce an adequate number of oocytes and hence embryos. This low number of embryos available for biopsy significantly reduces their prognosis of a succesful preimplantation genetic diagnosis cycle (PGD).
Multiple consecutive ovarian stimulation cycles combined with ICSI and serial vitrification of embryos obtained before the actual PGD could be an option to increase the chances for a healthy pregnancy in these patients. Until now, only one case report has been presented by Chung et al. (2012) where a normal birth was obtained after serial vitrification of oocytes from 5 consecutive ovarian stimulation cycles for a patient carrying reciprocal translocations.

Aim:

Our study evaluates the effectiveness a PGD program using serial vitrification of embryos produced from consecutive ovarian stimulation cycles in poor responder patients.

Results

Tabel 1: Patient characteristics and laboratory outcomes

Number of patients	10
Number of patients per indication	
Cystic fibrosis	1
SMN1	1
X-linked Microtubular myopathy	1
Repeated implantation failure	2
Recurrent miscarriage	5
Total number of ovarian stimulation cycles with vitrification of embryos and fresh embryos	24
Total number of embryos vitrified	44
Total number of embryos in final fresh cycle	28

Table 2: Laboratory and clinical outcomes

Total number of embryos warmed and percentage viable	44 100%
Number of embryos obtained in final fresh cycle	28
Total number of embryos for PGD	72
Mean number of all embryos (fresh and warmed) per patient for PGD	7,2
Number and percentage of patients with transfer of at least one healthy embryo	9 90%
Mean number of embryos per transfer	2,1
Number of patients with positive hCG test	6
Percentage of patients with positive hCG test	66,6%
Number of patients with healthy delivery	4
Percentage of patients with healthy delivery	44,4%

Conclusions

Poor responder patients can increase their number of embryos for PGD by cumulative vitrification of embryos obtained in multiple ovarian stimulation cycles and hence increase their chance for a healthy pregnancy. Vitrification is a powerful tool for PGD, especially for poor responder patients.

Materials and methods

Setting: Private fertility treatment centre, Embryolab, Assisted Reproduction Unit, 173-175 Ethnikis Antistaseos 551 34 Kalamaria, Thessaloniki, Greece.
Study design: Retrospective cohort study.
Cycles-patients studied: Ten poor responder patients entered our PGD program with the following indications: recurrent implantation failure, Cystic fibrosis, SMN1, X-linked Microtubular myopathy or recurrent miscarriage. Following counseling, couples opted for serial vitrification of embryos from consecutive ovarian stimulation cycles followed by PGD.
Patient's ovarian stimulation protocol consisted of standard down regulation protocol or antagonist protocol. Patient stimulations were repeated because a limited number of embryos were obtained in the first cycle and all embryos were vitrified. One or two extra stimulation cycles were initiated to obtain a sufficient number of embryos for each patient.
Oocyte collection was carried out 36 hours post hCG administration. Fresh semen samples were prepared by density gradient and wash (Sage).
ICSI was done according to standard procedures.
Check for fertilisation: 18-22 hours post oocyte collection oocytes were checked for presence of 2 pronuclei (2PN). Fertilised oocytes were group cultured in 0,7ml droplets (Cleavage medium, Sage). Embryo quality was checked daily.
Vitrification of embryos: good quality embryos were vitrified using the Cryotech vitrification method followed by storage in liquid nitrogen.
Warming of vitrified embryos: embryos were warmed according to Cryotech's guidelines.
PGD: Embryos were biopsied on day 3 of development and genetic testing was performed by FISH, PCR or CGH depending on the indication. Embryos were cultured individually in 50 μl droplets under oil until transfer. Embryo quality was checked daily.
Embryo transfer: Embryo'(s) were transferred to the patient using a Wallace or Labotect soft catheter under by ultra sound guidance.
Clinical pregnancy is defined as the presence of a gestational sac with foetal heartbeat by ultrasound at 8-10 weeks after embryo transfer.
The IVF laboratory at Embryolab has ***ISO 9001:2000 accreditation*** (2007) and has been assessed in accordance to ***ISO 15189-2007.***

Literature cited

Chung JT, Son WY, Zhang XY, Ao A, *et al.,* 2012, Normal birth following PGD for reciprocal translocation after serial vitrification of oocytes from a poor responder: a case report. RBMonline. 25, 521-6.

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