

Autologous mitochondrial transfer as a complementary technique to ICSI to improve oocyte and embryo quality in IVF patients. A Randomized Pilot Study.

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Study question:

Does Autologous mitochondrial transfer (AUGMENT® treatment) improve oocyte/embryo quality and pregnancy rates in patients with previously failed IVF treatments?

Summary answer:

AUGMENT does not seem to improve oocyte/embryo quality in this poor prognosis patients. No differences regarding live birth rates per embryo cohort were observed.

What is known already:

AUGMENT is a proprietary new technology launched in 2014 by OvaScienceSM. Previous clinical use suggested that the addition of autologous mitochondria during IVF is safe, improves embryo quality, increases the success of IVF and avoids concerns associated to heteroplasmy. Many studies described the existence of egg precursor cells (EPCs) in the outer lining of the ovarian cortex, however others have failed to find them. OvaScience reports that mitochondria isolated from EPCs are of high quality and morphologically like oocyte mitochondria.

Study design, size, duration:

Triple blind, randomized, single-center, controlled experimental pilot study.

Study period: October 2015- June 2017.

A biopsy of the ovarian cortex was performed to isolate the EPCs to obtain their mitochondria.

Sibling MII oocytes obtained after stimulation were allocated through computerized randomization to two groups: AUGMENT protocol (experimental) and Conventional ICSI (control).

Sample size was calculated to detect a 20% difference (15-35%) in the OPR between both groups.

An interim analysis was performed in 59 patients.

Participants/materials, setting, methods:

Infertile patients undergoing an IVF-PGT-A cycle, aged ≤42, BMI <30, AMH ≥4 pmol/mL, >5 million/mL motile sperm, ≥1 unsuccessful previous IVF cycle with ≥5 MII eggs collected and extremely low embryo quality.

Primary endpoint was ongoing pregnancy rate (>12w).

In the experimental group, \approx 1-2 picoliters of mitochondrial suspension were injected along with the sperm during ICSI. Viable blastocysts from both groups were biopsied and cryopreserved. The genetic content of the embryos was evaluated through CGH arrays.

Main results and the role of chance:

Two of 59 enrolled patients spontaneously conceived (one ended in miscarriage). A total of 57 ovarian cortex biopsies were performed. In one case, a suboptimal number of EPCs were isolated; a second biopsy was performed yielding sufficient EPCs for inclusion in the study. Twenty-six patients did not undergo embryo transfer for the following reasons: no blastocysts available for biopsy ($n = 16$); all aneuploid ($n = 8$); no fertilization ($n = 1$); no survival after thawing ($n = 1$). A total of 253 MII were inseminated in the AUGMENT and 250 in the Control group, with a fertilization rate of 64.0 % and 70.8%, respectively ($p = 0.11$).

Day 5 blastocyst formation rates were significantly reduced in the AUGMENT group (27.2%) compared to the Control group (43.5%), $p = 0.002$. The number of euploid blastocysts/biopsied blastocysts was 42.2% (19/45) in the AUGMENT and 50% (37/74) in the Control group ($p = 0.42$). Statistical differences in euploidy rate/MI I oocytes between both groups (7.5% vs. 14.8%, $p = 0.01$) were observed.

No differences were observed regarding mtDNA content in euploid embryos, $p = 0.56$.

The live birth rate per transferred embryo was 41.2% (7/17) in the AUGMENT and 39.1% (9/23) in the Control group ($p = 0.90$).

Limitations, reasons for caution:

The technique requires a laparoscopy. Isolation of EPCs and mitochondrial extraction was performed in a separated laboratory set up from OvaScience. Data regarding final mitochondrial quantity and quality was not available for this analysis.

Wider implications of the findings:

In this difficult to treat patient population, the ratio of euploid embryos obtained per MII was significantly lower with AUGMENT compared to the Control group. No differences regarding live birth rates per embryo cohort were seen. Therefore, the study is no longer being continued.

Trial registration number:

The www.clinicaltrials.gov registration number is NCT02586298

Yes

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