Abstract title:
The application of AOA-artificial oocyte activation in patients with previous unsuccessful attempt increases the ongoing pregnancy per treatment but not per transfer; a multivariable study

Biography
Dr. Aránzazu Galán was born in 1974, receiving her Chemistry Degree in 1999. She did her predoctoral research in embryo implantation and received her Ph.D. Degree in Chemistry in 2003 from the University of Valencia. She started as embryologist in 2000, becoming laboratory supervisor in 2004 and deputy director in 2018 in IVI Valencia. Her research area is focused on embryology, mainly in time-lapse. She has published several articles, made numerous presentations at national and international congresses and she is associate professor of the Master in Biotechnology from Valencia University

Study question:
To check the effectiveness of AOA in patients with previous very low or failed fertilization rates in terms of fertilization, implantation and ongoing pregnancy outcomes.

Summary answer:
After applying AOA the ongoing pregnancy rates of the patients per initiated treatment were enhanced, as well as a significant reduction in the cancellation rate.

What is known already:
Different authors have demonstrated better results after using AOA in couples with low or non-fertilization in previous treatments: (Heindryckx et al., 2005, Heindryckx et al., 2008, Montag et al., 2012). Recently, we have seen extensively described similar benefits by the use of AOA for couples with previous standard ICSI failure (Fawzy et al., 2018). The implementation of this technique in the current clinical routine has been possible after reporting no detrimental impact on neither human gametes (Ebner et al., 2015) nor on the offspring (Vanden Meerschaut et al., 2014).

Study design, size, duration:
Retrospective cohort study, from four consecutive years. We studied 509 oocytes from 66 patients who were treated with standard ICSI, and were compared to 616 oocytes from the same cohort of patients but using AOA.

Participants/materials, setting, methods:
66 patients were included in the study generating 163 cycles; standard group was composed of 509 oocytes generating 75 cycles (18 fresh cycles, 4 frozen cycles, 1 mixed and 52 cancelled cycles). AOA group included 616 oocytes resulting from the same patients, but creating 88 cycles (31 fresh cycles, 37 frozen cycles). AOA technique involves oocyte injection by spermatozoa and incubation for 10 minutes with calcium ionophore. Outcome analysis included a multivariable logistic regression model.

Main results and the role of chance:
Although no differences were observed in relation with the day of transfer (Day 3 vs Day 5) and maternal age at the time of the cycle, we performed a multivariable logistic regression including those variables as potential bias factors. The study was performed to assess the impact of AOA on ongoing pregnancy per cycle as well as per transfer. We observed that the application of AOA in our patients increased the chances of a viable pregnancy by more than 4 times (OR=4.57, p=0.008) per cycle but not per transfer (OR=0.964, Not significant). When embryos were available for transfer AOA did not increased the chances of a viable pregnancy.

**Limitations, reasons for caution:**
The retrospective analysis of this study may be a reason to take into consideration. Another limitation was not to study the PLCζ levels of the sperm, then we presumed that this dysfunction was presented in the spermatozoa and, in consequence, was the responsible for the fertilization failure.

**Wider implications of the findings:**
Our findings suggest the use of AOA for a particular population where the fertilization was failed in previous attempts. After AOA application, the fertilization rate was enhanced, increasing the chances of success per treatment. The use of AOA is comforting after checking non-existence of detrimental impact on the offspring.

**Keywords:**
calcium ionophore
oocyte activation
Ongoing pregnancy
non-fertilization
unsuccessful attempt