Can we help infertile couple suffering from in vitro fertilization arrest with ca2+ ionophore?

Intracytoplasmic sperm injection (ICSI) is an infertility treatment technique developed to help infertile couples to conceive child. ICSI is performed by injecting one spermatozoon (male gamete) into cytoplasm of an oocyte (female egg) *in vitro* in assisted reproductive laboratories. Once we find under microscope that the oocyte is fertilized, it is assumed to undergo mitotic division to form an embryo. This embryo will be transferred to the female uterus to implant, and continue embryological and fetal development for 9 months.

Fig. 1. Two centrally positioned, juxtaposed PNs with clearly defined membranes, 16-18 hours post insemination / ICSI.

Fertilization is a complex process starts when a spermatozoon interacts with an oocyte; this induces series of changes known as oocyte activation. Oocyte activation starts by increase in intracellular ca^{2+} transient that ends with formation of male and female pronucli (2PN) as shown in Figure 1 .By the end of fertilization process, high Ca^{2+} spikes are observed again in the early post-fertilization phase, to induce events initiating mitotic division (cleavage).

Although ICSI has become a hopeful treatment for thousands of infertile couples, some cases still suffer from fertilization failure or fertilization arrest, after performing ICSI as treatment procedure. Ca^{2+} ionophore was used as an effective treatment for cases with total or partial fertilization failure to get better fertilization, and embryo development. This is called artificial oocyte activation (AOA).

In this study, 4 infertile cases their oocytes suffered from inability to transit to cleavage stage after performing ICSI procedure, they arrested at 2PN stage and no more development. We used ca^{2+} ionophore prospectively on those four cases in another ICSI treatment cycle to try to overcome this developmental arrest problem.

Before treatment with Ca^{2+} ionophore activation, 22 oocytes out of 40 injected were fertilized (Fertilization rate= 55%). None of those zygotes started cleavage (Cleavage rate= 0%) showing 2PN stage arrest. As a result failed ICSI treatment cycles, and no Embryo transfer

In their second ICSI treatment cycle, Ca^{2+} ionophore was used with all injected oocytes. Fortunately, fertilized oocytes were 25 from 37 injected oocytes (Fertilization rate= 67.60 %), out of them 11 zygotes were cleaved (Cleavage rate= 44%).This time all patients had developed embryos to transfer, which resulted in one clinically pregnant case out of four cases enrolled the study.

The results from our research indicated that AOA of oocytes using Ca^{2+} ionophore in cases with previous cleavage failure dramatically shifts the fate of ICSI cycles from being cancelled treatment trials, to complete ones. It overcomes the problem of inadequate signaling events, and helps the embryos to reach more advanced stages. Consequently, patients got embryos to be transferred to their wombs, and some got successfully pregnant.

This is a new hope for this category of infertility patients to reach their dream of having babies, and overcome their infertility problem.

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