Intracytoplasmic sperm injection

Dimitra Leriou
Graduate Biomedical Scientist
Department of Biomedical Sciences/Medical Laboratories, University of West Attica
dmtrgmlcmb@gmail.com

George Bablekos
Assistant Professor
Department of Occupational Therapy, University of West Attica
gmpample@uniwa.gr

Abstract: Infertility is a serious issue affecting many couples worldwide, including those in Greece. Innovative assisted reproductive techniques have given hope to many individuals facing fertility challenges. Intracytoplasmic sperm injection (ICSI) is one of the most well-known and widely used methods, contributing to the birth of children among couples with reproductive difficulties. Scientific advancements in this field are ongoing, providing hope to an increasing number of couples experiencing fertility problems.

Keywords: Intracytoplasmic sperm injection, Infertility, Treatment.

Complete failure of fertilization is a particularly disappointing outcome for couples undergoing in vitro fertilization (IVF). To reduce the incidence of this failure, ICSI has been preferred over conventional IVF. However, while ICSI has shown positive results, its use in couples without a male infertility factor is not recommended. One strategy that could benefit conventional IVF is delayed rescue ICSI. This procedure involves performing ICSI 18-24 hours after conventional insemination on oocytes that have not shown signs of fertilization. Although this treatment has been reported as less efficient, recent observations indicate that embryos derived from it can be transferred with better results after cryopreservation in a freeze-thaw cycle. The results of this review suggest that delayed rescue ICSI (r-ICSI/Rescue ICSI), combined with frozen embryo transfer, can be a beneficial method for couples who are unable to conceive after conventional IVF cycles [1].

ICSI is usually effective for poor or absent fertilization in couples with clear abnormalities in sperm parameters. However, it is often combined with other surrogacy methods for various infertility factors even when sperm parameters are within regulatory standards, according to World Health Organization reports (2010) [2].

The ICSI technique has become one of the most popular fertilization methods in assisted reproduction technology due to its high efficiency, standardization and flexibility for integration into fertility centers worldwide. ICSI is the main option for treating severe male factor infertility, but its excessive use in cases of male factor infertility without sufficient supporting data is not recommended. Despite efforts to improve the positive outcomes and safety of ICSI through advanced sperm retrieval and cryopreservation methods, as well as sperm selection techniques with better chromatin integrity, overall pregnancy outcomes for infertile men remain low. Addressing the underlying male infertility factor before ICSI appears to be a promising approach to improving outcomes, but data are still lacking. Information collected over the last 25 years raises concerns about the health of ICSI offspring, including risks of congenital malformations, epigenetic disorders, chromosomal abnormalities, infertility, cancer, delayed psychological and neurological development and a reduced cardiometabolic profile [3]. These risks appear to be greater in babies born from ICSI compared to those conceived naturally. However, as infertility itself may influence risk estimates, it remains unclear whether adverse outcomes are primarily associated with parental factors or with ICSI [3].

In general, infertility affects up to 15% of couples of reproductive age. Gamete micromanipulation, such as ICSI, is an effective solution for couples with reduced sperm parameters [4]. The use of ICSI has increased significantly, now covering 65% of IVF cycles in Europe and 76% in the USA. Despite its continued use, no clear benefit has been established compared to conventional IVF. However, women of advanced age and low ovarian reserve may benefit from ICSI, due to reduced egg quality. Research on the effectiveness of ICSI in this age group is still lacking. The choice of ICSI should be based on sperm parameters and previous history. It is important to note that its use, due to the advanced age of the woman, has not shown any identifiable benefit compared to conventional IVF [5]. When prognostic indications are favorable, IVF/ICSI appears to be a beneficial alternative up to the age of 43 years old [6].

On the other hand, human gene therapy (HGT), which aims to cure or prevent disease through gene transfer, is often highlighted as a medical innovation. Unlike most existing drugs that address symptoms, gene therapy targets the root causes of diseases. Micro-assisted insemination, specifically ICSI, has brought significant progress for couples with reduced sperm quality and obstructive or non-obstructive azoospermia. This technique involves directly introducing a single sperm into the cytoplasm of a mature egg (oocyte) using a glass needle (pipette). Although ICSI achieves successful fertilization in 50% - 80% of cases, it may cause some damage to a small percentage of oocytes. Gene therapy offers new techniques for gene transfer and genome manipulation, including microinjection techniques such as ICSI – mediated transgenesis (ICSI –Tr), active diagenesis and pronuclear microinjection [7].

To optimize IVF results in advanced patients, ICSI is recommended over conventional insemination (CI). ICSI is often used to address issues with egg – sperm interaction and sperm penetration, particularly related to maternal age, but not sperm abnormalities.

Studies support the use of ICSI in elderly IVF patients to achieve higher fertilization rates and a greater number of high – quality embryos per IVF cycle. However, further research is needed to confirm ICSI as the primary approach for abnormal sperm – egg interactions related to advanced maternal age [8]. Other research highlights the advantages of conventional IVF over ICSI in cases of non – male factor infertility with five or fewer oocytes retrieved at an advanced age [9]. Additionally, intrauterine infusion of platelet – rich plasma (PRP) is being considered as an alternative method for women undergoing IVF or ICSI [10].

Sperm retrieval from testicular tissue can be challenging, often requiring 2 to 3 hours depending on sperm production rates and the cause of testicular failure. During this procedure sperm is released from the seminiferous tubules, and removed from the surrounding testicular tissue. These conditions necessitate assisted reproductive techniques, such as ICSI to confirm pregnancy [11]. Azoospermia, the absence of sperm in ejaculated semen, is a severe factor in male infertility, affecting about 5% of couples undergoing further testing. The advent of ICSI has advanced the treatment of azoospermia, with sperm retrieval possible from the epididymis or testicle, depending on the type of disease. However, there is insufficient evidence to identify a superior sperm retrieval technique for azoospermic men undergoing ICSI [12]. In men with azoospermia due to spermatogenic dysfunction, no significant difference in clinical pregnancy or fertilization rates has been observed between the use of fresh and cryopreserved - thawed testicular sperm [13]. Finally, ICSI is often useful in treating hypogonadotropic hypogonadism [14].

REFERENCES

Paffoni A, Reschini M, Pisaturo V, Guarneri C, Palini S, Viganò P. Should rescue ICSI be re-evaluated considering the deferred transfer of cryopreserved embryos in in-vitro fertilization cycles? A systematic review and meta-analysis. Reprod Biol Endocrinol. 2021;19(1):121. https://doi.org/10.1186/s12958-021-00784-3

Intracytoplasmic sperm injection (ICSI) for non-male factor indications: a committee opinion. Fertil Steril. 2020;114(2):239-245. (CN: Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. Electronic address: asrm@asrm.org ; AD: American Society for Reproductive Medicine and Society for Assisted Reproductive Technology, Birmingham, Alabama). https://doi.org/10.1016/j.fertnstert.2020.05.032

Esteves SC, Roque M, Bedoschi G, Haahr T, Humaidan P. Intracytoplasmic sperm injection for male infertility and consequences for offspring. Nat Rev Urol. 2018;15(9):535-562. https://doi.org/10.1038/s41585-018-0051-8

Teixeira DM, Barbosa MA, Ferriani RA, Navarro PA, Raine-Fenning N, Nastri CO, Martins WP. Regular (ICSI) versus ultra-high magnification (IMSI) sperm selection for assisted reproduction. Cochrane Database Syst Rev. 2013;(7):CD010167. https://doi.org/10.1002/14651858.CD010167.pub2

Tannus S, Son WY, Gilman A, Younes G, Shavit T, Dahan MH. The role of intracytoplasmic sperm injection in non-male factor infertility in advanced maternal age. Hum Reprod. 2017;32(1):119-124. https://doi.org/10.1093/humrep/dew298

Cabry R, Merviel P, Hazout A, Belloc S, Dalleac A, Copin H, Benkhalifa M. Management of infertility in women over 40. Maturitas. 2014;78(1):17-21. https://doi.org/10.1016/j.maturitas.2014.02.014

Navarro J, Risco R, Toschi M, Schattman G. Gene therapy and intracytoplasmatic sperm injection (ICSI) - a review. Placenta. 2008;29 Suppl B:193-9. https://doi.org/10.1016/j.placenta.2008.08.014

Farhi J, Cohen K, Mizrachi Y, Weissman A, Raziel A, Orvieto R. Should ICSI be implemented during IVF to all advanced-age patients with non-male factor subfertility? Reprod Biol Endocrinol. 2019;17(1):30. https://doi.org/10.1186/s12958-019-0474-y

Liu H, Zhao H, Yu G, Li M, Ma S, Zhang H, Wu K. Conventional in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI): which is preferred for advanced age patients with five or fewer oocytes retrieved? Arch Gynecol Obstet. 2018;297(5):1301-1306. https://doi.org/10.1007/s00404-018-4696-6

Maleki-Hajiagha A, Razavi M, Rouholamin S, Rezaeinejad M, Maroufizadeh S, Sepidarkish M. Intrauterine infusion of autologous platelet-rich plasma in women undergoing assisted reproduction: A systematic review and meta-analysis. J Reprod Immunol. 2020;137:103078. https://doi.org/10.1016/j.jri.2019.103078

Popal W, Nagy ZP. Laboratory processing and intracytoplasmic sperm injection using epididymal and testicular spermatozoa: what can be done to improve outcomes? Clinics (Sao Paulo). 2013;68 Suppl 1(Suppl 1):125-30. https://doi.org/10.6061/clinics/2013(sup01)14

Van Peperstraten A, Proctor ML, Johnson NP, Philipson G. Techniques for surgical retrieval of sperm prior to intra-cytoplasmic sperm injection (ICSI) for azoospermia. Cochrane Database Syst Rev. 2008;2008(2):CD002807. https://doi.org/10.1002/14651858.CD002807.pub3

Ohlander S, Hotaling J, Kirshenbaum E, Niederberger C, Eisenberg ML. Impact of fresh versus cryopreserved testicular sperm upon intracytoplasmic sperm injection pregnancy outcomes in men with azoospermia due to spermatogenic dysfunction: a meta-analysis. Fertil Steril. 2014;101(2):344-9. https://doi.org/10.1016/j.fertnstert.2013.10.012

Resorlu B, Abdulmajed MI, Kara C, Unsal A, Aydos K. Is intracytoplasmic sperm injection essential for the treatment of hypogonadotrophic hypogonadism? A comparison between idiopathic and secondary hypogonadotrophic hypogonadism. Hum Fertil (Camb). 2009;12(4):204-8. https://doi.org/10.3109/14647270903331139