

## Post-thaw Embryo Transfer Cycles as the Future Hope for Boosting IVF Success Rates

The history of IVF is synonymous with several millstones and each of these have led to a revolution in our understanding of human fertility or causes of male and female infertility, as well as introducing new treatment protocols for infertility. It can undoubtedly be claimed that one of the best of these was the introduction of ultra-rapid glass-like solidification of a solution without ice-crystal formation or vitrification method for cryopreservation of human embryos and gametes in 1990 (1).

Vitrification has brought about fundamental changes in cryopreservation and human fertility preservation. Vitrification of embryos at cleavage or blastocyst stage seems to be a promising procedure for improving implantation and pregnancy rate in IVF cycles. It improves cryosurvival rate of embryos close to 100% which is comparable to slow freezing through prevention of ice-crystal formation. Simplicity and speed and no need for expensive freezing machines are reasons for its rapid expansion. Vitrification has been improved and standardized for human gametes and embryos through large numbers of studies since 1990 (2).

However, two decades past the first live-birth from vitrified embryos, there are still some doubts on the safety of these methods and its probable deleterious effects on the health of children born from vitrified embryos or oocytes. There is concern that application of high concentrations of cryoprotectants may lead to genetic or epigenetic abnormalities with subsequent inborn malformations. Therefore, there is no consensus or scientific recommendations for the substitution of slow freezing method with vitrification worldwide. In spite of concerns about the toxic effects of high concentrations of cryoprotectants, most studies indicate that the survival rate, implantation and clinical pregnancy of post-thaw vitrified embryos is far better than those from slow freezing method, as substitution of slow rate freezing by vitrification increased pregnancy rate per cycle from 7% to 64% and delivery and live birth rate per cycle from 7% to 50%. But still slow freezing method is the only acceptable method for embryo and gametes cryopreservation in large numbers of IVF centers in Australia and European countries (2).

According to current practice, 3-4 cleavage embryos or 1-2 blastocyst embryos are frozen on loading devices such as Cryotop<sup>®</sup>. Following artificial endometrial preparation in none-stimulated cycles, the post-thaw survived embryos are transferred to uterus; however post-thaw survival alone is not enough to support their implantation, therefore, embryo culture is necessary to confirm resumed embryo cleavage. Embryo culture increases pregnancy rate following freezing/thawing cycles by preventing transfer of embryos with post-thaw cleavage arrest (3).

Several studies have revealed that controlled ovarian stimulation severely decreases endometrial receptivity for embryo, therefore, more attention and research on implantation is needed regarding synchronization of endometrium and embryo development to increase endometrial receptivity. Embryo transfer during implantation window is a critical factor in the success of IVF cycles but it is usually missed in most fresh cycles; although it is achievable through post-thaw embryo transfer cycles (3).

Later, several studies proposed freeze-all cycles in which all embryos are frozen in stimulation cycle and transferred at blastocyst stage following artificial preparation of endometrium. This method seems to increase embryo and endometrial synchronicity and decrease the number of transferred embryos and subsequent multiple pregnancies.

Moreover, some studies suggested transferring higher numbers of low quality embryos in fresh cycles and keeping high quality embryos which are later developed to blastocyst stage and are subsequently vitrified for future transfer without stimulation (4).

Although the present data supports the efficiency and potential safety of vitrification, but more profound studies on its details are still needed, including embryonic stage, loading devices, the media and practice protocols for its worldwide application. Finally, it could be claimed that future improvements in IVF success rates will depend on the role played by embryology field, especially control of in vitro conditions of embryo culture and cryopreservation of embryos and gametes, specifically vitrification method that would be the most important part of this scenario.

### References

1. Gordts S, Roziers P, Campo R, Noto V. Survival and pregnancy outcome after ultrarapid freezing of human embryos. *Fertil Steril*. 1990;53(3):469-72.

2. Kader AA, Choi A, Orief Y, Agarwal A. Factors affecting the outcome of human blastocyst vitrification. *Reprod Biol Endocrinol.* 2009;7:99.
3. Shapiro BS, Daneshmand ST, Garner FC, Aguirre M, Hudson C, Thomas S. Evidence of impaired endometrial receptivity after ovarian stimulation for in vitro fertilization: a prospective randomized trial comparing fresh and frozen-thawed embryo transfer in normal responders. *Fertil Steril.* 2011;96(2):344-8.
4. Aflatoonian A, Oskouian H, Ahmadi S, Oskouian L. Can fresh embryo transfers be replaced by cryopreserved-thawed embryo transfers in assisted reproductive cycles? A randomized controlled trial. *J Assist Reprod Genet.* 2010;27(7):357-63.

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