CLEAVAGE-STAGE TRANSFER

Cleavage-Stage Embryo Transfer

Type of embryo transfer where embryos are transferred 2-3 days after fertilization.

About Cleavage-stage transfer

Cleavage-stage embryo is transferred 2-3 days after fertilization. When woman undergoes an embryo transfer, embryos can be replaced at the stage of cleavage or blastocyst. Cleavage stage is a phase of early embryo development where a zygote undergoes rapid cell divisions to form a blastula. Usually, embryos contain of 4 cells on day 2 (Pic. 1) and 8 cells on day 3 (Pic. 2). At this developmental stage, embryos are driven by the maternal genome and subsequent development may failure to continue to grow past this stage. Only embryos from good quality eggs are able to continue in development under their own genomic control. Embryos that reach the day 3 cell stage can be tested for chromosomal or specific genetic defects prior to possible transfer by preimplantation genetic screening (PGS) resp. diagnosis (PGD).

During cell division process, not all the embryos divide correctly. The decision on which embryo to transfer is mainly based on the developmental competence of the embryo on the day of transfer by taking into account morphokinetical observations of that embryo at earlier time points. The scored morphological features include the number of cells, grade of fragmentation, cell size and multinucleation for cleavage stage embryos.

Embryos can be either “fresh” from fertilized egg cells of the same menstrual cycle, or “frozen”, that is they have been generated in a preceding cycle and undergone embryo cryopreservation, and are thawed just prior to the transfer, which is then termed “frozen embryo transfer” (FET). The outcome from using cryopreserved embryos has uniformly been positive with no increase in birth defects or development abnormalities, also between fresh versus frozen eggs used for intracytoplasmic sperm injection (ICSI).

In fact, pregnancy rates are increased following FET, and perinatal outcomes are less affected, compared to embryo transfer in the same cycle as ovarian hyperstimulation was performed. The endometrium is believed to not be optimally prepared for implantation following ovarian hyperstimulation, and therefore frozen embryo transfer avails for a separate cycle to focus on optimizing the chances of successful implantation. When transferring a frozen-thawed embryo, the chance of pregnancy is essentially the same whether it is transferred in a natural cycle or one with ovulation induction.

The uterine lining (endometrium) needs to be appropriately prepared so that the embryo(s) can implant. In a natural cycle the embryo transfer takes place in the luteal phase at a time where the lining is appropriately undeveloped in relation to the status of the present luteinizing hormone (LH). In a stimulated or a cycle where a “frozen” embryo is transferred, the recipient woman could be given first estrogen preparations (about 2 weeks), then a combination of estrogen and progesterone so that the lining becomes receptive for the embryo. The time of receptivity is the implantation window.

Success or failure factors

Generally, cleavage-stage transfer is recommended for those patients that have less than 3 eggs fertilized normally. In some cases, patient’s embryos are not enough viable and are not able to be cultured up to
blastocyst stage (day 5-6), therefore an embryo transfer would not be performed, so the cumulative clinical pregnancy rates are increased with cleavage stage transfer. This risk of insufficient number of embryos can be up to 10%. Cleavage-stage transfer is a good possibility for those patients. Additionally, if there are less than 4 good quality embryos at day 3, cleavage-stage transfer is preferred.

Cleavage-stage embryo transfer does not affect gender ratio compare to blastocyst transfer where higher rate of male offspring is detected. Additionally, there is a significantly higher odds of preterm birth and congenital anomalies among births having reached the blastocyst stage compared with cleavage stage. Twin pregnancies rate is also lower in cleavage-stage transfer compare to blastocyst transfer.

Complications

No significant differences in preeclampsia, antepartum/postpartum hemorrhage, placenta previa, placental abruption, after blastocyst versus cleavage-stage transfers were seen. However, one found higher chances of preterm birth associated with blastocyst-stage transfers (17%) in comparison to cleavage-stage transfers (14%).

However, embryo stage (blastocyst vs cleavage) does not appear to impact safety in infants.

Prognosis

Cleavage-stage transfer is associated with greater numbers of embryos available for freezing, while blastocyst transfer is associated with increased number of cycles with no embryos to transfer. Transfer day 2 instead of day 3 after fertilization has no differences in live birth rate. Cleavage stage transfer is less effective than blastocyst stage transfer in assisted reproductive technologies. It showed a small improvement in live birth rate per couple for blastocyst transfers. This would mean that for a typical rate of 31% in clinics that use early cleavage stage cycles, the rate would increase to 32% to 42% live births if clinics used blastocyst transfer (Pic. 3; Pic. 4). There is a higher clinical pregnancy rate in fresh cleavage-stage embryo transfers than frozen-thawed cleavage-stage transfers (Pic. 5). The cleavage-stage embryos did not induce self-selection through the extended culture so the ability of resistance may be weaker than blastocyst.

The significantly lower pregnancy rate achieved after single cleavage stage embryo transfer as compared to a double embryo transfer can be compensated by pregnancies resulting from the first thawed cycle. This finding underscores the important role of cryopreservation in enhancing the total reproductive potential of a single cycle. The introduction of the vitrification technique as an efficient cryopreservation technique promises to further increase the impact of cryo-technology on the cycle specific pregnancy rates.

## Gallery

### Pic. 3: Cleavage-stage transfer vs. Blastocyst transfer
Comparison with fresh cleavage-stage embryo transfer and fresh blastocyst transfer (age <35 years).

### Pic. 4: Cleavage-stage transfer vs. Blastocyst transfer
Comparison with fresh cleavage-stage embryo transfer and fresh blastocyst transfer (age ≥35 years).

Note: Values are presented as number, number (%) or mean±SD.
Sources

“Embryo transfer” —sourced from Wikipedia licensed under CC BY-SA 3.0

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