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Fresh embryo transfer versus frozen-thawed embryo transfer in assisted reproduction technique cycles: a systematic review and meta-analysis

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Introduction: Endometrial receptivity is an essential step for conception in natural and infertility treatment cycles. It is not known whether ovarian stimulation adversely affects endometrial receptivity in assisted reproduction techniques (ART) cycles. Its effects can determine suboptimal synchrony between endometrium and the transferred embryos and therefore can be responsible by many IVF cycle failures. In frozen-thawed embryo transfers (FET) the endometrial priming may be achieved with the use of estrogens and progesterone (for luteal phase support) and the endometrial receptivity can be controlled more precisely than in cycles of COH with gonadotropins.

The purpose of this review and meta-analysis was to examine systematically the literature and identify randomized clinical trials to answer the following question: Is cryopreservation of all viable embryos and posterior FET associated with best ART outcomes when comparing to fresh embryo transfer?

Material and Methods: An exhaustive electronic literature search in MEDLINE, EMBASE, and the Cochrane Library was performed and covered articles published up to December 2011. The review was restricted for articles written in English. The search combined terms and descriptors related to fresh and FET, endometrial receptivity and ART outcomes.

The review included randomized clinical trials comparing the outcomes of ART cycles between fresh embryo transfer and FET. The main outcomes were clinical pregnancy rate and miscarriage. We extracted outcome results per women randomized (intention-to-treat analysis). Two independent authors analyzed the titles and abstracts from the electronic search, at the first screening. In the final screening, inclusion or exclusion decisions were made on examination of the full text by the two reviewers. If needed, a third reviewer reached a consensus.

We pooled data for dichotomous outcomes from original studies, to obtain the relative ratio (RR) of the occurrence of an outcome event. From each study, outcome data were extracted in 2x2 tables and the results were pooled using Mantel-Haenszel statistic model when using the fixed effects model and the DerSimonian and Laird method when using random effects model, and are expressed as RR with 95% confidence intervals (CI). We evaluated the degree of variation across studies attributable to heterogeneity with the I^2 statistic. We conducted the meta-analyses using the Review Manager 5 software.

Results: A total of 64 studies that potentially were able to answer the research question were initially retrieved from the literature. Further evaluation based on study titles and abstracts and/or the full manuscripts identified three prospective randomized clinical trials that compared the ART cycles outcomes in fresh embryo transfer cycles to FET cycles. Overall, the current review summarizes information from 633 ART cycles (316 randomized to fresh embryo transfer and 317 to FET)

Our meta-analysis demonstrates that the probability of a clinical pregnancy is significantly increased in FET compared to fresh embryo transfer (RR: 1.31; CI: 1.10-1.56; p = 0.002). The miscarriage rates did not show significantly differences between the two groups (RR: 0.83; CI: 0.43-1.60; p=0.57)

Conclusion: This is the first meta-analysis addressing the question if the cryopreservation of all viable embryos and posterior FET is associated with improvements in ART outcomes when comparing to fresh embryo transfer. The pooled data demonstrates that the cryopreservation and subsequently FET may improve the outcomes of ART cycles. The data provide a rationale for conducting further randomized clinical trials assessing the consequences of COH on endometrial receptivity and in the ART outcomes and compare to the FET.