Is tubal embryo transfer of any value: a meta-analysis and comparison with the Society for Assisted Reproductive Technology database

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Authors' objectives
To compare pregnancy outcomes between uterine or tubal embryo transfer techniques, i.e. in vitro fertilisation and embryo transfer (IVF-ET) and zygote intrafallopian transfer (ZIFT).

Searching
MEDLINE was searched from 1966 to December 1998 for publications in the English language. The search terms included: 'ZIFT', 'PROST', 'TEST', 'TET', 'TPET', 'IVF', 'intrafallopian', 'tubal', 'intrauterine' and 'uterine transfer'. The references from reports, review articles and abstracts of the annual meetings of the American Society for Reproductive Medicine and the European Society for Human Reproduction, were manually searched.

Study selection
Study designs of evaluations included in the review
Only randomised controlled trials were included in the analysis.

Specific interventions included in the review
IVF-ET compared with ZIFT. The methods of pronuclear stage-embryo transfer (PROST), tubal pre-embryo transfer (TPET), tubal embryo-stage transfer (TEST), and tubal embryo transfer (TET) are known collectively as ZIFT.

Participants included in the review
Women with infertility. The mean age of the women was 31 years.

Outcomes assessed in the review
The main outcome measures were the rates of implantation and clinical pregnancy. The implantation rate was calculated by dividing the total number of gestational sacs by the total number of transferred embryos. Clinical pregnancy was defined by the presence of a gestational sac on transvaginal ultrasound, 4 to 6 weeks after transfer. The ectopic pregnancy rate was a secondary outcome measure. Other outcomes included pregnancies per retrieval, spontaneous abortion, and ongoing and multiple pregnancies.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The methodology of each study was assessed according to the recommendations of Mulrow and Oxman (see Other Publications of Related Interest no.1). This included an assessment of the following: randomisation; explicit inclusion and exclusion criteria; similarity in baseline characteristics between groups; the technique of ZIFT and IVF-ET; the follow-up of patients; and the reporting of outcomes of patients. Two reviewers independently assessed the methodology of each study.

Data extraction
The authors do not state how many of the reviewers performed the data extraction.

When some outcome data were not presented, it was obtained through correspondence with the original authors, who reanalysed the original raw data. The odds ratio (OR) with 95% confidence intervals (CIs) were calculated for dichotomous data for each study. The data tabulated for each study included: study identification; sample size; the
number of stimulated cycles; the number of retrievals; and the number of transfers (tubal versus uterine).

Methods of synthesis
How were the studies combined?
A pooled OR and its 95% CI were calculated using the fixed-effect model of Peto (see Other Publications of Related Interest no.2), or the random-effects model of DerSimonian and Laird (see Other Publications of Related Interest no.3). The continuous outcomes were pooled using the weighted mean difference with 95% CIs.

How were differences between studies investigated?
The chi-squared statistic was used to test for heterogeneity using a significance level of P less than 0.10. Sensitivity analyses were conducted by excluding those studies thought to contribute to differences in the outcome measures.

Results of the review
Six randomised controlled trials with 458 participants (548 stimulated cycles, 514 retrievals, 181 tubal transfers, and 207 intra-uterine transfers) were included in the analysis.

Heterogeneity was found in only one outcome measure, namely pregnancy rate per transfer (P<0.08).

Implantation rates.
There was a total of 72 (15%) documented gestational sacs in 481 replaced embryos in ZIFT, and 63 (12%) in 523 replaced embryos in IVF-ET. The implantation rate between the two transfer methods was not significantly different (OR 1.25, 95% CI: 0.87, 1.8).

Pregnancy rate per transfer.
Sixty-six pregnancies (36.5%) resulted from 181 transfers in ZIFT, and 65 (31.4%) from 207 pregnancies in IVF-ET; the difference was not significant (OR 1.23, 95% CI: 0.8, 1.89). However, a chi-square test showed heterogeneity (as above). After removing one of the studies that used cryopreserved embryos, no heterogeneity was observed, but the results remained non significant.

Ectopic pregnancy.
Two (3%) of the 66 pregnancies in ZIFT were ectopic, compared with one (1.5%) of the 65 pregnancies in IVF-ET. While there was a trend towards a two-fold greater chance of having an ectopic pregnancy in ZIFT than in IVF-ET, there was no significant difference between the methods (OR 2.05, 95% CI: 0.21, 20.22).

The rates of pregnancy per retrieval, miscarriage, multiple, and ongoing pregnancy were comparable between tubal and intra-uterine transfers.

Authors’ conclusions
Published randomised trials suggested that there was no difference in the implantation and pregnancy rates between women undergoing ZIFT and IVF-ET.

CRD commentary
The review question and the inclusion and exclusion criteria were clearly presented. Only one database was searched for English language publications. It is possible, therefore, that some studies may have been missed. The validity of the included papers appear to have been adequately assessed, although the results of the validity assessment were not reported in detail. The information presented on the individual studies was lacking in detail, e.g. the characteristics of the participants, outcome measures, and results. The authors did not state how many of the reviewers selected the studies or extracted the data, although two reviewers were reported to have assessed the methodology of each paper. It is unclear why the authors used ORs or weighted mean differences to examine some variables (e.g. age, etiology of
infertility, stimulation protocol used, peak oestradiol level). Moreover, the authors presented only the overall results of various 'outcome' data in the format of a forest plot; these data were also (and more appropriately) tabulated. The primary studies appear to have been summarised appropriately, with consideration of clinical heterogeneity. The results appear to follow the conclusions, although the review would benefit from a detailed reporting of the quality of the included studies.

**Implications of the review for practice and research**

**Practice:** The authors recommend that patients should be counselled regarding the risk of ectopic pregnancy if ZIFT procedures are performed. Currently, a significant advantage of the use of the more expensive, inconvenient and invasive technique cannot be demonstrated. With the advent of improvements in culture techniques in the in vitro fertilisation laboratory, intra-uterine transfer remains the technique of choice.

**Research:** The authors state that for ZIFT to become a viable treatment option, subpopulations where its use may be of benefit will need to be identified.

**Bibliographic details**

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**Other publications of related interest**


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