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Single embryo transfer is the cheapest and most effective strategy for assisted reproduction

Transferring single embryos to women's wombs over several assisted reproduction cycles that use both fresh and frozen embryos is more effective and cheaper than transferring two or more embryos at one time, according to data from the world's longest running series of patients who choose to have only one embryo implanted per cycle – elective single embryo transfer (eSET).

The authors of the Finnish study published online today (Wednesday 25 March) in Europe's leading reproductive medicine journal *Human Reproduction* [1], say that their results effectively refute any concerns there have been up to now about the cost implications of an eSET policy and any fears that it could result in a lower rate of live births. In addition, it halves the rates of multiple pregnancies – the cause of potential medical complications and death for both babies and mothers.

Dr Hannu Martikainen, Chief Physician of the Division of Infertility and Reproductive Endocrinology at the University of Oulu, Finland, said: "This is the first study to evaluate the cumulative effect of fresh cycles with subsequent cycles using frozen-thawed embryos in a complete, consecutive (and therefore unselected) patient population over an extended period of time. Our study, thus, reflects eSET in everyday practice with an outcome measure consistent with what patients actually want: a live healthy baby achieved in a cost-effective way.

"We found that a baby born alive at term using eSET was, on average, 19,889 euros less expensive than babies born as a result of double embryo transfer."

The researchers, led by Dr Martikainen, compared the outcomes of IVF/ICSI cycles in two periods at their fertility clinic: 1995-1999 when eSET was rarely used (4.2% of women), and double embryo transfer (DET) was much more common (called the "DET period" for the purposes of this study), and 2000-2004 when eSET was used more widely (46.2% of women) – the eSET period.

Over the ten-year period, 1,510 women younger than 40 were treated at the infertility unit at Oulu University Hospital. They had a total of 2,386 cycles when fresh embryos were transferred, followed by 1,272 cycles when frozen-thawed embryos were transferred (FET). About 90% of deliveries in both periods occurred within the first four treatment cycles, suggesting that the time to delivery with eSET is no longer than that for DET.

The researchers found there was a significant difference between the DET and eSET periods in terms of effectiveness and cost. The cumulative pregnancy rate and cumulative live birth rate per egg retrieval ("ovum pick-up") and the cumulative live birth rate per

woman were all higher in the eSET period. Cumulative pregnancy rate per ovum pickup was 38.2% (eSET) versus 33.1% (DET), cumulative live birth rate per ovum pickup was 28% versus 22.5%, and cumulative live birth rate per woman was 41.7% versus 36.6%. In addition, the cumulative multiple birth rate was significantly lower in the eSET period (8.9% versus 19.6% in the DET period).

Dr Zdravka Veleva, from the same team, who is responsible for the economic analysis of the study, showed that the total treatment cost per woman in the eSET period was, on average, five per cent less than in the DET period (ranging from 2-20% less). In terms of euros, the total treatment cost per woman decreased by an average of 275 euros (ranging between 164-1184 euros) from the DET to the eSET period. When the researchers calculated the incremental cost-effectiveness ratio (ICER) [2] they found that 19,889 euros was saved per live baby born at term (after 37 weeks) in the eSET period compared with the DET period.

Dr Martikainen said: “There are few IVF centres in the world with greater experience than ours of eSET over such a long period of time. This study shows that the implementation of an eSET policy, together with an effective embryo freezing programme, results in a better outcome and lower treatment cost for women under the age of 40 having in vitro fertilisation, intra-cytoplasmic sperm injection (ICSI) or both. This refutes any concerns about the cost implications or efficacy of an eSET policy.

“At a time when there is an intense debate in many countries about how to reduce multiple pregnancy rates and provide affordable fertility treatment, policy makers should be made aware of our results. Hopefully this will encourage them to improve the reimbursement of assisted reproduction treatment, especially as it shows that a limit of only one reimbursed cycle will not necessarily result in lower costs once you take into account the far higher social and financial costs of treating the complications caused by multiple births arising from dual or multiple embryo transfer.

“These data should also encourage clinics to evaluate their embryo transfer policy and adopt eSET as their everyday practice for women younger than 40.”

In a second paper also published online in *Human Reproduction* [3], researchers in The Netherlands used a mathematical model to determine the “real world” cost-effectiveness of eSET, DET and combinations of these strategies. The model was based on a maximum of three consecutive IVF cycles.

Led by Dr Audrey Fiddelers, a clinical researcher and epidemiologist at the Academic Hospital Maastricht (The Netherlands), the researchers found that combining several different transfer policies (eSET, DET or standard treatment: eSET in good prognosis patients, with DET for the rest) was not cost-effective.

“A choice has to be made between three cycles of eSET, DET or standard treatment,” said Dr Fiddelers. “It is not cost effective to switch between these three treatment methods during the period of the three cycles of treatment.

“From a cost-effectiveness point of view, the choice of which policy to implement depends, however, on society’s willingness to pay. If society is willing to pay less than 7,350 euros for one extra live birth, then three cycles of eSET are to be preferred. If society is willing to pay between 7,350 and 15,250 euros, three cycles of standard treatment are to be preferred, and if society is willing to pay more than 15,250 euros per extra live birth, three cycles of DET are to be preferred. A policy of eSET would result in fewer live births than the other strategies, while a DET policy would result in more multiple births.”

Dr Fiddelers said that patients, practitioners and policy makers needed to consider more than just the cost-effectiveness when deciding which strategy to implement.

“If society is willing to pay more than 15,250 euros per extra live birth, three cycles DET are preferred from a cost-effectiveness point of view. However, in order to make proper conclusions on which strategy to choose, long-term costs and consequences of IVF singletons and twins should also be considered. Apart from the children born, the well-being of their parents and other family members should be considered. For example, involuntary childlessness could have an influence on the well-being of the couples, and a severely handicapped child may have a considerable impact on the well-being of both the parents and siblings, especially twin siblings. So, for a balanced approach with respect to the long-term costs and effects of eSET, STP or DET, all these issues should be considered,” she concluded.

(ends)

[1] Elective single embryo transfer with cryopreservation improves the cumulative live birth rate, diminishes the costs and reduces the multiple pregnancy rate of IVF/ICSI. *Human Reproduction*. doi:10.1093/humrep/dep042

[2] The incremental cost-effectiveness ratio (ICER) is a term used in cost-effectiveness analysis in health economics. It is defined as the ratio of the change in costs of a therapeutic intervention (compared to the alternative, in this case eSET versus DET) to the change in effects of the intervention.

[3] Cost effectiveness of seven IVF strategies: results of a Markov decision-analytic model. *Human Reproduction*. doi:10.1093/humrep/dep041

Notes:

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