Preimplantation genetic screening will play a dominant role in selecting embryos for single embryo transfer

Sir,

In a recent Editorial in this Journal, the Editor-in-Chief predicted that in the future single embryo transfer (SET) would be almost universally applied in IVF and that our successors, in the year 2020, would wonder how it could ever have been different (Barlow, 2005). To be successful, he admitted, this would require optimal stimulation, and the ability to select from a group of embryos with ‘reasonably valid’ assessment tools. He suggested a policy based on a Belgian model that used age, and the number of previous failed IVF cycles to determine when more than one embryo should be transferred (Ombelet et al., 2005). Some patients would still have two or even three embryos transferred. The Belgian model, or indeed any model with less than a strict SET policy for all, will not eliminate twin births or even triplet births due to IVF. The question of whether elimination of twin births due to IVF is desirable for all couples or would have an impact at a national level has been argued previously in this Journal (Dickey et al., 2004).

In the same Editorial, Barlow (2005) stated that preimplantation genetic diagnosis (PGD) and related procedures would have a clinical impact for only a minority of patients undergoing IVF. It is our opinion, based on 22 years of IVF experience, >10 000 infertility pregnancies from all types of treatment since 1977, and recent developments (Sermon et al., 2005; Wilton, 2005), that PGD and preimplantation genetic screening (PGS) will not only have a major impact on IVF in the future but are essential if SET is to become the standard of care. In the same issue of Human Reproduction Update in which the Belgian model was described, Wilton (2005) reviewed the current status of chromosome analysis of blastomers by comparative genomic hybridization (CGH). Using CGH, complete karyotyping at the single cell level can now be achieved. Also, chromosomal breakage, translocations and partial aneuploidies can be detected. At present, fluorescent in-situ hybridization (FISH) is used to detect the most common chromosome aneuploidies associated with birth defects and early pregnancy loss. Typically five (13, 16, 18, 21, 22) or nine (X, Y, 13, 14, 15, 16, 18, 21, 22) chromosomes are analysed for PGS (Sermon et al., 2005). Using FISH nearly all monogenetic disease, e.g. Tay–Sachs, Huntington’s disease, Fragile X syndrome, and others can now be detected on single blastomers.

Soon, technology will be available to IVF laboratories to determine all clinically significant human genes. It will be possible to determine that every embryo is normal before it is transferred and SET will then become standard for couples that desire single births. Already, DNA microarrays (Genome chip) are available on a research basis, to detect human genes associated with diabetes, obesity, hyperlipidaemia, prostate cancer, breast cancer, and a number of other conditions. New gene microarrays for additional diagnoses are being made available almost weekly.

These technological advances will present clinical and ethical dilemmas. Some patients, especially those who are older or have had repeated IVF failure, will have no normal embryos to transfer. Currently 5% of our IVF cycles include PGS for age or IVF failure, and 30% of these have no normal embryos. A large multinational series has reported similar results (Sermon et al., 2005). There will be a problem in some countries with discarding abnormal but potentially viable embryos. Eventually, in vitro genome therapy for some inheritable diseases may be possible and embryos could be cryopreserved until that time. Along with detection of abnormalities, it will be possible to determine somatic characteristics: height, eye and hair colour. How this ability will be used will have to be decided in advance. Perhaps the most common dilemma that will be encountered for SET is which sex to transfer when normal embryos of both sexes are available. This will not be a problem for patients who desire twins, who are healthy and who able to carry a twin pregnancy to ≥34 weeks.

The future for infertility couples requiring IVF has never been brighter. We believe the time when all embryos are evaluated by new advanced technologies before transfer is not 15 years in the future but 10 and possibly no more than 5 years away. Wise decisions will need to be made about how physicians and infertile couples use these technologies. At a minimum patients will be able to choose to have SET with the assurance that they will almost certainly become pregnant and that their baby will be normal. Ultimately decisions should be the couple’s alone, aided by consultation with geneticists and their personal physician. Governments should not intercede in their decision about the sex or number of their children.

References


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