Reducing multiple pregnancy from assisted reproduction treatment: educating patients and medical staff

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ABSTRACT

- Multiple pregnancy, with its adverse outcomes, is a significant problem in assisted reproductive technology.
- Single embryo transfer (SET) is the only feasible solution for reducing the rate of multiple pregnancy.
- Many patients and some clinicians remain to be convinced that SET is a better clinical option.
- Adequate education, based on available evidence, is one important way to promote the use of SET.

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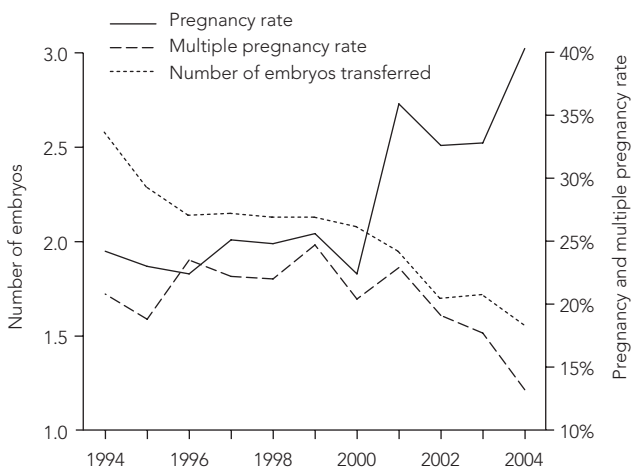
One of the major problems of assisted reproductive technology (ART) treatment is the high rate of multiple pregnancy. Based on the latest published Australian data in 2002, 18.3% of ART deliveries were twins and 0.6% were triplets.[1] The risk of adverse outcomes is much higher for both pregnant women and children born from multiple pregnancy. As the chance of multiple pregnancy from in-vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI) is directly associated with the transfer of multiple embryos, single embryo transfer (SET) in IVF/ICSI cycles has been strongly promoted as the most effective means of reducing the occurrence of twin and high order multiple pregnancy. One recent randomised trial has shown that elective SET and, if needed, subsequently transferring one frozen-thawed embryo, can achieve a similar pregnancy rate and live birth rate as double embryo transfer.[2]

In Australia, there are voluntary clinical guidelines to promote the use of SET in several IVF clinics. Some countries have mandatory legislation. For example, in Belgium, the introduction of a new law increased SET from 14% to 49% of IVF/ICSI cycles, providing a significant decrease in the twin pregnancy rate without affecting the overall pregnancy rate.[3] In Australia, the accreditation system operated by the Fertility Society of Australia (Reproductive Technology Accreditation Committee, RTAC) requests clinics generally transfer no more than two embryos in one treatment cycle. Many clinicians would transfer two embryos per cycle, although SET has been proposed as the better clinical option.[4] Despite increased attention to the risk of multiple births in patient information and counselling practice, many Australian IVF clinics and a large proportion of patients continue to choose double embryo transfer. In 2002, less than 30% of Australian women undergoing IVF received a single embryo transfer per IVF cycle.[1] Although this proportion will almost certainly have increased in the past few years, the implantation rates (the chance of an embryo implanting in utero and initiating a pregnancy) have improved greatly in many IVF clinics following the introduction of new culture techniques, and this leads to a high likelihood of twin implantation with double embryo transfer. The prevalence of twin pregnancy will be significantly reduced only when the use of SET is also substantially increased. Box 1 indicates that pregnancy rates have improved while fewer embryos per cycle have been transferred.

Information on the chance of pregnancy and risk of possible adverse outcomes, in a form that is easily understandable, is essential for patients' treatment decision-making process. The choice is often dependent upon their understanding and acceptance of the information.[5] Clinicians usually respect patient preference for treatment options, especially within the guidelines. The multicentre Australian study of SET had to be stopped because of the difficulty in recruiting patients, largely caused by their reluctance to be randomised once adequate information had been provided. At the same time, clinicians have great influence on patients' choice depending on how they interpret the existing evidence. There may be a tension in the consideration between the safety and long-term benefits to children and the desire for achieving a pregnancy in a treatment cycle. Patients often accept or even desire twins, possibly because of the desire for pregnancy and reduction of the cost and inconvenience of IVF, and only realise the extra burden of twins on their life later.[6] Some may even like to reach the objective of a complete family in one treatment cycle through the birth of twins.

1 Trends in pregnancy rates and number of embryos transferred*



* Mean number of embryos transferred per cycle, and pregnancy and multiple pregnancy rates (%) at an Adelaide IVF clinic (Repromed). ◆

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2 Risk of some major pregnancy and obstetric outcomes for twins conceived by assisted reproduction technologies compared with singletons, based on 2002 Australia data[1]

	Singleton	Twin
Birth weight (g)	3279	2379
Low and very low birth weight	8.2%	48.4%
Gestation (weeks)	38.4	35.0
Caesarean section	42.4%	71.1%
Perinatal mortality (per 1000 births)	10.9	29.3

For many, there can be a genuine lack of appreciation of the risk of multiple pregnancy and its consequences. It is not enough just to inform patients about the chance of twin or multiple pregnancy — it may be necessary to provide information to patients about the increased risk of serious complications, like cerebral palsy. It is unclear whether information can change patients' choice, as one study failed to show that additional information had increased patients' acceptance of elective SET.[7] Our own experience in recruiting patients for a SET trial indicated that provision of detailed information on the risk of twins and associated adverse outcomes may have contributed to the increase of 17% SET in 2001 to nearly 50% SET in 2004 in our patient population.

Education of clinicians is equally important, as patients are strongly influenced by both the official policy of the clinic and the clinicians' advice. Medical personnel have a good knowledge of increased risk of adverse outcomes of twins (Box 2). Although outcomes are similar for twins conceived by ART and naturally conceived twins,[8] it is clear that twins conceived by ART have much poorer outcomes than singletons conceived either naturally or by ART. One study of more than 700 ART twin pregnancies in Australia showed that the perinatal mortality rate for the twins was much higher than for singletons conceived by ART (44.8 v 11.7 per 1000 births).[9] Some recent publications have highlighted particular risks in twins conceived by ART, such as high discordant birth weight and increased admissions to neonatal intensive care units.[10] Growing evidence suggests that the high rate of in-utero death in a twin pregnancy or vanishing twins (around 25%)[9] as a result of double embryo transfer may be a cause of adverse outcome in singletons conceived by IVF.[11] More important for infertility clinics and many clinicians is the gradual accumulation of quality evidence that elective SET can achieve the same pregnancy rate as double embryo transfer in patients who have good prognosis. Therefore, promoting SET does not jeopardise patients' chance of achieving pregnancy. Elective SET is substantially cheaper in health economic terms than double embryo transfer in women younger than 38 years in their first IVF/ICSI cycle when maternal, neonatal and total costs are considered.[12]

For both patients and clinicians, the chance of achieving a pregnancy is a major determining factor when considering the number of embryos to be transferred. Pregnancy rate per cycle is an important indicator of treatment efficacy, and most patients can comprehend it clearly. However, with the relatively generous Medicare cover in Australia for multiple cycles of ART, many couples undergo more than one treatment cycle, including frozen embryo transfers, leading to the observation that the overall chance of achieving a successful pregnancy over the course of treatment is more relevant. A positive long-term view based on cumulative pregnancy rates may encourage patients to accept SET.

Communicating evidence for effective patient participation in decision-making is a key issue in the patient–physician relationship and the practice of evidence-based medicine.[13] There should be a full appreciation of the risk of twins and promotion of SET as the solution by clinicians. To improve the education of both patients and clinicians, further research is needed to study the process of patient decision-making to evaluate the influence of various types of medical information, including the content and style of medical advice, on this process.

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Competing interests

Michelle Lane and Robert Norman are involved in the delivery of an assisted reproduction service. Jim Wang is involved in research using data from an assisted reproduction service.

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