DEBATE

Prevention of multiple pregnancy in ART

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Since several years back now, we have seen very convincing evidence from many studies to show that triplets or more after ART carries with them a very substantial increase of perinatal mortality and of short and long term morbidity. In addition we also know that the psycho-social consequences often are huge.

Twins carry with them similar problems at a significant but somewhat lower scale. The mothers suffer from a large increase of obstetrical complications.

At the recent ESHRE Annual Meeting in Copenhagen, two additional strong reasons to avoid at least high order of multiple pregnancy after ART were presented.

First, the economy. Two reports, one from the Nordic countries and one from France clearly demonstrated that the total cost, including cost for deliveries and post-natal complications, were very much higher with a clinical policy leading to high proportions of multiples. The myth, therefore, that multiples would help reducing cost is totally false because it does not include cost for complications.

Second, national statistics showing the feasibility of a national policy of a high proportion of elective single embryo transfers (e-SET). National data from Finland and Sweden and also from Belgium now show, with treatments during 2004, that a high proportion of e-SET (over 50%) is proven to be compatible with a continuously high pregnancy rate per embryo transfer in fresh cycles (over 30%) leading to a substantial decrease of multiple deliveries to now below 10% of twins and virtually no triplets.

The conclusion is, that high order of multiple pregnancy after ART, can no longer be defended by economical evidence or evidence of low effectiveness.

A shift over to a clinical policy to avoid high order of multiple deliveries and to at least to decrease the proportion of twins is therefore only logical.

How can that be achieved, in clinical practice? Several suggestions put forward may be summarized as follows:

1. Select, for e-SET, women under 38 years of age, during their first (and possibly second) IVF cycle.
2. Select, for e-SET, women with an obstetrical increased risk with multiple gestation.
3. Stimulate for 10-12 eggs, at aspiration.
4. Transfer the best embryo and freeze the other suitable embryos one by one. Transfer them one by one.
5. Use high quality freezing equipment and monitor transfer cycles closely.
6. To present success, use combined fresh and frozen delivery rates, i.e. delivery rates by aspiration procedure.
7. Transfer 2 embryos otherwise, but never three.
8. Convince your staff and your patients that such a policy is founded on very sound evidence, and is in the best interest of all parties involved, and that it is not counter productive for efficacy or cost.

Are there any negative sides to such a policy?

1. Q: Is it more cost-effective with multiples?
   A: No, it is not. It may appear so, in the ultra-short term, if only direct treatment cost is included, but
in a longer perspective that is not at all true.

2. Q: Do multiples save time for the couple to achieve their reproductive goal for a larger family? 
A: Only marginally so. And it saves quality of life for children and families alike.

So, all evidence available on
a/ medical risks,
b/ psycho-social problems,
c/ economy and
d/ feasibility for effectiveness 
all speak the same language: A shift in clinical policy to avoid, totally, high order of multiple pregnancy (triplets or more) and to decrease the proportion of twins is logical, rational and beneficial to all parties involved.

REFERENCES


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Women undergoing in vitro fertilization (IVF) have been shown to have a higher percentage of twin, triplet and even higher order deliveries than their non-IVF counterparts. This has even been estimated to reach as high as a 20-fold increased risk of twins and a 400-fold increased risk of high order pregnancies (1). ART surveillance on multiple pregnancy rates in the USA, for the years 2000 and 2001, demonstrated that the twin deliveries rates were 44% and 46%, respectively (2, 3). In addition, the triplet and higher deliveries rate were 9% and 8% respectively. Also, the European ART registry for the same years reported twin deliveries rates at 24.4% and 24% and the triplet delivery rates at 2% and 1.5% respectively (4, 5). Furthermore, the Middle East IVF registry for the year 2000 (6) reported a twin deliveries rate of 27% and triplet and higher deliveries rate of 5%. It has been well recognized that multiple pregnancy is associated with an increased risk of maternal and perinatal morbidity and mortality (7 - 9). Preventative measures to reduce the multiple pregnancy rate include: a) soft ovulation induction, b) reducing the number of embryos per embryo transfer, c) optimizing embryo cryopreservation, and d) secondary prevention by multifetal pregnancy reduction as a back-up procedure.

One of the most important factors affecting the multiple delivery rates is the number of embryos transferred per cycle. Most European centers now have moved away from the traditional three-embryo to a new two-embryo transfer policy. Consequently, triplet rates have fallen, however, the twin rates still remain almost unchanged (4).

In the USA, from 1995 to 2001, the average number of embryos per transfer began decreasing in 1997, with an 11% decrease between 1998 and 1999. In contrast, the number of live birth per cycle has steadily increased. Furthermore, even though the rate of twin pregnancies did not change significantly, the multiple pregnancy rates with three or more has significantly decreased; with a marked decline of 20.8% between 1998 and 1999 (10).

The residual problem is how to decrease this high rate of twin pregnancies (25 - 45%). Obviously, a strategy using single embryo transfer would eliminate the problem of a high twin pregnancy rate. Even though, some important questions still remain to be answered about the single embryo transfer before it becomes the standard: a) Will it lower the overall birth rate? b) Who is at a significant risk for twin pregnancy? c) What are the definite criteria to select the best embryo? d)