LETTERS TO THE EDITOR

Final-ART success rates: a 10 years survey

Sir,

We would like to congratulate Gnoth et al. (2011) on their recent paper, stressing the point that consecutive ART treatments may result in a high cumulative live birth rate (CLBR), as long as the couple and physician are confident in continuing treatment.

To prevent confusion, we would like to point out that blastocyst culture was never forbidden in Germany. However, ongoing culture of more pronucleate embryos than intended for transfer (maximum of three) is not allowed.

One should be aware that inclusion only of couples entering assisted reproduction treatment (ART) and those coming for subsequent treatment after a birth will have a favorable influence on the outcome. The assumption that patients discontinuing the treatment after failure to conceive have the same chances of conceiving in any given cycle if they proceed being treated, may be considered optimistic; a fact acknowledged by the authors. Individual counseling about chances will always be based on an estimation.

Gnoth et al.’s data have to be interpreted cautiously and cannot necessarily be extrapolated to other countries with different health insurance systems and embryo protection laws.

For instance, in Germany the national health system covers half the costs of three ART treatments, in couples with private insurance up till six attempts. This may facilitate the decision to see a specialist and start a cost-intensive treatment, more so than in countries where there is no reimbursement of costs.

On the other hand, just 10% of all Germans are insured privately, 90% are covered by the national health system and, as stated by the authors, a large proportion of the ART couples underwent three cycles, with a CLBR of ~50%. The comparison of ART and natural cycles seems to be critical as the proportion of couples that stopped treatment after three cycles due to financial reasons can be considered to be high (although unknown). This cost variable could have a strong impact on the shape of the Kaplan–Meier curve of ART patients but not on the curve of the natural cycle patients.

Furthermore, cryopreservation in Germany is supposed to take place in the pronucleate stage, which will give rise to lower pregnancy rates in a cumulative consideration than, e.g. vitrified blastocysts. As indicated by the authors, cryopreservation and storage is not paid for by any insurance. We consider that it would be worthwhile to start a prospective RCT to investigate cumulative pregnancy rate/birth rate in couples with frozen—thawed pronucleate embryos versus cleavage stages embryos, compaction or blastocysts.

In making these calculations, one has to be aware of considerable fertility center hopping, which makes it difficult to appreciate the whole picture. The dissatisfied tend to discontinue treatment and admission policies of new couples and age limits will change the cohort.

Finally, the number of embryos upon transfer strongly influences the number of cycles needed to treat in order to obtain a live birth.

Comparing CLBR from natural conception cycles, assumed the couples will keep on trying to conceive, with couples continuing ART treatment, proves a filtering effect of the observation and therefore disapproval of the Kaplan–Meier hypothesis.

ART cannot solve all (sub)fertility problems, especially not the general tendency to postpone the implementation of the wish to start a family.

Reference


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Reply: Final-ART success rates: a 10 years survey

Sir,

We appreciate the comments of our colleagues Scholtes et al. on our paper ‘Final-ART success rates: a 10 years survey’ published in Human Reproduction 2011 (Gnoth et al., 2011).

We confirm that blastocyst culture was never forbidden in Germany, but blastocyst culture for embryo selection is not allowed and the legal restrictions and their interpretation are currently a matter of intensive discussions, for which our paper is important.

We also agree with Scholtes et al. that because of the nature of Kaplan–Meier estimations, an individual counselling of the couples is always necessary.

Different national restrictions and different national reimbursement situations influence decisions of couples to start or continue a cost-intensive treatment. Hence it is astonishing that, in spite of all formal and therapeutic differences, the cumulative birth rate compared with a single centre in the USA is nearly the same! This points to general biological and interventional limitations of ART which is also supported by the fact that comparable pregnancy rates are seen after ART and natural conception.

The efficiency of cryopreservation at the pronucleate stage in comparison with vitrified blastocysts is still a matter of scientific discussion.

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