Developmental capacity and pregnancy rate of tetrahedral- versus non-tetrahedral-shaped 4-cell stage human embryos

T. Ebner · P. Oppelt · R. B. Mayer · O. Shebl

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Dear Editor,

With great interest we read the recently published study of Cauffman et al. [1] dealing with the developmental fate of 4-cell embryos depending on the arrangement of their blastomeres.

Although this manuscript is discussed in great detail carefully addressing current scientific knowledge we have the feeling that our data [4] have been somewhat misinterpreted. As Paternot et al. [5] noted correctly our working group focused on a particular subgroup of non-tetrahedral embryos characterized by presumed incomplete cleavage resulting in a tetrafoliate-clover shape, as being depicted in Fig. 2 (left image) of the Cauffmann paper [1]. This fact nicely explains why the frequency of “planar embryos” in our prospective analysis was only 3 % as compared to 21 % in other studies [5, 1]. In this context we would like to state that neither our hypothesis of an involvement of the male centrosome nor the finding that the vast majority of clover-shaped embryos were found to be aneuploid apply to regular non-tetrahedral cleavage caused by two consecutive equatorial or meridional cleavages. It would be interesting to see whether the large data set of Cauffman et al. [1] reveals a potential paternal influence if re-analyzed under this premise.

Speaking of re-evaluation, the existence of natural cycles in the present study [1] would have allowed working out a possible difference in growth pattern in contrast to stimulated cycles. Obviously, there is actually no difference in the performance of the embryos between long and antagonist protocol [1]. In addition, Paternot et al. [5] did not find a correlation between the presence of a non-tetrahedral day-2 cleavage pattern and the

type of culture medium. In fact the embryo quality was identical irrespective of the fact whether the authors used a sequential medium (Cook medium, Sidney IVF, Australia) or a global one (GM501, Gynemed, Germany). Since Cauffman et al. [1] used three alternative sequential media but failed to present the pertaining data re-evaluation of their data might shed some light on this interesting aspect. However, although the generation of non-tetrahedral embryos more or less is sufficiently explained by the altered orientation of the cleavage planes (Fig. 1; [1]) as well as by a failed shaping function of the zona pellucida [2, 3] any influence of controlled ovarian hyperstimulation or culture conditions on embryo cleavage is still under debate.

It seems that there is consensus that non-tetrahedral embryos have an impaired in vitro development as assessed by rates of top quality embryos and/or blastulation [4, 1, 5]; however, any potential negative impact on treatment outcome is discussed controversially [1, 5]. This might in part be due to the retrospective character of such studies but most likely these authors had a higher risk of comparing apples and oranges since they pooled all types of planar embryos for analysis [1, 5].

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T. Ebner (✉) · P. Oppelt · R. B. Mayer · O. Shebl
Department of Gynecological Endocrinology and Kinderwunsch
Zentrum, Landes- Frauen- und Kinderklinik, Krankenhausstr. 26-30,
4020 Linz, Upper Austria, Austria
e-mail: Thomas.ebner@gespag.at