The mental, motor, socio-emotional and language development of 2-year-old twins born after PGD/PGS and parental well-being

Sir,

In this letter, we would like to update readers of Human Reproduction on the development of twins born after embryo biopsy in addition to the articles published on PGD/PGS singletons by our research group (Nekkebroeck et al., 2008a,b; Desmyttere et al., 2009). In our studies, 2-year-old singletons born after embryo biopsy applied in PGD/PGS present similar prenatal and early postnatal linear growth compared with ICSI children and naturally conceived (NC) children and appear not to be at higher risk of congenital malformations and surgical interventions (Desmyttere et al., 2009). Moreover, reassuring results were found as to the mental, motor, socio-emotional and language development of 2-year-old PGD/PGS singleton children compared with ICSI and NC children and the well-being of their respective parents (Nekkebroeck et al., 2008a,b). Convinced of the importance to assess all 2-year-old PGD/PGS children (singletons as well as twins) at the time of recruitment, 16 PGD/PGS twins were assessed and compared with 16 ICSI twins and 15 NC twins for mental, motor, socio-emotional and language developmental outcomes and parental well-being. Data obtained from this small sample are reported here and are so far, the only indicators on PGD/PGS twins’ neurodevelopment and psychological well-being.

PGD/PGS (and ICSI) twins were recruited from the register of the Centre for Medical Genetics of the UZ Brussel. Of the 30 PGD/PGS twins who were 2 years of age at the time of assessment 19 twins met the inclusion criteria and 16 participated in the study resulting in a participation rate of 84%. The participation rate was 94% in the ICSI group (n = 16 twins) and 75% in the NC group (n = 15 twins). For a more detailed description of the methodology, we refer to the studies on singletons by Nekkebroeck et al. (2008a,b) since the procedure and the outcome measures that were used are identical. However, the statistical analyses were adapted. As our data have a nested structure—individuals are clustered into twin couples; the dependence of the within-cluster data and the estimation of within-cluster and between-cluster variance and covariance require multilevel analyses (Raudenbush and Bryk, 2002). In a first step we estimated and tested a one-way analysis of variance with random effects with the aim of determining the proportion of within cluster (twin) variability and the proportion of between cluster variability of each outcome variable. In the second and final step, a full model was tested in which both at the within cluster level and at the between cluster level all relevant predictors were included in order to test the effect of mode of conception on the dependent variable after controlling for the covariates. A significance level of 0.05 was accepted throughout. The results are summarized in Table I and show that conception after embryo biopsy in the case of PGD and PGS has no adverse impact on the mental, motor, language or socio-emotional development of 2-year-old twins when compared with ICSI and NC twins or for that matter on the well-being of their respective parents as expressed in parenting stress levels and general health measures. However, significant conception group effects were found in which the control groups (ICSI, NC) deviated from each other or in which one of the control groups deviated from the other two conception groups. However, the PGD/PGS group never deviated on its own from both control groups together. For language development significant conception group effects favouring the assisted reproductive techniques (ART) conception groups were found for the number of words understood and produced. Where motor development is concerned, the ICSI twins scored lower than the two other conception groups. However, the results need to be put in perspective, since none of the average scores in any of the three conception groups fell within a clinical range, which suggests that most of the children in all three conception groups display normal language and motor development. Another important finding is that the mothers and fathers of the ICSI twins reported that their children had fewer emotional/behavioural problems, especially externalizing behavioural problems. This finding is in accordance with the findings in our previous study on ICSI singleton children (Nekkebroeck et al., 2008b) in which ICSI mothers and fathers reported fewer externalizing behaviour problems in their offspring than did the PGD/PGS and NC parents. The mothers in the NC group reported lower than average temperament scores in their twins than did the mothers in the PGD/PGS and ICSI conception groups. Again, the scores in all three conception groups were within the average range (2.71–3.93). The ICSI mothers reported fewer ‘mental health problems’ than the mothers in the NC and PGD/PGS conception groups. For ‘parenting stress’, no differences between the mothers and fathers in all three conception groups were found.

Although results are reassuring some major limitations need to be considered. Participation rates were high but sample sizes remained very small and the return of some questionnaires was relatively poor. Therefore, the generalizability of our findings is limited, and the results need to be interpreted with caution and are of a preliminary nature. Moreover, the twins were assessed using a test of developmental abilities whereby the predictability for later intellectual and motor functioning remains inconclusive. Continuing assessment at later ages is therefore essential. Unfortunately, twins have often been excluded from ART child follow-up studies because of possible...
confounders (e.g. prematurity and birthweight) that might interfere with developmental outcome (Miceli et al., 2000). On the other hand, ART are associated with high rates of multiple pregnancies, and this is also true in the case of PGD/PGS (Harper et al., 2008). Therefore, this large proportion of the ART child population, one that moreover is more prone to neonatal complications that may lead to long-term neurodevelopmental problems (Olivennes et al., 2005), deserves special attention and should be investigated independently from singletons. We hope to encourage other centres involved in ART child follow-up to report on data obtained from ART twins. Since these results are obtained from a single-centre study mainly focussing on singletons, confirmatory investigations are strongly needed involving other centres so larger cohorts of twins at later ages can be assessed.

### References


### Appendix

Letter to the Editor


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