The prevention of hereditary breast and ovarian cancer by PGD is 'feasible'

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Preimplantation genetic diagnosis (PGD) for the breast cancer genes BRCA1/2 is now feasible and established, with good success rates for those treated, according to investigators from the reproduction, oncology and genetics centres of the university hospitals of Maastricht and Brussels. The results follow a review of the largest number of PGD treatments for BRCA1/2 in Europe and were presented today at the annual meeting of ESHRE (European Society of Human Reproduction and Embryology) by Professor Willem Verpoest from the Centre for Reproductive Medicine at Vrije Universiteit Brussel, Belgium.

Behind his vote of confidence lie 145 PGD cycles for BRCA1/2 mutations performed in 70 couples at the two centres (a mean of 2.1 cycles per woman). Almost 60% of the mutation carriers were female, two-thirds with a BRCA1 mutation. Just over one quarter (26.2%) of female carriers had undergone a prophylactic bilateral mastectomy.

Following IVF, 717 embryos were found suitable for genetic analysis, and of these 43.1% were diagnosed as affected by the mutation, with 40.7% unaffected and thus suitable for transfer (the remainder had an abnormal genotype or the analysis was inconclusive). Hence, 62.1% of the PGD cycles led to fresh embryo transfer - with 3.6% transferred from one or two frozen-thawed unaffected embryos - resulting in 42 pregnancies in 40 women. Pregnancy rates were 41.4% per fresh embryo transfer and 23.1% per frozen. The overall pregnancy rate was 29%.

The series also included three cases of PGD on embryos previously

cryopreserved for fertility preservation prior to chemotherapy, and these too resulted in two ongoing pregnancies.

Two female BRCA1 carriers were diagnosed with breast cancer within three months of the PGD treatment, despite breast screening shortly before treatment. One had a history of breast cancer, the other patient hadn't. The former patient went on to have healthy twins three years after the second breast surgery and chemotherapy, and following frozen/thawed embryo transfer.

So far, PGD for BRCA1 and BRCA2 gene mutations has been considered controversial. While most PGD procedures are indicated to remove completely the risk of inherited sex-linked and single-gene diseases (such as cystic fibrosis) in the children of affected couples, PGD for the breast cancer mutations cannot remove the risk completely - because the 10% background risk of breast cancer remains, even after PGD. Moreover, breast and ovarian cancers are usually of late onset, with prevention and therapeutic options constantly improving - so the chances of successful treatment, and many years of healthy life, are high.

Nor is breast cancer inevitable for a woman (or man) carrying a BRCA1/2 mutation. The controversy thus rests on the fact that a mutation in the BRCA genes increases susceptibility to breast or ovarian cancer, but does not reflect an inevitability for developing the diseases. However, with female carriers of a mutation in either gene having a lifetime risk of 60-80% for breast cancer, and a risk of 30-60% (BRCA1) or 5-20% (BRCA2) for ovarian cancer, many authorities have recognised the gravity of the risk and accepted a BRCA gene mutation as an indication for PGD.

So far, only five pregnancies after PGD for BRCA1/2 have been reported since the first was described in 2008.(1) The slow uptake

reflects not just the controversial nature of the procedure, but also concerns over patient selection and the safety of hormonal stimulation for IVF in women at risk themselves of breast and ovarian cancers.

Professor Verpoest emphasised that the results, representing by far the biggest series of PGD for breast cancer in Europe, are robust, with a good unaffected pregnancy rate.

"We now believe that this technique offers an established option for those couples seeking to avoid the risk of inherited BRCA in their children," he said. "However, although there is no evidence of increased carcinogenesis in patients having ovarian stimulation for PGD in this population, the screening and monitoring measures - as well as multidisciplinary management - must still be in place.

"Our results suggest that PGD for BRCA1 and 2 mutations is feasible, with a good treatment outcome, but controversy will still remain over the ethical acceptability of PGD for a susceptible - yet preventable - condition."

More information: 1. See news.bbc.co.uk/1/hi/health/7792318.stm

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