Preimplantation Genetic Testing for monogenic disorders in transport service

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Introduction

In vitro fertilization … through ICSI.

Genetic diagnosis … either by performing PCR or SNP array.

Transfer to the women’s uterus … of one or two genetically transferable embryos.

Embryo biopsy … either at day 3 (1 or 2 blastomeres) or day 5/6 of development (4-8 trophectoderm cells).

Ranking of embryos … in genetically transferable or genetically not transferable.

Figure 1. Overview of the steps regarding a PGT clinical cycle: ICSI intracytoplasmic sperm injection.

Materials & Methods

This is a combined retrospective and prospective cohort analysis of transport PGT-M from January 2006 until February 2021. Data were collected on patient inclusion, genetic indications, preclinical workup, and clinical cycle outcome. Figure 2 shows an overview of the cycles initiated.

The biopsy/genetic testing strategy was either targeted PCR-based testing of single blastomeres (2-cell biopsy), removed on day 3 of embryonic development, or genome-wide SNPArray-based testing of few trophectoderm cells, biopsied on day 5 or 6 of embryo development. Targeted testing was already available in 2006, while genome-wide testing became possible from 2015.

Figure 2. Overview of the cycles initiated. LBDR: live birth delivery rate.

Preimplantation genetic testing (PGT) is a procedure based on the diagnosis of in vitro fertilized embryos prior to their transfer, thus avoiding the transmission of genetic disorders (Fig. 1). It is subdivided into three categories – PGT for monogenic disorders (PGT-M), PGT for chromosomal structural rearrangements (PGT-SR) and PGT for aneuploidies (PGT-A).

Transport PGT is an adaptation of the conventional way – embryos are biopsied in a satellite IVF center and the biopsy cells samples are transported to a specialized genetic unit for testing. A transport service between the Genetics Department of Faculty of Medicine in University of Porto and the Center of Medical Genetics of UZ Brussel has been in place since 2006.

Aim

The main aim of the project is to compare, for specific parameters, day 3 biopsy/targeted testing with day 5/6 biopsy/genome-wide testing in transport service.

A secondary aim is to compare this cohort of transport cycles with other datasets (in-house and ESHRE PGT consortium).

Results

Since 2006, 284 couples have requested PGT treatment in transport service. More than half of the indications for PGT-M were autosomal dominant (AD) diseases, followed by 22 % of autosomal recessive (AR) indications (Fig. 3). This is in line with data of the ESHRE PGT consortium (64 % AD, 21 % AR and 15 % X-linked). The most common AD indication for these patients was polycystic kidney disease, which was unexpected - the top five PGT-M indications requested in Europe are Huntington disease, followed by Cystic Fibrosis, Neurofibromatosis, Breast-ovarian cancer and Myotonic dystrophy (unpublished data).

Test diagnosis efficiency, based on the percentage of embryos with a diagnosis, is statistically different between test strategies (p = 0.006) (Fig. 4). Failure of amplification is the main cause for the significant higher percentage of embryos without diagnosis tested with the PCR-based strategy compared with the SNP array strategy. Other causes of no diagnosis such as ADO, contamination or recombination were not significantly different between both test strategies (results not shown).

For the 166 couples that started a clinical cycle (n = 377 cycles), 297 embryos were transferred, which resulted in 42 term pregnancies, and 47 babies. The live birth delivery rate for this cohort was statistically not different between test strategies (20.5 % for PCR-based diagnosis and 30 % for SNPArray-based diagnosis).

Conclusion

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References


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