NONINVASIVE PREIMPLANTATION GENETIC TEST FOR ANEUPLOIDY (NIPGT-A) X INVASIVE PGT-A: LESS INVASIVE, LOWER FALSE POSITIVE RATE

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Introduction: Recently, a new technology (niPGT-A) has arisen using cell-free DNA present in the spent culture media of human blastocysts. Unlike invasive PGT-A that uses only trophoblastic cells, niPGT-A reflects the ploidy status of trophoblastic cells and inner cell mass, suggesting that this new technology could be less prone to errors, being more reliable than invasive test. This study aimed to compare the results of plody embryo analysis from niPGT-A and PGT-A

Material and Methods: This cohort study included a total of 56 blastocysts vitrified on day 5 that were previously biopsied for invasive PGT-A and presented a diagnosis of aneuploidy. The embryos were donated under informed consent by patients following the Human Medical Authority regulations. Blastocysts were thawed and cultured in 15µl drops of culture medium under oil. After their expansion (4-8hours), the blastocysts were transferred to NGS tubes and their corresponding spent media were collected for analysis.

The DNA of all samples (spent culture medium and whole embryo) was amplified by the MALBAC. Technology (Yikon Genomics). The samples were subjected to next-generation sequencing (NGS) using Illumina MiSeq. System. The ploidy status results obtained from ChromGo™ software (Yikon Genomics) for culture medium and whole embryo were compared to determine the accuracy of niPGT-A for screening chromosomal abnormalities in each embryo.

Results: DNA from all 56 spent media samples and whole embryos were successfully amplified. Comparing the results of NIPGT-A (abnormal=46) and whole embryos sequencing, the positive predictive value (PPV) was 93.5% and the false positive rate (FPR) was 6.5%. On the other hand, comparing the whole embryo and invasive PGT-A results (abnormal=56), the PPV was 76.8%, and the FPR was 23.2% (p=0.01; Fisher test)

Table 1. NIPGT-A and Invasive PGT-A results

| Whole embryo | | | | Whole embryo | |
|------------------------|------------|--------|-------------------------|--------------|--------|
| niPGT-A | Aneuploidy | Normal | iPGT-A | Aneuploidy | Normal |
| Abnormal | 43 | 3 | Abnormal | 43 | 13 |
| Normal | 0 | 10 | Normal | 0 | 0 |
| PPV:93.5% / FPR = 6.5% | | | PPV:76.3% / FPR = 23.1% | | |

Conclusion: niPGT-A has a lower FPR than invasive PGT-A and does not require micromanipulation skills, avoiding trophectoderm biopsies trauma and seems to provide more accurate results corresponding to the ploidy status of the whole embryo.