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Noninvasive preimplantation genetic testing for aneuploidies (NIPGT-A) x Preimplantation genetic testing for aneuploidies (PGT-A): NIPGT-A IS MORE RELIABLE THAN PGT-A

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INTRODUCTION

After many years of using PGT-A, there are still many concerns, such as risks of invasive action and difficulties in the correct interpretation of mosaicism, which could lead to errors in the interpretation of false-positive and false-negative results. Recently, a new technology (NIPGT-A) has arisen using cell-free DNA present in the spent culture media of human blastocysts. Unlike 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 and thus more reliable than invasive tests.

STUDY QUESTION

Does NIPGT-A have lower false-positive rates (FPR) than PGT-A?

METHODS

This multicentric cohort study included a total of 56 blastocysts vitrified on day/5 that were previously biopsied for PGT-A(all these embryos presented a diagnosis of aneuploidy). The embryos were donated under informed consent by patients following the Human Medical Authority regulations.

Table 1. NIPGT-A X Whole Embryo: results

NIPGT-A	Whole Embryo		
	Aneuploid	Euploid	Total
Aneuploid	43	3	46
Euploid	0	10	10
Total	43	13	56

PPV: 93.5% FPR: 6.5%

Blastocysts were thawed and cultured in 15µL drops of culture medium under oil. After their expansion(4-8hours), the blastocysts and their corresponding spent culture media were transferred to PCR tubes and stored at -20ºC until analysis. The DNA of all samples (spent culture medium and whole embryo) was amplified by the MALBAC® technology (Yikon Genomics). The DNA concentration of the amplified product was measured using Qubit 3.0 Fluorometer (Thermo Fisher Scientific). The samples were subjected to next-generation sequencing (NGS) using Illumina MiSeq® System. The ploidy status results obtained from ChromGo™ software (Yikon Genomics) for spent culture medium and whole embryo were compared to determine the accuracy of NIPGT-A for screening chromosomal abnormalities in each embryo.

Table 2. PGT-A X Whole Embryo: results

PGT-A	Whole Embryo		
	Aneuploid	Euploid	Total
Aneuploid	43	13	56
Euploid	0	0	0
Total	43	13	56

PPV: 76.8% FPR: 23.2%

RESULTS

DNA from all 56 spent culture media samples and whole embryos were successfully amplified. Comparing the results of NIPGT-A and whole embryos sequencing, the positive predictive value (PPV) was 93.5% and the FPR was 6.5% (**Table 1**). On the other hand, comparing the whole embryo and PGT-A results, the PPV was 76.8%, and the FPR was 23.2% (**Table 2**). NIPGT-A had a negative predictive value (NPV) of 100% and a false negative rate (FNR) of 0%.

CONCLUSION

When DNA from whole embryo cells was used as the gold-standard, the FPR of NIPGT-A was 3.57-times smaller than that obtained with PGT-A.NIPGT-A has a lower FPR than PGT-A and does not require micromanipulation skills, avoiding trophectoderm biopsy trauma and seems to provide more accurate results corresponding to the ploidy status of the whole embryo. Thereby NIPGT-A should be considered as the test of choice for genetic evaluation of the embryo.