Non-invasive Preimplantation Testing for the Study of Embryonic Aneuploidies

Meriam Ben Tekaya, Marwa Ben Amor, Olfa Abdelkefi,Tarak Rebai, Salima Daoud, Afifa Sellami

Laboratory of Histology Embryology and Biology of Reproduction Medical School Sfax Tunisia

Preimplantation Genetic Diagnosis (PGD) is an invasive method that allows for the detection of serious hereditary diseases or non-viable chromosomal anomalies in embryos resulting from in vitro fertilization (IVF) before implantation into the uterus. A biopsy of one or more embryonic cells is necessary to obtain genetic material for analysis. Recently, new non-invasive methods for studying embryonic aneuploidies have emerged, relying on the analysis of biomarkers contained in embryonic culture media or on the study of morphokinetic parameters of embryonic development provided by time-lapse technology (TLT).

In this work, we propose to present the new non-invasive methods for detecting embryonic aneuploidies. An updated international literature review was conducted using the following keywords: "PGD," "aneuploidy," "biomarkers," and "non-invasive genetic tests."

Non-invasive Preimplantation Genetic Testing (niPGT) has been proposed as an alternative to invasive embryonic biopsy, avoiding potential alterations to the implantation and future development potential of the embryo, and reducing the risk of miscarriages. niPGT involves analyzing acellular DNA contained in the culture medium after amplification by next-generation sequencing (NGS) or comparative genomic hybridization (aCGH) array. These tests, based on embryonic acellular DNA, show high concordance with biopsies of the trophectoderm, inner cell mass, and whole blastocyst. niPGT can now be performed for the definitive diagnosis of trisomy 21, certain recessive and X-linked disorders. However, the main limitation is embryonic mosaicism.

On the other hand, a new non-invasive approach involves measuring certain biomarkers in spent embryonic culture media, such as specific miRNAs or proteins. Overexpression of miR-191 has been observed in the culture media of aneuploid embryos, suggesting their use as biomarkers for embryonic aneuploidies. Analysis of glutamine levels in culture media by gas chromatography and mass spectrometry has shown a significant increase in glutamine consumption in aneuploid embryos. Glutamine has been proposed as a molecular indicator for evaluating embryonic ploidy. Protein secretome analysis of blastocysts in spent culture media has shown different profiles based on embryonic ploidy. Increased and differentially significant expression of lipocalin-1 in the secretome of aneuploid blastocysts compared to euploid blastocysts suggests the potential use of this protein as a biomarker for embryonic aneuploidy.

In addition to the secretome, other non-invasive methods focus on morphological and morphokinetic parameters of embryos derived from Time-Lapse incubator systems. Euploid embryos exhibit faster kinetics of segmentation and blastocyst expansion. The combination of these data with artificial intelligence has allowed the development of algorithms to predict embryonic ploidy with high efficiency.

While non-invasive methods for studying embryonic aneuploidies are less disruptive to the embryo and more efficient in terms of time and cost than invasive PGD, further studies are needed to validate these methods and determine the extent to which they reflect the true genetic status of the embryo.