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EDITORIAL

NON-INVASIVE PRENATAL TESTING OF FETAL CHROMOSOMAL ANEUPLOIDIES: WHAT SHOULD BE CHANGED?

TESTE PRÉ-NATAL NÃO INVASIVO DE ANEUPLOIDIAS CROMOSSÓMICAS FETAIS: O QUE DEVE SER MUDADO?

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In Portugal, as in many other countries, the use of combined ultrasound and biochemical screening is part of the basic routine for the prenatal detection of the most frequent aneuploidies. Briefly, in the first trimester, pregnant women undergo a routine ultrasound study that determines gestational age, the anatomical normality of the fetus and the presence of ultrasound markers - increased nuchal translucency, the absence of the nasal bone, the presence of tricuspid regurgitation and a-wave inversion of ductus venosus. These findings are then combined with biochemical screening and a predicted risk value is determined. Cases where an increased risk for aneuploidy is detected are selected for prenatal counseling and may undergo an invasive study (chorionic villus sampling or amniocentesis) so that a definitive cytogenetic or molecular diagnosis can be established. Nevertheless, performing an invasive method for fetal diagnosis is not absent of risk, and parents must be advised as the risk of fetal loss is considerable. Even though, this method has been used for decades in Fetal Medicine and showed a remarkable sensitivity with obvious advances in prenatal diagnosis.

In recent years, a new and safe blood test is available and is rapidly changing the prenatal testing paradigm.[1,2] This test is known as non-invasive prenatal testing (NIPT) and was demonstrated, for the first time in a study in 2011, as an easy to implement and clinically useful test in the practice of Fetal Medicine.[2] The purpose of this first study was to report the initial experience of noninvasive prenatal diagnosis of fetal Down syndrome in a clinical setting.[1] The authors report that NIPT was a highly specific test, and unnecessary invasive tests and associated fetal losses could be avoided in almost all women who have a normal fetus.[1]

NIPT offers an intermediate step between serum screening and invasive diagnostic testing or can be considered to be implemented as a replacement for serum screening. Its high sensitivity (high probability of detection or high proportion of actual positives that are correctly identified as such) and specificity (high proportion of actual negatives that are correctly identified as such) make it an attractive alternative to the serum screens and invasive tests currently in use.[1,3,4]

NIPT involves analyzing the cell-free fetal DNA (cfDNA) present in a sample of maternal blood to determine the likelihood of a fetal aneuploidy. NIPT is more accurate than serum screening and produces fewer false positives, but is not currently diagnostic. The only physical risks associated with the procedure are those normally associated with a blood draw and there is no risk of miscarriage.2 Despite this, in the presence of a fetal structural anomaly, the indications for fetal karyotyping and/or microarray testing should not be modified by a normal NIPT result. Therefore, the clinicians should be aware that fetal ultrasound should be performed before NIPT screening to ascertain whether there is an indication for another prenatal test.

As defined by the International Society of Ultrasound in Obstetrics & Gynecology guidelines, « three options should be considered for women who wish to have a further risk assessment for trisomy 21 and, to a lesser extent, trisomies 13 and 18: (1) Screening strategies based on individual risk calculated from maternal age and nuchal translucency measurement and/or maternal serum markers and/or other ultrasound markers in the first trimester (defined by the conventional crown–rump length range of 45–84 mm); (2) cfDNA testing as a first-line screening test (cfDNA testing should not replace first-trimester ultrasound and should not be offered when an ultrasound anomaly or markedly

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increased NT is detected. Using cfDNA in low-risk patients might be endorsed as a widely available option only when more data emerge and cfDNA costs decrease); (3) Invasive testing based on a woman's preference or background risk (maternal age, previous history, fetal ultrasound anomaly) with no further individual risk calculation».[5,6]

The evidence clearly supports that the test performance of NIPT is better than that of first-trimester screening. However, unfortunately, the currrent cost of cfDNA testing is too high to be adopted as the primary method of screening.[7-10] For this reason it is necessary to create financing models that should be based on a perspective of improvement of results achieved, favouring gains for the patient and the health system, ensuring the principle of sustainability, optimizing health outcomes for individuals, communities, and society.

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