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ORIGINAL ARTICLE

Duo test and aneuploidy detection in women under 35 years of age with high-risk pregnancy at the Hospital General de México

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KEYWORDS
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Abstract Non-invasive procedures for prenatal diagnosis are the most frequently used methods in the first trimester of pregnancy in pregnant women under 35 years of age because they do not involve risk of pregnancy loss; however, they are not considered to be a definitive diagnosis method. During the first trimester the duo test (PAPP-A and free βhGC), cell-free fetal DNA in maternal blood and structural ultrasound scans are the principal tools used; the quadruple marker test (αFP, E3, β-hCG, inhibin A) is used in the second trimester. However, the definitive diagnosis is performed by cytogenetic analysis through amniocentesis.

Methods: Thirty women, under 35 years of age with high-risk pregnancy, were studied with duo test and structural ultrasound in the first trimester and amniocentesis in weeks 15–18.

Results: Only five duo tests were positive: three showed risk of trisomy 18 and one of Turner syndrome, they all corroborated with the cytogenetic study; the fifth showed a risk of Down's syndrome, however it was a chromosomally normal product. Three patients with a negative duo test cytogenetically detected with karyotypes with structural abnormalities, which were: deletion of the short arm of chromosome 18 [46,XY, del(18)(p11)], Robertsonian translocation between chromosome 13 and 14 [45,XY, rob(13:14)] and a chromosome derived from X [46,X, der(X)]. The duo test is a very useful tool for the diagnosis of numerical chromosome abnormalities, but not for detecting structural chromosome aberrations. However, it is essential to perform amniocentesis to definitively rule out chromosomal aberrations in products of conception.

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PALABRAS CLAVE
Dúo test;
Aneuploidía;
Embarazo de alto riesgo

Dúo test y detección de aneuploidías en mujeres menores de 35 años con embarazo de alto riesgo en el Hospital General de México

Resumen Los procedimientos de diagnóstico prenatal no invasivos están siendo los métodos más usados en el primer trimestre del embarazo en mujeres embarazadas menores de 35 años, ya que no implican riesgo de pérdida gestacional; sin embargo, no se consideran un método diagnóstico definitivo. Durante el primer trimestre de gestación se utiliza el dúo test (PAPP-A y βhGC libre), DNA fetal libre de células en sangre materna y la ultrasonografía estructural; durante el segundo trimestre se usa el cuádruple marcador (αFP, E_3, β hGCH, Inhibina A). Sin embargo, el diagnóstico definitivo se lleva a cabo mediante el análisis citogenético a través de la amniocentesis.

Métodos: Se estudiaron 30 mujeres menores de 35 años con embarazo de alto riesgo a las cuales se les realizó ultrasonido estructural y dúo test en el primer trimestre del embarazo y amniocentesis en la semana 15-18.

Resultados: Únicamente cinco dúo test fueron positivos, de los cuales tres mostraron riesgo de trisomía 18 y uno para síndrome de Turner, todos corroborados con estudio citogenético; el quinto mostró riesgo de síndrome de Down, sin embargo fue un producto cromosómicamente normal. En tres pacientes con dúo test negativo, se detectaron citogenéticamente cariotipos con anomalías estructurales, las cuales fueron: pérdida parcial del brazo corto del cromosoma 18 [46,XY,del(18)(p11)], translocación robertsoniana entre el cromosoma 13 y 14 [45,XY,rob(13:14)] y un cromosoma derivado del X[46,X,der(X)]. El dúo test representa una herramienta muy útil para el diagnóstico de alteraciones cromosómicas numéricas, no así para detectar aberraciones estructurales de los cromosomas, sin embargo es imprescindible la realización de la amniocentesis para descartar definitivamente aberraciones cromosómicas del producto en gestación.

Introduction

Prenatal diagnosis, using invasive procedures such as amniocentesis and chorionic villus sampling, in women with a high risk of having babies with chromosomal and structural abnormalities[1] is a very useful tool which is widely used nowadays. However, these invasive procedures involve a significant risk of miscarriage (1 in 200).[2] For this reason, these procedures are restricted only to pregnant women who are over 35 years of age or younger women with biochemical markers or positive ultrasound tests for chromosomopathy. Currently, non-invasive procedures are considered to be a very useful tool for making decisions with regard to the continuity of pregnancies with genetic diseases.[3] These studies have become very relevant in recent years, although they are not considered to be diagnostic procedures, but only screening procedures. The triple marker test, which determines the beta fraction of human chorionic gonadotropin (βhCG), unconjugated estriol (E3) and alpha-fetoprotein (αFP), was one of the first biochemical markers used in screening for chromosomal abnormalities in the product of conception.[4] At a later date, the determination of inhibin A was added, and it was then referred to as the quadruple marker test. The quadruple marker test is performed between weeks 15 and 20 of pregnancy. Subsequently, the duo test was established. This is performed in the first trimester of pregnancy (11–13.6 weeks). It determines the multiples of the median of the pregnancy-associated plasma protein (PAPP-A) and free βhGC. The duo test is complemented by the fetal ultrasound which measures nuchal translucency and nasal bone. A non-invasive prenatal diagnosis test based on next-generation sequencing (NGS), which consists of the analysis of cell-free fetal DNA in maternal blood, has recently been developed. This procedure is increasingly gaining importance in the screening for chromosomopathy, especially in trisomies 21, 18 and 13.[5–8] All these screening procedures make it possible to select patients who require invasive procedures, such as amniocentesis and chorionic villus sampling, in a more appropriate manner. Amniocentesis should be directly indicated for patients over 35 years of age, in whom biochemical markers do not have a relevant use for predicting aneuploidy in products of conception. The objective of this study is to identify the use of the duo test in detecting numerical chromosomal abnormalities in patients under 35 years of age in a sample of Mexican women with high-risk pregnancy who came to the Hospital General de México. A high-risk pregnancy is defined as that in which there are conditions present which compromise the health or life of the pregnant mother and/or her baby.

Material and methods

This project consisted of a descriptive, comparative study, with analysis, using a two-by-two table, between the duo test and amniocentesis. The determination of free βhGC and pregnancy-associated plasma protein (PAPP-A) in serum

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