Use of Commercial Tests for Aneuploidy Screening Using Cell-free Fetal DNA in Clinical Practice (Poster)

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ABSTRACT:

Objective: To characterize the use of the new commercial tests for aneuploidy screening using cell-free fetal DNA (cffDNA) by women at high risk for fetal aneuploidy.

Study Design: This is a retrospective cohort study of all women undergoing cffDNA testing in the first 6 months the tests were offered in the Lehigh Valley Health Network Maternal Fetal Medicine practice. All patients were high risk for fetal aneuploidy defined as advanced maternal age, abnormal aneuploidy screening, abnormal ultrasound findings and/or personal/family history. Medical records were reviewed for patient demographics, indication for testing, other tests performed, pregnancy outcomes (maternal and fetal) and insurance information.

Results: A total of 142 patients underwent cffDNA testing from 1/1/12 to 6/30/12. The mean age of patients having the test performed was 32.3 ± 6.5 years. Most patients were Caucasian (72%), non-hispanic (83%), multiparous (64%), married (58%), had private obstetrician (77%), had private insurance (51%) and were singleton gestations (95%). The median gestational age the test was performed was 18 5/7 weeks (range 10 2/7 – 28 3/7). Most tests were performed in the second trimester (73%). Insurance coverage varied and evolved significantly during this time period. Four patients had positive test results (3%) and three had uninformative results (2%). There was one false negative and there were no false positives. Sensitivity, specificity, positive predictive value and negative predictive value were 80%, 100%, 100% and 99%, respectively.

Conclusion: Our study provides some information on the use of new commercial tests for aneuploidy screening using cffDNA in clinical practice in a non-research setting. Although the potential for these tests to provide women with information regarding their pregnancies without the risk of an invasive procedure is exciting, additional studies are needed to validate their performance in both low and high risk populations, and providers and patients need to be aware of their limitations.

INTRODUCTION:

In the past two decades, numerous strategies for the detection of fetal aneuploidy have been developed, although definitifve diagnosis is possible only through the use of invasive procedures. In the fall of 2011, non-invasive tests for the diagnosis of common aneuploidies first became commercially available for the diagnosis of common trisomies and sex chromosome abnormalities. These tests work by identifying cffDNA in maternal blood with a high degrees of sensitivity and specificity, and have the advantage of providing the patient with highly accurate information without the discomfort or risk of an invasive procedure. The purpose of this study is to characterize the use of cell-free fetal DNA tests used at our institution for women at high risk for fetal aneuploidy.

METHODS:

- Retrospective cohort study of all women undergoing cffDNA testing through Lehigh Valley Health Network Maternal Fetal Medicine practice from 1/1/12 to 6/30/12.
  - CffDNA testing was offered only to women at high risk for aneuploidy based on maternal age, abnormal screening results, abnormal ultrasound findings, and/or family/personal history of aneuploidy.
  - All women underwent genetic counseling prior to cffDNA testing.
  - Women with positive results were strongly encouraged to undergo invasive testing to confirm results.
- Women were identified by review of a MFM clinical database developed to track patients that underwent cffDNA testing.
- Medical records were reviewed for baseline characteristics, indications for testing, test results and pregnancy outcomes. Neonatal records were reviewed when available.
- Descriptive statistics were generated for baseline characteristics and test indications. Sensitivity, specificity, positive predictive value and negative predictive value were calculated for trisomies 13, 18 and 21.

RESULTS:

Table 1. Baseline Characteristics of Women Undergoing Cell-free Fetal DNA Testing*

Mean maternal age (years)	32.3±6.5
Advanced maternal age	73/141 (52%)
Ethnicity	
Caucasian	102/142 (72%)
Black	10/142 (7%)
Asian/Indian	8/142 (6%)
American Indian	3/142 (2%)
Arabic	1/142 (1%)
Mixed	3/142 (2%)
Unknown	15/142 (11%)
Non-hispanic	109/132 (83%)
Multiparous	84/132 (64%)
Married	77/133 (58%)
Private obstetrician	102/132 (77%)
Private insurance	65/127 (51%)
Singleton gestation	125/132 (95%)
High school graduate	85/95 (89%)
College graduate	40/95 (42%)
Median gestational age (weeks)	18.64 (10.29 – 28.43)
Trimester	
First	33/132 (25%)
Second	94/132 (71%)
Third	5/132 (4%)

* Not all characteristics available for all subjects

Data in n (%), mean +SD or median (range). GA, gestational age.

Table 2. Primary Indications for Cell-free Fetal DNA Testing

AMA only	26 (18%)
Abnormal screen only	41 (29%)
Abnormal ultrasound only	52 (37%)
Abnormal screen and abnormal ultrasound	19 (13%)
History indicated	3 (2%)
Unspecified	1 (1%)

Data are in n (%).

Table 3. Summary of Cell-free Fetal DNA Results

135 negative

- One false negative. Indication: abnormal serum screen, increased nuchal translucency and AMA. No major structural abnormalities. Diagnosis of trisomy 21 suspected at delivery and confirmed by postnatal karyotype.

4 Positive for Trisomy 21

- Indication: AMA only. IVF pregnancy started as di/di twin gestation with embryonic demise of Twin A in first trimester. Remaining fetus had no abnormalities on ultrasound. Declined amniocentesis. Opted to continue pregnancy. Delivered healthy child. Suspect demise twin to be source of aneuploidy. No karyotype done on placenta.
- Indication: cystic hygroma. Declined amniocentesis. Opted to continue the pregnancy. Duodenal atresia and CHD suspected prenatally and confirmed postnatally. Delivered at 31 weeks for abnormal antenatal testing, trisomy 21 confirmed.
- Indication: increased NT. Declined amniocentesis. Opted to continue pregnancy. CHD subsequently suspected on ultrasound. CHD and trisomy 21 confirmed postnatally.
- Indication: CHD at time of level 2 ultrasound. Confirmed with amniocentesis. Pregnancy terminated.

AMA, advanced maternal age. CHD, congenital heart disease.

Table 4. Performance of Cell-free Fetal DNA Tests to Detect Trisomy 13, 18,21

Sensitivity	80%
Specificity	100%
Positive Predictive Value	100%
Negative Predictive Value	99%

CONCLUSIONS:

Our study provides some information on the use of new commercial tests for aneuploidy screening using cffDNA in clinical practice in a non-research setting. Although the potential for these tests to provide women with information regarding their pregnancies without the risk of an invasive procedure is exciting, additional studies are needed to validate their performance in both low and high risk populations, and providers and patients need to be aware of their limitations.