Prenatal Screening for Aneuploidy: Should cfDNA Replace Traditional Methods?

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Prenatal Screening for Aneuploidy: Should cfDNA replace traditional methods?

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Abstract

In 2011, advances in research in medical genetics led to the advent of prenatal cell-free DNA (cfDNA) screening or testing (NIPS). This screen consists of analysis of placental DNA circulating in maternal blood. NIPS has had a major impact on prenatal screening for aneuploidy. Mixed opinions and data exist as to whom this test is most appropriate for. The sensitivity and specificity of this screen in detecting common fetal aneuploidies has been well documented as superior to other screens in high-risk populations, but less so in low-risk obstetric populations. This paper will compare and contrast NIPS to more traditional screening methods such as first trimester maternal serum biochemical assay of human chorionic gonadotropin (hCG) and pregnancy associated plasma protein A (PAPP-A), and second trimester markers which include hCG, unconjugated estriol, inhibin A, and maternal serum alpha-fetoprotein.

Introduction

Screening for chromosome abnormalities prenatally is a complex topic and should be employed as an essential component of comprehensive obstetric care. Various screening options are available to screen for the most common fetal aneuploidies, namely Trisomy 21 (Down syndrome), Trisomy 18, and Trisomy 13. Each screening tool has advantages and disadvantages, and informed decision making between patient and provider is essential for selection of which screen suits each patient, if any.

The traditional methods of screening will be compared to NIPS including gestational age at which these screens may be performed, sensitivity and specificity for Trisomy 13, 18, and 21, and for which populations these screens are most appropriate.

Statement of the Problem

With an increase in the amount of options for screening for fetal aneuploidy, awareness and understanding of the disadvantages and advantages of each screening tool is necessary in providing comprehensive obstetric care. Patients must first be counseled on the existence and possibility of fetal chromosome abnormalities; and informed decision making between patient and provider should ensue regarding which, if any, screening tool best suits the patient.

Research Question

Why should prenatal screening be offered? What are the current options for screening for fetal aneuploidy? Should NIPS replace standard screening for aneuploidy?

Literature Review

Why should prenatal screening be offered?

It is well documented that the risk of carrying a fetus affected by any chromosome abnormality increases with maternal age.

<table>
<thead>
<tr>
<th>Age at Test</th>
<th>Risk of Trisomy 21 (%)</th>
<th>Risk of Any Chromosomal Abnormality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35-36 weeks</td>
<td>1 in 190</td>
<td>1 in 140</td>
</tr>
<tr>
<td>37-38 weeks</td>
<td>1 in 165</td>
<td>1 in 125</td>
</tr>
<tr>
<td>39 weeks</td>
<td>1 in 145</td>
<td>1 in 110</td>
</tr>
</tbody>
</table>

Table 1: Risk of Chromosomal Abnormalities Based on Maternal Age at Test

What are the current options for screening for aneuploidy?

• **First trimester screening**: Maternal serum hCG and PAPP-A + nuchal translucency ultrasound at 11 to 14 weeks
  
  • **Second trimester screening**: Quad screen analyzes four biochemical markers which include hCG levels, alpha-fetoprotein, unconjugated estriol, and dimeric inhibin A.
  
  • **Integrative/Sequential screening**: First trimester nuchal translucency study with ultrasound, hCG and PAPP-A levels, as well as a second trimester quad screen
  
  • **NIPT/cfDNA**: Analysis of placental DNA circulating in maternal blood

Table 2: Characteristics, Advantages, and Disadvantages of Common Screening Tools for Aneuploidy

<table>
<thead>
<tr>
<th>Screening Tool</th>
<th>Characteristics</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quad screen</td>
<td>Includes four biochemical markers</td>
<td>High detection rates for the most common aneuploidies</td>
<td>Only screen for high-risk populations</td>
</tr>
<tr>
<td>Nuchal translucency</td>
<td>Includes ultrasound</td>
<td>Can be performed any time after 10 weeks gestation</td>
<td>Unreliable with multiples</td>
</tr>
<tr>
<td>cfDNA</td>
<td>Analyzes placental DNA</td>
<td>Versatile test for all ages</td>
<td>Only one blood draw needed</td>
</tr>
</tbody>
</table>

FIGURE 1: Risk of Chromosomal Abnormalities Based on Maternal Age at Test

Advantages of NIPS

• High detection rates for the most common aneuploidies
• Can be performed any time after 10 weeks gestation
• Only one blood draw needed

Disadvantages of NIPS

• Only detects Trisomy 21, 18, and 13
• Mixed data on PPV in non-high-risk populations
• Unreliable with multiples

Discussion: Should cfDNA replace traditional methods?

According to a survey published by the Journal of Maternal-Fetal and Neonatal Medicine in September of 2016, obstetric care providers identified NIPS as clinically superior to other screening tools (Brewer, Demers, & Musci, 2016). The survey stated that 81.5% of respondents believed that NIPS is a superior test in screening for aneuploidy regardless of maternal age. The survey also stated that most respondents would like ACOG to formally recommend this screening tool to all pregnant women, regardless of age.

Applicability to Clinical Practice

The research as stated in this review is highly applicable to clinical practice due to the fact that offering prenatal screening for aneuploidy to all women is an important part of providing comprehensive obstetric care. Physician Assistants in both the primary care setting and women’s health setting may be providing obstetric care to patients, and knowledge of not only the existence of chromosome alterations but how to screen for them is of utmost importance in providing quality care. ACOG recommends offering screening to every pregnant patient.

Knowledge of the benefits, limitations, and drawbacks of each screening test is an integral part of appropriate genetic counseling.

References


Acknowledgements

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