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Genetic Counselling In Prenatal Screening: A Review

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Abstract

Prenatal screening for aneuploidy and prenatal diagnostic testing have expanded dramatically over the past two decades. Driven in part by powerful market forces, new complex testing modalities have become available. The responsibility for offering prenatal tests lies primarily on the obstetrical care provider, Medical Geneticist/Genetic Counselor, and has become more burdensome as the number of testing options expands. Genetic testing in pregnancy is optional, and decisions about undergoing tests, as well as follow-up testing, should be informed and based on individual patients' values and needs. Careful pre- and post-test counseling is central to supporting informed decision-making. This article explores the technical expansion in genetic testing of prenatal screening for fetal aneuploidies and provides insights aimed at enabling the obstetrical practitioner to better support the patients.

Keywords

Genetic counseling; prenatal diagnosis, genetic screening.

Introduction

In the past five years, dramatic advances in genomic medicine have led to significant changes in the types of genetic tests available to pregnant women. New testing modalities in prenatal screening have moved from the laboratory to clinical care. These new prenatal screening tests are aimed at providing more information about potential risk of possibility of fetal disorders in response to women's and obstetricians' general desire for information that will serve to either reassure the woman that abnormalities are absent, or to inform both the obstetrician and the pregnant woman about the presence of a probable genetic condition. This probable risk might signal the need for additional confirmatory prenatal testing to provide more clarity by confirmation of the risk of fetal chromosomal abnormality shown by prenatal screening tests, lead to changes in obstetric or pediatric management, precipitate consideration of taking irreversible decision whether to continue or not[1]. Although more information can be known, this information may be ambiguous, complicating decision-making and raising ethical issues.

The use of genetic technologies in prenatal care has always presented ethical challenges, but debates have intensified as prenatal testing options expand to include genetic tests that are easily obtained in the obstetric care center. Discussion has focused on the extent to which the accessibility of these new tests will routinize their use, erode informed consent and stigmatize individuals living with certain disabilities[2]. It is likely that genetic screening in the future will include testing for more disorders. In the face of the common notion that "more is better", many

pregnant woman may accept screening without considering the downstream consequences, including possible anxiety created by additional information, especially if it is uncertain. In most instances, prenatal genetic screening and carrier testing options are first offered to patients through their obstetrician, midwife, or other primary obstetrical care provider and obstetrical care providers remain the primary initial source of information for women about new testing modalities[3].

Currently, numerous professional guidelines recommend that women offered prenatal screening and testing for genetic disorders be given education and pretest counseling aimed at helping them to understand and weigh the benefits, risks and limitations of various testing modalities, and then make an autonomous decision that is most consistent with individual values and preferences. Although the general public is increasingly aware of the availability of new tests through the mass media, direct marketing or social networks, consumers frequently hold exaggerated views of the utility of genomic tests, and may underestimate their limitations. When options for genetic testing are introduced by the obstetrical care provider, some minimal information should be included in the pretesting discussion, including:

1. Genetic testing is optional and the decision to undergo or decline genetic testing in pregnancy should be based on the personal values and needs of each patient;
2. General Information about the conditions being tested for, including variability and common features;
3. Nature of the testing (screening, carrier screening, diagnostic);
4. Available alternative testing options and the risks, benefits and limitations of each;
5. Possible results of testing (positive, negative, unclear, unexpected);
6. Implications of positive results and follow-up options and available resources if the testing is positive;
7. Cost of testing and expectation regarding insurance coverage;
8. The availability of genetic counseling to provide additional information and risk assessment, to assist with decision-making about testing or discuss follow-up regarding results[4].

To maximize time for consideration of testing choices and to allow for appropriate follow-up, education and counseling about genetic tests should ideally be accomplished in the first or second prenatal visit, generally occurring in the first trimester of pregnancy, or in the case of carrier screening, even pre-conceptionally. The integration of counseling regarding optional genetic tests into early prenatal care is complicated by several factors including delays in initiating prenatal care by the patient, anxiety and uncertainty about pregnancy outcome that frequently occurs in the first trimester, and the significant volume of education and information that is necessary to discuss during a relatively short clinical encounter. Time constraints coupled with increasing complexity of available testing options increase concerns that women are being expected to make decisions after receiving only minimal information and with poor understanding of what they are consenting to. Furthermore, intense marketing pressure as well as concern for wrongful life suits may lead providers to encourage testing rather than supporting autonomous decisions about testing by the patient.

In response to these concerns it has been suggested that all women should meet with a genetic counselor early in pregnancy to review personal genetic risks and available testing options. Genetic counselors are trained professionals who work in a variety of clinical, research and commercial settings. Consultation with a genetic

counselor in the prenatal setting involves detail review of the family and medical history of the patient and her reproductive partner; review of risks and/or test results, discussion of testing options to include overview of risks, benefits, limitations, alternatives and potential next steps; review of conditions that may be tested for; and most importantly, clarification of patient values regarding prenatal testing options. The goal of genetic counseling is to provide the risk assessment, support, education and resources needed to facilitate patient decision making that best supports the individual patient's personal needs and values. Historically, prenatal genetic counselors have worked in academic medical centers, healthcare systems and perinatology practices. However, over the past decade, genetic counselors are increasingly working in less traditional settings including telephone/Skype based genetic counseling services as well as commercial testing laboratories. In some cases, laboratory-based genetic counselors directly interface with patients providing pre-test counseling and/or in follow-up of test results. The potential for conflict of interest associated with counseling provided by a laboratory counselor should be considered carefully, and the American College of Obstetricians and Gynecologists (ACOG) caution that neutral counseling may be compromised through "use of patient educational materials or counselors that are provided by a company that may profit from a patient's decision to undergo testing"[5].

While it would be ideal for all pregnant women to have the opportunity to meet with a genetic counselor, such a goal is not realistic given the number of trained genetic counselors and the finite number of training slots currently available. As a means to provide education to women, various modalities to evaluate risk and to inform women about prenatal tests and support decision-making have been developed and evaluated, and a method for rapidly creating and updating educational materials has been called for. Such resources may support the work of the primary obstetrical care provider in providing pre-test counseling and follow-up of genetic test results[6].

This review will provide information to aid obstetrical care providers in providing information and support to patients regarding new technologies that are being increasingly integrated into prenatal care.

Over the past three decades, prenatal screening options for Down syndrome and other common aneuploidies have moved from an assessment based on age and family history alone, to screening using maternal serum markers only, to screening using both maternal serum and ultrasonographic markers, and most recently, to include screening using circulating cell free (cf) DNA present in maternal blood. Screening was initially performed in the second trimester, but is now more typically performed in the late first trimester. As the timing, sensitivity and specificity of screening tests have improved, the utilization of invasive procedures, such as amniocentesis and chorionic villus sampling, by pregnant women seems to be declined.

These welcome advances also involve an unprecedented degree of complexity that has challenged our current approaches. In 2007, ACOG updated their practice guidelines about prenatal screening for aneuploidy to recommend that all pregnant women be offered screening, and that invasive testing for chromosomal aneuploidy be made available to all pregnant women, regardless of their risk for fetal aneuploidy. The 2007 ACOG guidelines along with the shift to tests that are offered in the first trimester and often in the obstetrician's office have led to the need to educate more patients about more screening options at an earlier stage of pregnancy. This has fueled concerns that more women will be making decisions with insufficient education concerning the risks, benefits and

limitations of various available options. Pretest counseling by obstetrical providers, including medical geneticist/genetic counselors, will have a major impact on utilization and efficacy of screening modalities of prenatal tests[7].

Pre-test Genetic Counseling

The number of prenatal screening and prenatal diagnostic options currently available, and the complexity of prenatal tests, will challenge the clinician's ability to adequately inform women of all available options, and the pregnant woman's ability to make informed decisions about their use. In order to meet this challenge, obstetrical providers must develop new methods of pre-test counseling of prenatal tests that present the important elements of testing options in a framework patient can comprehend. Written and web-based educational materials that are understandable and unbiased for patients may also enhance the pre and post-test counseling process. The content of educational materials produced by commercial prenatal labs varies tremendously and may have an underlying message to support uptake of some prenatal tests rather than informed and autonomous patient decisions. Several scientific organizations recommend that education should include information about the conditions that the test screens for, the availability of follow-up, the implications of a positive results, the need for confirmatory testing following positive results, the availability of alternatives (such as invasive testing), and the possibility of false positive and false negative results[8].

Several sources recognize the validity of various combinations of methods and approaches to prenatal screening. Given the value of first trimester ultrasound, and the wide availability and proven cost effectiveness of first trimester screening, patients may prefer to start with first trimester screening. Prenatal screening can detect the risk for Down syndrome, it will identify pregnancies with or at increased risk for other birth defects and obstetrical factors important in patient care. First trimester screening also involves a two-step process involving measurement of the fetal nuchal translucency by ultrasound and analysis of biochemical serum markers prior to generating results that allows patients more time for and information about individual risk. Likewise, given the provision of definitive results and relative safety of CVS and amniocentesis, high risk patients should be advised that they may elect to undergo invasive prenatal diagnosis without undergoing any screening[9].

Further, they should know in advance that the clinical utility of screening for rare microdeletions in low risk populations has not been established and that the positive predictive value for these uncommon conditions is low.

Post-test Genetic Counseling

In general, pre-test prenatal counseling should prepare patients for possible positive results. Obstetrical providers should be prepared to deliver these results, provide post-test counseling and make referrals. Preparing patients for possible unanticipated results has always been an important goal in genetic counseling. Positive prenatal screening results are associated with considerable anxiety, and providers should be prepared to allow time for patients to react and process the implications of results. Patients should be informed about the availability of invasive testing for confirmation of findings and offered genetic counseling. More than one visit may be optimal, or the initial obstetrical providers contact may be followed by a genetic counseling visit the next day, allowing patients time to consider results and testing options. Prenatal genetic counselors can assist with interpreting results and providing follow-up that may be critical in meeting the patient's needs[10].

Obstetrical providers should include the concept of false positive results and explain the difference between the

detection rate (sensitivity) and positive predictive value (chance that positive result is a true positive) to patients in pre-test counseling. While prenatal screening is often advertised as being highly accurate, patients should be aware that in the event of a positive result, the likelihood that the pregnancy is affected depends on factors including her age, results of other screening tests and her pregnancy and family history. In the low risk population, the chance that a positive result is a false positive result may be similar to or even exceed the likelihood of a true positive. For those with a positive prenatal screening result, amniocentesis and chorionic villus sampling (CVS) provide near definitive results. However, patients should be made aware that laboratory testing of villi obtained via CVS may occasionally differ from the fetus (Maternal contamination/placental mosaicism). In these cases, testing may reveal abnormal cells which could be present in the placenta, but not reflective of the fetal karyotype, a phenomenon known as placental mosaicism. It has been shown that cell free DNA in maternal blood also originates from the cytotrophoblast and is therefore of "placental" not fetal origin. For patients electing CVS or amniocentesis, microarray analysis or specific DNA testing may be included in prenatal testing[11]. Depending on the presence or suspicion of an abnormality or specific genetic condition, other specialized fetal evaluation may be indicated, such as fetal echocardiography or MRI and consultation with pediatric specialists for better prediction of prognosis and better patient counseling. Genetic counselors may be utilized in coordinating these referrals.

Conclusion

The complexity of prenatal genetic testing options offered to patients in preconception and prenatal care would continue to grow, and most probably with swift pace due to introduction of new molecular and bioinformatics technologies. These rapidly evolving technologies may provide beneficial information for some patients but shall also pose genetic counseling challenges for obstetricians and gynecologists. Therefore, in order to deliver most accurate prenatal patient care, it is imperative for prenatal care specialists to be well-informed and abreast with new genetic technologies. Not only it is essential to understand the striking features but also it is equally important to know about the limitations of various prenatal testing options. It would be an ideal situation for each pregnant woman to avail benefits from the genetic counselling services. A partnership between obstetricians/gynecologists and genetic counsellors becomes indispensable for delivering high quality education and genetic counseling for all women aspiring for reproductive genetic testing.

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