Has Noninvasive Prenatal Testing Impacted Termination of Pregnancy and Live Birth Rates of Infants With Down Syndrome?

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ABSTRACT

Noninvasive prenatal testing (NIPT) for aneuploidy using cell-free DNA (cfDNA) has become widely available and popular for detection of Down syndrome (DS) because of its high sensitivity (99%) and specificity (99.5%). The acceptance of NIPT as an alternative to the first-trimester combined test has greatly reduced the use of invasive prenatal diagnostic testing. Widespread implementation of NIPT may result in an increase in parents opting for prenatal testing and subsequent reduction in those born with DS as pregnancies are terminated following a high-risk result.

This literature review aimed to determine the impact that the introduction of NIPT has had on the number of parents choosing to continue their pregnancy following detection of DS. A systematic search of articles related to NIPT and published from when NIPT entered clinical practice (January 1, 2011, to September 25, 2017) was conducted using the PubMed database. A separate, similar search was conducted to establish country-specific abortion rates prior to the introduction of NIPT. Two audits on termination rates following detection of high risk for DS by NIPT, calculated as a proportion of all pregnancies, were conducted in the United Kingdom and Singapore.

A total of 14 studies were included in review. The studies' objectives and design were diverse, 8 prospective and 6 retrospective, whereas only 1 aimed to determine pregnancy outcome and patient decision making following NIPT. The data showed that a significant proportion of pregnancies where NIPT indicated a high risk of DS were continued to live birth in the United States, the United Kingdom, and the Netherlands, whereas there were no live births with DS in the studies from China, Hong Kong, Taiwan, France, and Spain. The audit in Singapore found that 2 of 6 pregnancies were continued to live birth following a high-risk NIPT result, whereas the UK audit found 15 of 43 continued the pregnancy.

This study found that many pregnancies were continued to live birth despite receiving a high-risk diagnosis for DS using NIPT. The results also found that the rate of abortion since the clinical implementation of NIPT is unchanged or slightly decreased compared with historical rates. There were numerous instances of women receiving a high-risk result from NIPT and declining to undergo confirmatory invasive testing. These situations suggest some women's intent to undergo NIPT for the sake of obtaining information about the health of their child, however, and unwillingness to risk miscarriage or pursue termination despite the results. Participant numbers were low in many of the studies included, weakening the ability of this review to draw an association between modern and historical termination rates. Larger-scale population-based studies are needed to determine the effect of NIPT on the rates of children born with DS.

EDITORIAL COMMENT

(Since introduction in 2011, the uptake of cfDNA screening has increased rapidly. With very high sensitivity and very low false-positive rates, this test represents a tremendous advance in DS detection. However, because the detection rate is higher, some disability rights advocates and others in the DS community have worried that the increased use of these tests will result in higher termination rates for DS and lower rates of DS birth.

In this abstracted article, the authors investigated the impact of cfDNA screening on termination and live birth rates for DS in a number of different settings, including in the United Kingdom and the United States. Compared with termination rates...
prior to the introduction of cfDNA, the rates of termination were actually found to be unchanged or lower. However, the authors acknowledge that true population studies are needed to determine the true impact on DS birth.

The premise behind this study is a bit confusing, but reflects the concerns of many bioethicists that the introduction of cfDNA screening will lead to higher rates of pregnancy termination. What these individuals perhaps do not recognize is that prenatal aneuploidy screening has been on a trajectory of improved diagnosis over the past 2 decades, and integrated screening with serum analytes and nuchal translucency ultrasound has a very high detection rate of approximately 93% (Baer) (Obstet Gynecol 2015;126(4):753–759). While the relatively low positive predictive value of integrated screening leads some women to decline diagnostic testing, those who value diagnostic certainty and, presumably, those who felt they would seriously consider termination for an affected child, generally have chosen to undergo amniocentesis or chorionic villus sampling. Those women who wished to avoid a risk of pregnancy loss or did not value diagnostic certainty would generally decline invasive diagnostic testing during the pregnancy. The authors state that “many parents who would not have previously opted for prenatal testing because of the risk of miscarriage would be willing to have NIPT.” Unfortunately, it appears that these authors, despite being highly regarded prenatal genetics experts, continue to consider NIPT as an alternative to diagnostic testing, rather than an alternative screening test.

Cell-free DNA represents merely another option for aneuploidy screening. Those who feel that suddenly women would be having prenatal testing who never would have chosen this option in the past are missing this important point and perhaps are not aware that, prior to introduction of cfDNA, we offered pregnant women an excellent aneuploidy screening test. The paradigm has not changed, and it is not clear why some would anticipate higher rates of termination. Rates of diagnostic testing and rates of termination began decreasing in the United States long before the introduction of cfDNA; this is a cultural trend that has not been much impacted by cfDNA.

I think the other important point that is not appreciated by many nonclinicians is that finding out the fetal sex is a primary consideration in patients’ decision to elect cfDNA. Most women are optimistic and assume their fetus will be healthy, but excitedly anticipate finding out if it is a boy or girl. In the past, this had to wait until 20 weeks’ gestation when the routine anatomic survey is performed. Now, cfDNA far earlier in pregnancy can answer the question. A recent study by Palomaki and colleagues (Genet Med 2017;19(7):778–786) found that more than 80% of women who chose cfDNA screening indicated that they did so to learn the fetal sex as early as possible.

Interestingly, we are quite good at predicting new technologies that will be developed and introduced, but quite poor at predicting how our culture will change. There was a quote in Time magazine in 1966 that stated, “Remote shopping, while entirely feasible, will flop—because women like to get out of the house, like to handle merchandise, like to be able to change their minds.” If Jeff Bezos had listened to these words of wisdom, the world would be a quite different place. Likewise, we have poorly predicted how women would use cfDNA screening. This test was introduced at about the same time as chromosomal microarray, which can detect a far broader array of serious abnormalities. In addition, the loss rate from diagnostic testing has become far lower. Yet, women continue to prefer cfDNA to these other options, much to the surprise of prenatal “experts.” As the field of prenatal genomics further expands with introduction of genomic sequencing, who knows where our patients will take us? It will be fascinating to see.—MEN)