Optimal screening for Down syndrome: non-invasive prenatal testing?

Key words: Down syndrome, screening, technology, non-invasive prenatal diagnosis, evidence based midwifery

Statistics from the WHO on Down syndrome estimate an effect size of 1:1000 to 1:1100 live births each year (WHO, 2014). Recent UK statistics, produced from the National Down Syndrome Cytogenetic Register (Morris et al, 2014), report the rate 2.7:1000 births for babies born in England and Wales. They also report a significant increase in the proportion of women diagnosed prenatally, from 45% in 2008 to 77% in 2012 for women under 35 years, and from 68% in 2008 to 80% for women over 35 in 2012.

Historically, recognition of Down syndrome was evidenced three centuries ago by Dr John Langdon Down, a medical doctor from Cornwall, who first described and classified Down syndrome in 1862 under the label of a ‘Mongolian idiot’ (Dunn, 1991). Today, it is the most common chromosomal abnormality present at birth and has become a major focus for prenatal screening worldwide. New screening technologies have made remarkable advances in the past 15 years and this is most visible when we look back at recommendations from the UK National Screening Committee in 2001, which advised that all pregnant mothers should be offered one of the available screening tests for Down syndrome. The committee recommended that by 2010 the screening tests should have a positive rate of less than 3% and a detection rate of more than 75%. Major advances in screening technology have taken place since and the American College of Medical Genetics and Genomics (2012) refer to the current gold standard antenatal screening for Down syndrome as a combination of data from the first trimester collected between 11 and 14 weeks’ gestation, including assessment based on maternal age, ultrasound for nuchal translucency thickness and maternal serum analytes (free beta human chorionic gonadotrophin and pregnancy-associated plasma protein A). They report this assessment has 90% sensitivity and 95% specificity for predicting Down syndrome.

Technology has advanced rapidly and we have next-generation sequencing of circulating cell-free DNA in maternal plasma capable of identifying nearly all Down syndrome pregnancies with low false-positive rates based on a single maternal blood test for non-invasive prenatal screening (Glen et al, 2012). The blood test is undertaken around 10 weeks’ gestation and the results are available within 10 to 14 days.

The test costs between £99 and £800, depending on the provider (currently available from medical staff in Harley Street in London and independent diagnostic companies). It is not free within the NHS at this time, but may become so following the results of the National Institute for Health Research funded UK study looking specifically at non-invasive prenatal testing (NIPT) for Down syndrome. The study is being led by the RAPID team from Great Ormond Street Hospital for Children in London and involves six sites where women who have a risk of a Down syndrome baby – >1:1000 – will be offered NIPT. There is some persuasive research evidence reporting NIPT tests have 100% sensitivity and 100% specificity (Zimmermann et al, 2012). However, amniocentesis or chorionic villus sampling is still being performed for confirmatory diagnosis.

Recent UK research explored NIPT preferences of 335 women and 181 health professionals using discrete choice experiments (Hill et al, 2012). The results demonstrated preference for ‘safe’ tests conducted early in pregnancy, with high accuracy. For women, the key attribute was ‘no risk of miscarriage, whereas for health professionals it was accuracy’.

In 10 years, based on current knowledge of personalised medicine, epigenetics and values-based medicine, one can envision a maternity service where optimal NIPT for Down syndrome and other chromosomal abnormalities will be incorporated into everyday antenatal care. The technology used in NIPT can scan the entire genetic code of the fetus leading to the need for sound bioethical principles to be put in place. The challenge for us as midwives is to remain committed to listening to the voices of the women we serve, while maintaining our professional, legal, moral and academic integrity in the midst of a sea of turbulent cultural and technological change.

References


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