Executive summary

Health Council of the Netherlands. Population Screening Act: noninvasive prenatal test for increased risk of trisomy. The Hague: Health Council of the Netherlands, 2013; publication no. 2013/35

The national NIPT consortium has applied for a permit for a pilot introduction of screening with non-invasive prenatal testing (NIPT) of women at high risk of carrying a foetus with Down syndrome (trisomy 21) and two other chromosomal abnormalities (trisomy 13 and 18). This requires a permit under the Population Screening Act. The Committee on Population Screening of the Health Council of the Netherlands advises the Minister of Health, Welfare and Sport about granting this permit.

Prenatal screening and NIPT

Currently the first step in prenatal screening for trisomy is the (first trimester) combined test, which is used to estimate the risk of carrying a foetus with trisomy. The factors combined in this test are, the age of the pregnant woman, a foetal nuchal translucency measurement and the outcome of two biochemical markers in the mother's blood. If the risk estimate is 1 in 200, or greater, then the woman in question can opt for further testing to obtain certainty. The usefulness of the combined test is independent of the woman's age, as age is an integral part of this test. Women aged 36 or above can also benefit from doing an initial combined test, before considering further testing. Currently such further testing consists of chorionic villus sampling or amniocentesis. These invasive tests have a small, but significant, risk of miscarriage or other complications. Published studies indicate that this happens three to five times in every thousand tests.

For trisomy screening NIPT is a new type of blood test. It detects trisomy by means of foetal DNA that is present in the pregnant woman's blood. Studies conducted in other countries indicate that the test gives good results when used in women who are at relatively high risk of carrying a foetus with trisomy. This raises the question of exactly how effective the test will be in the target group of Dutch high-risk pregnant women, who have a lower risk than the subjects in most of the studies that were performed outside the Netherlands. Basically, there should not be too many false positive results (where the test indicates a foetus with trisomy when in fact there is not) and not too many false negative results (where the test fails to spot trisomy when it is actually present).

Permit request

The aim of the project for which a permit is being requested is to investigate the introduction of NIPT in the Dutch prenatal screening programme for women at increased risk of carrying a foetus with trisomy. During this pilot introduction the women will be required to give written consent before receiving NIPT. If NIPT has a positive result (indicating that the foetus is affected) and the woman in question needs absolute certainty (e.g. if she is considering an abortion), then further invasive tests (with chorionic villus sampling or amniocentesis) will have to be carried out. This is because in about 5 out of every 100 women with a positive NIPT (after a positive combined test), the foetus will not have trisomy. Nevertheless, this approach means that, after the combined test, far fewer women will have to undergo an invasive test than is presently the case, that is less than 1 in 500 instead of 1 in 28.

Advice

The Committee advises the Minister of Health, Welfare and Sport to grant the permit. It has been sufficiently established that, as a second test after the combined test, NIPT does indeed have added value. For the moment, the use of NIPT as initial test (instead of the combination test) is not an option, as the test is not sufficiently reliable. Furthermore, the design of the proposed population based screening programme is scientifically sound and meets the legal requirements for medical practice.

Recommendations

The Committee does have a number of recommendations. It feels that, as an initial test, the combination test offers benefits to all women, independent of age. The risk to pregnant women aged 36 and above does not suffice as direct indication for further testing. If women aged 36 and above first do the combination test, then the required number of (further) invasive tests will sharply decline. This is advantageous for the women concerned, because as a consequence the risk of miscarriage related to the procedure will be much smaller than currently is the case.

The Committee also believes that the study should carefully examine those cases in which NIPT fails. The test is known to be less effective in overweight women, and there may be other reasons for failure of NIPT.

The Committee also recommends that data be collected about women's prenatal screening choices and the extent to which these are modified by NIPT: does it facilitate useful reproductive risk control options for more women (the purpose of this screening)?

Finally, the Committee proposes it is important to carry out a cost-effectiveness study to determine the cost-effectiveness of introducing NIPT. In other words, is NIPT worth any additional costs it may involve? The Committee recommends that data should be collected for such a study during the pilot introduction of NIPT, even though this is not mandatory under the terms of the Population Screening Act. This is because the pilot phase offers a unique opportunity to collect such data.