Cheap, simple, noninvasive blood test may replace invasive diagnostic techniques in early pregnancy

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Researchers in The Netherlands believe they are on the verge of developing a simple, prenatal blood test that would be able to detect accurately chromosomal abnormalities in the developing foetus. At present, the only reliable way to do this is through amniocentesis or chorionic villus sampling, both of which are invasive and carry the risk of triggering a miscarriage.

Dr Suzanna Frints, a clinical geneticist at Maastricht University Medical Centre (Maastricht, The Netherlands), will tell the 26th annual meeting of the European Society of Human Reproduction and Embryology in Rome today (Tuesday), that she and her colleagues have been able to use molecular genetic probes to detect DNA belonging to the foetus in blood samples taken from pregnant women.

So far, they have been successful in identifying DNA from the Y chromosome, indicating that the foetus is a boy and therefore could be at risk of inheriting an X-linked disorder such as Duchenne's muscular dystrophy and haemophilia. [1]

The researchers believe the same method can be used to detect trisomy 21 (where an extra chromosome 21 causes Down's syndrome) and they are investigating this next, followed by trisomy 13 and 18 (responsible for causing Patau and Edward's syndromes respectively). [2]

Dr Frints and her colleagues are using the "Multiplex Ligation-dependent Probe Amplification" (MLPA), technique to detect foetal DNA that is present in the blood of women who have been pregnant for at least six to eight weeks. The MLPA test is part of an existing kit that is already used around the world to detect chromosomal abnormalities in invasively obtained amniotic fluid or chorionic villi samples from pregnant women. The kit is cheap and fast, delivering results within 24-62 hours, but, until now, it has only been used on samples taken during invasive procedures; it was not known whether it would work on cell free foetal DNA circulating in blood samples of pregnant women.

"It is inexpensive compared to the costs of invasive prenatal diagnosis, and could easily be implemented at low cost, between 30-150 Euros per kit per person, with a small apparatus in every hospital in the world. Blood samples can be taken during routine antenatal visits," said Dr Frints.

The study started in 2009 and is expected to continue to 2012 or longer. The researchers are recruiting women who are at high risk of an abnormal pregnancy and undergoing prenatal screening and invasive diagnostic procedures. To obtain MLPA proof of principle, they have recruited 14 women who had a pregnancy termination between 14-22 weeks gestation because of trisomy 13, 18 or 21 detected by invasive prenatal diagnosis (group A), four women who had non-invasive prenatal screening at 12-14 weeks gestation (group B), three women who had invasive prenatal diagnosis because of being at least 36 years old (group C), and nine non-pregnant control women who had had up to three children (group D). A total of 20, 715, 40 and 30 women are needed in each group respectively to complete the clinical trial to test the reliability of the MLPA technique.

"The MLPA test results obtained in 2009 were compared with the results of amniocentesis, chorionic villus sampling and pregnancy outcome. All

but one sample correlated with the non-invasive MLPA test results, detecting foetal Y-chromosome sequences," said Dr Frints. "At the moment, the reliability of the test is about 80% due to false negative results, but we are working to improve the accuracy of the MLPA probe.

"Although we need to test and refine this MLPA technique further, our results so far are promising. This is innovative translational research and when we succeed in developing the MLPA procedure for use in maternal blood, we will be able to offer a safe, cheap, fast, reliable and accurate non-invasive test, which will be of immediate benefit to pregnant women, young and old, all over the world."

The researchers hope the test may be available in the clinic in two to five years' time.

More information: [1] Most X-linked disorders are recessive. This means that females, who have two X chromosomes, need two copies of the affected gene to show the disorder, but because males have only one X chromosome, they show the disorder if they inherit one copy of the affected gene. Genetic abnormalities that are carried on the X chromosome include Duchenne's muscular dystrophy and haemophilia. [2] Patau syndrome occurs in approximately one in 10,000 births and Edward's syndrome in approximately one in 6,000 births. They both cause numerous physical and mental abnormalities and most babies do not survive beyond infancy.

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