EDİTÖRE MEKTUP/LETTER TO THE EDITOR
J Turgut Ozal Med Cent 2015;22(2):141-2

Journal of Turgut Ozal Medical Center
www.jtomc.org

Non-Invasive Prenatal Testing

Non-İnvaziv Prenatal Tanı

Cemal Ekici

İnönü University, Faculty of Medicine, Department of Medcial Biology and Genetics, Malatya, Turkey

Dear Editor,

The rate of newborns with trisomy 21 (Down syndrome) who have been referred to our pediatric newborn clinic is very high. This shows that prenatal screening in the region is not carried out well. Prenatal diagnosis and screening methods include invasive prenatal diagnosis methods (amniocentesis, chorionic villus sampling (CVS), and cordocentesis) and non-invasive prenatal diagnosis (NIPT) which cell free fetal DNA (cffDNA) screening of maternal blood samples. After the discovery of the signs of fetal DNA in maternal blood in 1997 and parallel to advancements in molecular genetics and technology, NIPT has become a widely used method in the world in the last few years (1).

Non-invasive prenatal diagnosis is a test without risks both for the mother and for the fetus. A 4-5 cc peripheral blood sample taken from the mother's arm is sufficient for the diagnosis. This method scans the 13, 18, 21, and sex chromosomes (X/Y) in the 8th week of pregnancy. The test involves whole genome scanning or targeted screening for trisomy or monosomy in mother's blood in search of cffDNA fragments of the fetus. The test results within a few days, thus eliminating maternal anxiety and, if there are pathological results, providing enough time to terminate pregnancy in its early weeks. Other invasive prenatal tests can only be applied in later weeks of pregnancy compared to NIPT. For instance, CVS can be done in the 11th-12th weeks of pregnancy while amniocentesis can be applied in the 16th-18th weeks of pregnancy. Still, patients need to wait for an average of 3 weeks for the results in these tests. Moreover, even in experienced hands, both CVS and amniocentesis carry the risk of abortion at a rate of 1/50 and 1/200, respectively.

Recent studies on trisomy 21 with NIPT method show that practitioners may achieve results with high sensitivity and specificity without the need for long cell culture. In addition to frequent screening for fetal trisomy, screening of mother's blood for single gene disorders of the fetus will eventually become a routine practice; there are already many studies underway to this end. The most controversial aspect of this method is the ethical aspect; geneticists and obstetricians share different opinions about this issue (2).

Table 1. Sensitivity and specificity results of eight different studies for Down syndrome screening by NIPT.

Authors – Year of Publication	Method	P	FP	N	FN	Sensitivity	Specificity
Enrich et al. 2011(3)	Whole Genome	39	0	410	1	100	99.7
Palomaki et al. 2011(4)	Whole Genome	212	3	1471	3	99.6	99.8
Bianchi et al. 2012(5)	Whole Genome	89	0	404	0	100	100
Ashoor et al. 2012(6)	Targeted Screening	50	0	297	0	100	100
Sparks et al. 2012(7)	Targeted Screening	36	0	123	0	100	100
Norton et al. 2012(8)	Targeted Screening	81	0	2888	1	100	99.97
Futch et al. 2013(9)	Whole Genome	154	2	5515	1	98.72	99.98
Liang et al. 2011(10)	Whole Genome	40	0	372	0	100	100

P: Positive; FP: False positive; N: Negative; FN: False negative

NIPT has certain advantages; it is harmless to the mother and fetus while it also provides early diagnosis as early as the 8th week of pregnancy and the option of early termination in cases with aneuploidy. Besides, the results of NIPT can be obtained within a few days, which is another plus side for this method. Whereas, there are also some disadvantages of this method such as its inability to provide information about all the structural and numerical chromosome abnormalities, the fact that it is not 100% reliable for common trisomies, and its comparatively high cost. NIPT is a routinely applied screening method in some developed countries. In Turkey, through some local private laboratories, samples are sent to centres abroad to be studied. I believe that offering NIPT as an alternative method in addition to other invasive

prenatal diagnostic methods will be beneficial for the patients in our region.

REFERENCES

1. Lo YM, Corbetta N, Chamberlain PF, Rai V, Sargent IL, Redman CW, Wainscoat JS. Presence of fetal DNA in maternal plasma and serum. Lancet 1997;16;350(9076):485-7.
2. Vanstone M, King C, Vrijer B, Nisker J. Non-invasive prenatal testing: ethics and policy considerations. J Obstet Gynaecol Can 2014;36(6):515-26.
3. Ehrich M, Deciu C, Zweifellhofer T, Tynan JA, Cagasan L, et al. Non-invasive detection of fetal trisomy 21 by sequencing of DNA in maternal blood: a study in a clinical setting. Am J Obstet Gynecol 2011;205:1–11.
4. Palomaki GE, Kloza EM, Lambert-Messerlian GM, Haddow JE, Neveux LM, et al. DNA sequencing of maternal plasma to detect Down syndrome: an international clinical validation study. Genet Med 2011;13:913–20.
5. Bianchi DW, Platt LD, Goldberg JD, Abuhamad AZ, Sehnert AJ. On behalf of the Maternal Blood IS Source to Accurately diagnose fetal aneuploidy (MELISSA) Study Group Genome-Wide Fetal Aneuploidy Detection by Maternal Plasma DNA Sequencing. Obstet Gynecol 2012;119:890–901.
6. Ashoor G, Syngelaki A, Wagner M, Birdir C, Nicolaides KH. Chromosome-selective sequencing of maternal plasma cell-free DNA for first-trimester detection of trisomy 21 and trisomy 18. Am J Obstet Gynecol 2012;206:322–5.
7. Sparks AB, Struble CA, Wang ET, Song K, Oliphant A. Non-invasive prenatal detection and selective analysis of cell-free DNA obtained from maternal blood: evaluation for trisomy 21 and trisomy 18. Am J Obstet Gynecol 2012;206:319–9.
8. Norton ME, Brar H, Weiss J, Karimi A, Laurent LC, et al. Non-Invasive Chromosomal Evaluation (NICE) Study: results of a multicentre prospective cohort study for detection of fetal trisomy 21 and trisomy 18. Am J Obstet Gynecol 2012;207:137-8.
9. Futch T, Spinosa J, Bhatt S, de Feo E, Rava RP, et al. Initial clinical laboratory experience in non-invasive prenatal testing for fetal aneuploidy from maternal plasma DNA samples. Prenat Diagn 2013;33:569–74.
10. Liang D, Lv W, Wang H, Xu L, et al. Non-invasive prenatal testing of fetal whole chromosome aneuploidy by massively parallel sequencing. Prenat Diagn 2013;33:409–15.

Received/Başvuru: 21.08.2014, Accepted/Kabul: 21.08.2014

Correspondence/İletişim

Cemal EKİCİ
İnönü Üniversitesi Tıp Fakültesi, Tıbbi Biyoloji ve Genetik, MALATYA, TÜRKİYE
E-mail: cemalekici@yahoo.com

For citing/Atıf için

Ekici C. Non-ınvasive prenatal testing. J Turgut Ozal Med Cent 2015;22:141-2- DOI: 10.7247/jtomc.2014.2352