Bölüm
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YARDIMLA ÜREME TEKNİKLERİNDE PREİMPLANTASYON GENETİK TEST

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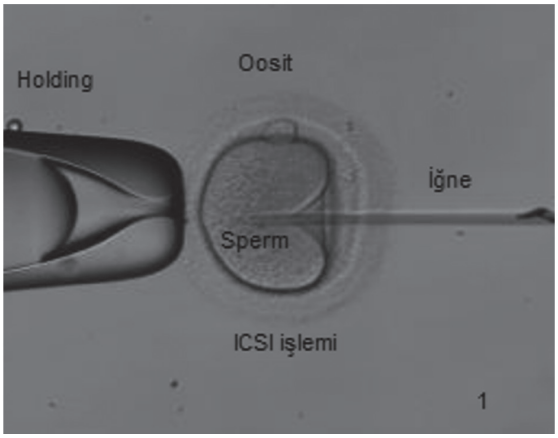
Yardımla Üreme Teknikleri (YÜT) kullanılarak geliştirilen embriyolarda yapılan genetik incelemelere Preimplantasyon Genetik Tanı (Preimlantation Genetic Diagnosis = PGD) denir. PGD işleminde, hastalığa sebep olabilecek genin veya kromozom bozukluğu olan embriyoların tespit edilip sağlıklı embriyoların seçilmesi sağlanır (1) . Tek gen hastalıklarında ve yapısal kromozomal düzensizliklerde PGD terimi kullanılırken, kromozomal anöploidi taraması için Preimlantasyon Genetik Tarama (Preimlantation Genetic Screening = PGS) terimi kullanılır.



Şekil 1

Laboratuvar ortamında sperm ile yumurta hücrelerinin döllenmesi sonucunda gelişen embriyolardan 3. günde 1 - 2 adet, 5 - 6 günde ise 4 - 6 adet hücre alınması

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Bu yöntem diğer yöntemlere göre daha avantajlıdır. Fazla hücre alınmasından dolayı sonucun doğruluk oranını artırır. Yapılan teknik işlem ile embriyonun zara görme olasılığı minimalize edilmiş olur. Anne ve babadan gelen genetik materyaller incelenmiş olur. Embriyonik aşamadan, blastokistlik aşamaya kadar laboratuvar ortamında kültüre edildiğinde kromozomu bozuk olan embriyolar elenmiş olur (21). Çoğul gebeliklerin önüne geçmek için tekli embriyo transferi yapılmasına olanak tanır (15).

REFERANSLAR

1. Alan R. Thornhill and Karen Snow Molecular Diagnostics in Preimplantation Genetic Diagnosis J Mol Diagn. 2002 Feb; 4(1): 11–29. doi: 10.1016/S1525-1578(10)60676-9 PMCID: PMC1906968 PMID: 11826184
2. Angell, R.R. et al. (1983) Chromosome abnormalities in human embryos after in vitro fertilization. Nature 303, 336–338.
3. Angell, R.R. et al. (1986) Chromosome studies in human in vitro fertilization. Hum. Genet. 72, 333–339.
4. Niebuhr E, Sparrevohn S, Henningsen K, Mikkelsen M. A case of liveborn triploidy (69,XXX). PMID: 4622018 DOI:10.1111/j.1651-2227.1972.tb15925.x
5. Edwards, R.G. and Gardner, R.L. (1967) Sexing of live rabbit blastocysts. Nature 214, 576–577.
6. Steptoe, P.C. and Edwards, R.G. (1978) Birth after the reimplantation of a human embryo. Lancet 2, 366.
7. Handyside, A.H. et al. (1990) Pregnancies from biopsied human preimplantation embryos sexed by Y-specific DNA amplification. Nature 344, 768–70.
8. Treff NR, Su J, Tao X, Levy B, Scott RT Jr. Accurate single cell 24 chromosome aneuploidy screening using whole genome amplification and single nucleotide polymorphism microarrays. Fertil Steril 2010;94:2017.
9. Hassold, T. and Hunt, P. (2001) To err (meiotically) is human: The genesis of human aneuploidy. Nat. Rev. Genet. 2, 280–291.
10. Hassold, T. and Hunt, P. (2009) Maternal age and chromosomally abnormal pregnancies: what we know and what we wish we knew. Curr Opin Pediatr 21, 703–8.
11. Munne, S. et al. (1995) Embryo morphology, developmental rates, and maternal age are correlated with chromosome abnormalities. Fertil Steril 64, 382–91.
12. Kuliev, A. and Verlinsky, Y. (2005) Preimplantation diagnosis: a realistic option for assisted reproduction and genetic practice. Curr. Opin. Obstet. Gynecol. 17, 179–183.
13. Mastenbroek, S. et al. (2007) In vitro fertilization with preimplantation genetic screening. N Engl J Med 357, 9–17.
14. Fritz, M.A. (2008) Perspectives on the efficacy and indications for preimplantation genetic screening: where are we now? Hum Reprod 23, 2617–21.
15. Forman, E.J. et al. (2014) Obstetrical and neonatal outcomes from the BEST Trial: single embryo transfer with aneuploidy screening improves outcomes after in vitro fertilization without compromising delivery rates. Am. J. Obstet. Gynecol. 2014 Feb;210(2):157.e1-6.
16. Staessen, C. et al. (2004) Comparison of blastocyst transfer with or without preimplantation genetic diagnosis for aneuploidy screening in couples with advanced maternal age: a prospective randomised controlled trial. Hum Reprod 19, 2849–58.
17. Hardarson, T. et al. (2008) Preimplantation genetic screening in women of advanced maternal age caused a decrease in clinical pregnancy rate: a randomized controlled trial. Hum Reprod 23, 2806–12.
18. Debrock, S. et al. (2007) Preimplantation genetic screening (PGS) for aneuploidy in embryos after in vitro fertilization (IVF) does not improve reproductive outcome in women over 35: a prospective controlled randomised study. Fertil Steril 88, S237.

19. Meyer, L.R. et al. (2009) A prospective randomized controlled trial of preimplantation genetic screening in the "good prognosis" patient. Fertil Steril 91, 1731–8.
20. Mersereau, J.E. et al. (2008) Preimplantation genetic screening in older women: a cost-effectiveness analysis. Fertil. Steril. 90, 592–598.
21. Northrop LE, Treff NR, Levy B, Scott RT., Jr SNP microarray-based 24 chromosome aneuploidy screening demonstrates that cleavage-stage FISH poorly predicts aneuploidy in embryos that develop to morphologically normal blastocysts. Mol Hum Reprod. 2010;16:590–600. doi: 10.1093/molehr/gaq037.
22. Fiegler H, Geigl JB, Langer S, et al. High resolution array-CGH analysis of single cells. Nucleic Acids Res. 2007;35:e15. doi: 10.1093/nar/gkl1030.
23. Treff NR, Levy B, Su J, Northrop LE, Tao X, Scott RT., Jr SNP microarray-based 24 chromosome aneuploidy screening is significantly more consistent than FISH. Mol Hum Reprod. 2010;16:583–9. doi: 10.1093/molehr/gaq039.
24. Brezina PR, Kutteh WH. Preimplantasyon genetik testlerinin klinik uygulamaları. BMJ (Clin Res Ed) 2015; 350 : g7611.
25. Handyside AH. PGD and aneuploidy screening for 24 chromosomes by genome-wide SNP analysis: seeing the wood and the trees 2011; 23 : 686-91. doi: 10.1016 / j.rbmo.2011.09.012.
26. Brezina PR, Benner A, Rechitsky S, Kuliev A, Pomerantseva E, Pauling D, et al. Single-gene testing combined with singles nucleotide polymorphism microarray preimplantation genetic diagnosis for aneuploidy: a novel approach in optimizing pregnancy outcome. Fertil Steril 2011;95:1786.e5-8.
27. Treff NR, Tao X, Ferry KM, Su J, Taylor D, Scott RT., Jr Development and validation of an accurate quantitative real-time polymerase chain reaction-based assay for human blastocyst comprehensive chromosomal aneuploidy screening. Fertil Steril. 2012;97:819–24. doi: 10.1016/j.fertnstert.2012.01.115.
28. Treff NR, Scott RT., Jr Four-hour quantitative real-time polymerase chain reaction-based comprehensive chromosome screening and accumulating evidence of accuracy, safety, predictive value, and clinical efficacy. Fertil Steril. 2013;99:1049–53. doi: 10.1016/j.fertnstert.2012.11.007.
29. Capalbo A, Treff NR, Cimadomo D, et al. Comparison of array comparative genomic hybridization and quantitative real-time PCR-based aneuploidy screening of blastocyst biopsies. Eur J Hum Genet: EJHG. 2015;23:901–6. doi: 10.1038/ejhg.2014.222.
30. Wells D, Delhanty JD. Comprehensive chromosomal analysis of human preimplantation embryos using whole genome amplification and single cell comparative genomic hybridization. Mol Hum Reprod 2000;6:1055.
31. Tiegs, A.W., Hodes-Wertz, B., McCulloh, D.H. et al. J Assist Reprod Genet 2016;33:893. doi:10.1007/s10815-016-0695-3.
32. Buermans HPJ, den Dunnen JT. Next generation sequencing technology: Advances and applications. Biochimica et Biophysica Acta. 2014;1842(10):1932-41.
33. Maxwell SM, Colls P, Hodes-Wertz B, McCulloh DH, McCaffrey C, Wells D, Munné S, Grifo JA. Why do euploid embryos miscarry? A case-control study comparing the rate of aneuploidy within presumed euploid embryos that resulted in miscarriage or live birth using next-generation sequencing. Fertil Steril 2016. pii: S0015-0282(16)62686-9. doi: 10.1016/ j.fertnstert.2016.08.017.
34. Delhanty JD, Harper JC, Ao A, Handyside AH, Winston RM. Multicolour FISH detects frequent chromosomal mosaicism and chaotic division in normal preimplantation embryos from fertile patients. Hum Genet 1997;99:755.
35. Norbert Gleicher, Andrea Vidali, Jeffrey Braverman, Vitaly A. Kushnir, David H. Barad, Cynthia Hudson, Yang-Guan Wu, Qi Wang, Lin Zhang, David F. Albertini and the International PGS Consortium Study Group. Accuracy of preimplantation genetic screening (PGS) is compromised by degree of mosaicism of human embryos. Reproductive Biology and Endocrinology 2016;14:54.

36. Sachdev NM, Maxwell SM, Besser AG, Grifo JA. Diagnosis and clinical management of embryonic mosaicism. Fertil Steril. 2016. pii: S0015-0282(16)62921-7. doi: 10.1016/ j.fertnstert.2016.10.006.
37. Greco E, Minasi MG, Fiorentino F. Healthy babies after intrauterine transfer of mosaic aneuploid blastocysts. N Engl J Med 2015;373: 2089.
38. J. Gontar ,Kazachkova ,I. İlyin ,N. Buderatska , A.Fedota ,O. Parnitska ,K. Ilyina ,E. Kapustin ,S. Lavrynenko ,Y. Lakhno PGT-A, a new dance for two couples: NGS with FISH and trophectoderm cells with blastocelic fluid. Reprod Bio Online.2019 DOI: https://doi.org/10.1016/j.rbmo.2019.03.069.
39. Nicolaidis P,Petersen MB.Origin and mechanisms of non-disjunction in human autosomal trisomies. Hum Reprod 1998;13:313–319
40. Montag M, Köster M, Strowitzki T, Toth B. Polar body biopsy. Fertil Steril. 2013; 100 (3):603–607. doi: 10.1016/j.fertnstert.2013.05.053.
41. Geraedts J, Sermon K. Preimplantation genetic screening 2.0: the theory. MHR Basic Sci Reprod Med. 2016; 22 (8):839–844. doi: 10.1093/molehr/gaw033.