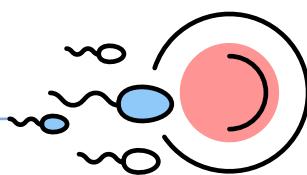


BÖLÜM 10

ERKEK İNFERTİLİTESİNİN NEDENLERİ



Serdar YİĞİT¹

GİRİŞ

Sağlıklı bir kadın partneri ile düzenli ve korunmasız olarak cinsel ilişkiye girmesinin sonucunda çocuk sahibi olamaması haline infertilite denilmektedir. Eşler arasında bu durumun görülmeye sıklığı %9 ile %15 arasındadır (1). Infertilite nedenleri kadın ve erkek kaynaklı olabileceği gibi her ikisinden kaynaklıda olabilmektedir. Kadın kaynaklı infertilitenin nedenleri genetik etiyoloji, hastalıklar psikolojik faktörler nedeniyle bozulabilmektedir (2,3). Infertilite etiyolojisinde erkek faktörü %30 kadın faktörü %40–50 hem erkek hem de kadın kaynaklı ortak infertilite %20 olarak bilinmektedir (4,5). Bu verilere göre doğrudan ve dolaylı olarak erkek kaynaklı infertilite oranı %50 olarak görülmektedir (6). Infertilite eşler açısından duygusal olarak stresli tedavisi ise maddi olarak sıkıntılı bir süreçtir (7). Erkek kaynaklı infertilite nedenleri bu bölümde, non-obstrüktif infertilite, idiopatik erkek infertilitesi, obstrüktif infertilite olarak ayrıntılı olarak anlatılacaktır.

NON-OBSTRÜKTİF İNFERTİLİTE

Non-obstrüktif infertilite testislerin yeterli sayıda ve harekette sperm üretmemesi olarak bilinmektedir. Bu oranda yaklaşık olarak %60'dır. Non-Obstrüktif İnfertilili-

¹ Arş. Gör. Dr., Kafkas Üniversitesi Tıp Fakültesi Histoloji ve Embriyoloji AD., yiğitserdar85@gmail.com

KAYNAKLAR

1. Greenhall E, Vessey M. The prevalence of subfertility: a review of the current confusion and a report of two new studies. *Fertil Steril* 1990; 54 (6), 978-983.
2. Vogler A. Obravnava neplodnega para. In: Vrtačnik Bokal E, Jančar N, eds. Sodobne oblike zdravljenja neplodnosti/IV spominski sestanek akad. prof. dr. Lidiye Andolšek-Jeras. Ljubljana: Slovensko društvo za reproduktivno medicine, 2007; p. 10-4
3. Zorn B. Moška neplodnost. In: Takač I, Geršak K, eds. Ginekologija in perinatologija. 1st edn. Maribor: Medicinska fakulteta. 2016; p. 206-16
4. Knez J, Vlaisavljević V. Ženska neplodnost. In: Takač I, Geršak K, eds. Ginekologija in perinatologija. 1st edn. Maribor: Medicinska fakulteta; 2016. p. 170-9
5. Raheem A, Ralph D. Male infertility: causes and investigations. *Trends Urol Men's Health*. 2011;2 (5):8-11.
6. Jungwirth A, Diemer T, Kopa Z, Krausz C, Minhas S, Tournaye H. EAU Guidelines on Male Infertility. *European Association of Urology*; 2019.
7. Pasch LA, Gregorich SE, Katz PK, Millstein SG, et al. Psychological distress and in vitro fertilization outcome. *Fertil Steril* 2012; 98 (2), 459-464
8. Karagöz Can, N. (2018). erkek infertilitesi tanısı almış bireylerin spermlerinde otofaji belirteçlerinin araştırılması
9. Hoffman AR, Crowley WF. Induction of Puberty in Men by Long-Term Pulsatile Administration of Low-Dose Gonadotropin-Releasing Hormone. *New Engl J Med*. 1982;307 (20):1237-41
10. Belchetz PE, Plant TM, Nakai Y, Keogh EJ, Knobil E. Hypophysial responses to continuous and intermittent delivery of hypothalamic gonadotropin-releasing hormone. *Science*. 1978;202 (4368):631-3.
11. Vicari E, Mongioi A, Calogero AE, Moncada ML, Sidoti G, Polosa P, et al. Therapy with human chorionic gonadotrophin alone induces spermatogenesis in men with isolated hypogonadotropic hypogonadism—long-term follow-up. *International journal of andrology*. 1992;15 (4):320-9.
12. Finkel DM, Phillips JL, Snyder PJ. Stimulation of spermatogenesis by gonadotropins in men with hypogonadotropic hypogonadism. *N Engl J Med*. 1985;313 (11):651-5.
13. Pitteloud N, Hayes FJ, Dwyer A, Boepple PA, Lee H, Crowley WF, Jr Predictors of outcome of long-term GnRH therapy in men with idiopathic hypogonadotropic hypogonadism. *The Journal of clinical endocrinology and metabolism*. 2002;87 (9):4128-36.
14. Margioris, A. N., & Chrousos, G. P. (Eds.). Adrenal disorders. Springer Science & Business Media. (2001).
15. Foresta C, Ferlin A, Gianaroli L, Dallapiccola B. Guidelines for the appropriate use of genetic tests in infertile couples. *European Journal of Human Genetics* 2002; 10 (5), 303-312.
16. Ferlin A, Garolla A, Foresta C. Chromosome abnormalities in sperm of individuals with constitutional sex chromosomal abnormalities. *Cytogenetics and Genome Research* 2005; 111 (3-4), 310-316.
17. Mau-Holzmann UA. Somatic chromosomal abnormalities in infertile men and women. *Cytogenetics and Genome Research* 2005; 111 (3-4), 317-336.
18. Foresta C, Moro E, Ferlin A. Y chromosome microdeletions and alterations of spermatogenesis. *Endocrine Reviews* 2001; 22 (2), 226-239.

19. Ferlin A, Arredi B, Speltra E et al. Molecular and clinical characterization of Y chromosome microdeletions in infertile men: a ten year experience in Italy. *Journal of Clinical Endocrinology and Metabolism* 2007; 92 (3), 762-770
20. Kuroda-Kawaguchi T, Skaletsky H, Brown LG et al. The AZFc region of the Y chromosome features massive palindromes and uniform recurrent deletions in infertile men. *Nature Genetics* 2001; 29 (3), 279-286
21. Stuppia L, Gatta V, Fogh I et al. Genomic organization, physical mapping, and involvement in Yq microdeletions of the VCY2 (BPY 2) gene. *Genomics* 2001; 72 (2), 153-157.
22. Repping S, Skaletsky H, Lange J et al. Recombination between palindromes P5 and P1 on the human Y chromosome causes massive deletions and spermatogenic failure. *American Journal of Human Genetics* 2002; 71 (4), 906-922
23. Foresta C, Garolla A, Bartoloni L et al. Genetic abnormalities among severely oligospermic men who are candidates for intracytoplasmic sperm injection. *Journal of Clinical Endocrinology and Metabolism* 2005; 90 (1), 152-156.
24. Foresta C, Ferlin A, Gianaroli L, Dallapiccola B Guidelines for the appropriate use of genetic tests in infertile couples. *European Journal of Human Genetics* 2002; 10 (5), 303-312.
25. Damsgaard, J. et al. Varicocele is associated with impaired semen quality and reproductive hormone levels: a study of 7035 healthy young men from six European countries. *Eur. Urol* 2016; 70 (6), 1019-1029.
26. Wang, Y. J., Zhang, R. Q., Lin, Y. J., Zhang, R. G. & Zhang, W. L. Relationship between varicocele and sperm DNA damage and the effect of varicocele repair: a meta-analysis. *Reprod. Biomed. Online* 2012; 25 (3), 307-314
27. Vigil, P., Wohler, C., Bustos-Obregon, E., Comhaire, F. & Morales, P. Assessment of sperm function in fertile and infertile men. *Andrologia* 1994; 26 (2), 55-60.
28. Abdelrahim, F. et al. Testicular morphology and function in varicocele patients: pre-operative and post-operative histopathology. *Br. J. Urol.* 1993; 72 (5), 643-647.
29. Dubin, L. & Hotchkiss, R. S. Testis biopsy in subfertile men with varicocele. *Fertil. Steril.* 1969; 20 (1), 50-57
30. Etriby, A., Girgis, S. M., Hefnawy, H. & Ibrahim, A. A. Testicular changes in subfertile males with varicocele. *Fertil. Steril.* 1967; 18 (5), 666-671.
31. Cayan, S. et al. The effect of microsurgical varicocelectomy on serum follicle stimulating hormone, testosterone and free testosterone levels in infertile men with varicocele. *BJU Int.* 1999; 84 (9), 1046-1049.
32. Agarwal, A., Hamada, A., & Esteves, S. C. (2012). Insight into oxidative stress in varicocele-associated male infertility: part 1. *Nature Reviews Urology*, 9 (12), 678-690.
33. Hurtado de Catalfo, G. E., Ranieri-Casilla, A., Marra, F. A., de Alaniz, M. J. & Marra, C. A. Oxidative stress biomarkers and hormonal profile in human patients undergoing varicocelectomy. *Int. J. Androl* 2007; 30 (6), 519-530.
34. Sakamoto, Y., Ishikawa, T., Kondo, Y., Yamaguchi, K. & Fujisawa, M. The assessment of oxidative stress in infertile patients with varicocele. *BJU Int.* 2008; 179 (4S), 635-636.
35. Zini A, Boman JM. Varicocele: red flag or red herring? *Semin Reprod Med.* 2009; 27 (2). pp. 171-178
36. Dubin L, Amelar RD. Varicocele size and results of varicocelectomy in selected subfertile men with varicocele. *Fertil. Steril.* 1970; 21 (8), 606-609.

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37. Steeno O, Knops J, Declerck L, Adimoelja A, van de Voorde H. Prevention of fertility disorders by detection and treatment of varicocele at school and college age. *Andrologia* 1976; 8 (1), 47-53.
38. Inci K, Hascicek M, Kara O, Dikmen AV, Gürgan T, Ergen A. Sperm retrieval and intracytoplasmic sperm injection in men with nonobstructive azoospermia, and treated and untreated varicocele. *J Urol* 2009; 182 (4), 1500-1505.
39. Fideleff HL, Boquete HR, Suarez MG, Ruibal GF, Sobrado PG, Azaretsky M, Pujol AB, Sequera AM, Giuseppucci J, Poncino R. Controversies in the evolution of paediatric-adolescent varicocele: clinical, biochemical and histological studies. *Eur J Endocrinol* 2000; 143 (6):775-781
40. Kass EJ, Stork BR, Steinert BW. Varicocele in adolescence induces left and right testicular volume loss. *BJU Int* 2001; 87 (6):499-501
41. Krieger JN, Nyberg L Jr, Nickel JC. NIH consensus definition and classification of prostatitis. *JAMA* 1999; 282 (3):236-7
42. Ludwig M, Vidal A, Huwe P, et al. Significance of inflammation on standard semen analysis in chronic prostatitis/chronic pelvic pain syndrome. *Andrologia* 2003; 35 (3):152-6.)
43. Henkel R, Ludwig M, Schuppe HC, et al. Chronic pelvic pain syndrome/ chronic prostatitis affect the acrosome reaction in human spermatozoa. *World J Urol* 2006; 24 (1):39-44
44. Campbell MF. Gonococcus epididymitis: observations in three thousand cases from the urological service of Bellevue hospital. *Annals of Surgery*, 1927; 86 (4), 577.
45. Berger, R. E., Kessler, D., & Holmes, K. K.. Etiology and manifestations of epididymitis in young men: correlations with sexual orientation. *The Journal of infectious diseases* 1987;155 (6), 1341-1343
46. Berger, R. E., Alexander, E. R., Monda, G. D., Ansell, J., McCormick, G., & Holmes, K. K. Chlamydia trachomatis as a cause of acute "idiopathic" epididymitis. *New England Journal of Medicine*, 1978; 298 (6), 301-304.
47. Doble, A., Taylor-Robinson, D., Thomas, B. J., Jalil, N., Harris, J. R. W., & WITHEROW, R. O. N.. Acute epididymitis: a microbiological and ultrasonographic study. *British journal of urology* 1989; 63 (1), 90-94.
48. Kaver, I., Matzkin, H., & Braf, Z. F.. Epididymo-orchitis: a retrospective study of 121 patients. *Journal of Family Practice*, 1990 ;30 (5), 548-552.
49. Pilatz, A., Ceylan, I., Schuppe, H. C., Ludwig, M., Fijak, M., Chakraborty, T., & Wagenlehner, F. Experimental Escherichia coli epididymitis in rats: assessment of testicular involvement in a long-term follow-up. *Andrologia* 2015; 47 (2), 160-167.
50. Hedger, M. P Immunophysiology and pathology of inflammation in the testis and epididymis. *Journal of andrology*, 2011; 32 (6), 625-640.
51. MD, P. T. C., & Schlegel, P. N. (). Inflammatory conditions of the male excurrent ductal system. Part I. *Journal of andrology* 2002; 23 (4), 453-460.
52. Pilatz A, Fijak M, Wagenlehner F, Schuppe HC. Orchitis . *Urologe A*. Jun 2019;58 (6):697-710
53. Krieger JN. Epididymitis, orchitis, and related conditions. *Sex Transm Dis*. 1984 ;11 (3):173-49.
54. Kanda T, Mochida J, Takada S, Hori Y, Yamaguchi K, Takahashi S. Case of mumps orchitis after vaccination. *Int J Urol*. 2014 ;21 (4):426-8
55. Silva CA, Cocuzza M, Carvalho JF, Bonfá E. Diagnosis and classification of autoimmune orchitis. *Autoimmun Rev*. Apr-May 2014;13 (4-5):431-4

56. Ochsendorf FR. Sexually transmitted infections: impact on male fertility. *Andrologia* 2008; 40 (2): 72–5
57. Rusz A, Pilatz A, Wagenlehner F, et al. Influence of urogenital infections and inflammation on semen quality and male fertility. *World J Urol* 2012; 30 (1): 23–30.
58. Pappas G, Bliziotis IA, Falagas ME. In: Schlossberg D (Ed). Clinical Infectious Disease. 2nd ed. Cambridge: Cambridge University Press; 2015: p.386-391.
59. World Health Organization. WHO laboratory manual for the examination and processing of human semen. 5th ed. Geneva: World Health Organization; 2010.
60. Aziz N, Agarwal A, Lewis-Jones I, Sharma RK, Thomas AJ. Jr Novel associations between specific sperm morphological defects and leukocytospermia. *Fertil Steril*. 2004; 82 (3), 621-627
61. Lackner JE, Herwig R, Schmidbauer J, Schatzl G, Kratzik C, Marberger M. Correlation of leukocytospermia with clinical infection and the positive effect of antiinflammatory treatment on semen quality. *Fertil Steril*. 2006; 86 (3), 601-605
62. Domes T, Lo KC, Grober ED, et al. The incidence and effect of bacteriospermia and elevated seminal leukocytes on semen parameters. *Fertil Steril* 2012; 97 (5):1050–5
63. Punab M, Loivukene K, Kermes K, et al. The limit of leucocytospermia from the microbiological viewpoint. *Andrologia* 2003; 35 (5):271–8
64. Wolff H. The biologic significance of white blood cells in semen. *Fertil Steril* 1995; 63 (6):1143–57
65. Yanushpolsky EH, Politch JA, Hill JA, et al. Is leukocytospermia clinically relevant? *Fertil Steril* 1996; 66 (5):822–5
66. Hadziselimovic F, Herzog B. Importance of early postnatal germ cell maturation for fertility of cryptorchid males. *Horm Res*. 2001; 55 (1), 6-10.
67. Gross RE, Jewett TC., Jr Surgical experiences from 1,222 operations for undescended testis. *J Am Med Assoc*. 1956; 160 (8), 634-641
68. Gilhooly PE, Meyers F, Lattimer JK. Fertility prospects for children with cryptorchidism. *Am J Dis Child*. 1984; 138 (10), 940-943
69. Lee PA, O'Leary LA, Songer NJ, Coughlin MT, Bellinger MF, LaPorte RE. Paternity after unilateral cryptorchidism: a controlled study. *Pediatrics*. 1996; 98 (4), 676-679
70. Lee PA, O'Leary LA, Songer NJ, Coughlin MT, Bellinger MF, LaPorte RE. Paternity after bilateral cryptorchidism: a controlled study. *Arch Pediatr Adolesc Med*. 1997; 151 (3), 260-263.
71. Lee PA, Coughlin MT, Bellinger MF. Inhibin B: comparison with indexes of fertility among formerly cryptorchid and control men. *J Clin Endocrinol Metab*. 2001; 86 (6), 2576-2584.
72. Raheem AA, Ralph D. Male infertility: causes and investigations. *Trends in Urology & Men's Health* 2011; 2 (5): 8-11.
73. Huang WY, Chen YF, Chang HC, Yang TK, Hisieh JT, Huang KH. The incidence rate and characteristics in patients with testicular torsion: a nationwide, population-based study *Acta Paediatrica* 2013, 102 (8), e363-e367..
74. Türk H, Çelik O, İşoğlu S, Tarhan H, İlbel YÖ. Erişkinde Testis Torsiyonu, Tepecik Eğit. *Hast Derg*. 2014; 24 (1): 73-76.
75. Coursey Moreno C, Small WC, Camacho JC, et al. Testicular tumors: what radiologists need to know--differential diagnosis, staging, and management. *Radiographics* 2015; 35 (2), 400-415.

- Temel ve Klinik Yönleriyle İnfertilite

76. Thaper,D.; Prabha, V. Molecular mimicry: An explanation for autoimmune diseases and infertility. *Scand. J. Immunol.* 2018; 88 (2), e12697.
77. Kanduc, D. The role of proteomics in defining autoimmunity. *Expert Rev. Proteom.* 2021; 18 (3), 177-184.
78. Pashnina, I.A.; Krivolapova, I.M.; Fedotkina, T.V.; Ryabkova, V.A.; Chereshneva, M.V.; Churilov, L.P.; Chereshnev, V.A. Antinuclear Autoantibodies in Health: Autoimmunity Is Not a Synonym of Autoimmune Disease. *Antibodies* 2021;10 (1), 9.,
79. Krassas, G. E., & Pontikides, N. (2004). Male reproductive function in relation with thyroid alterations. *Best Practice & Research Clinical Endocrinology & Metabolism*, 18 (2), 183-195.
80. Chereshnev, V. A., Pichugova, S. V., Beikin, Y. B., Chereshneva, M. V., Lukhta, A. I., Stroev, Y. I., & Churilov, L. P.. Pathogenesis of Autoimmune Male Infertility: Juxtacrine, Paracrine, and Endocrine Dysregulation. *Pathophysiology*, 2021; 28 (4), 471-488.
81. Pryor JP, Hendry WF. Ejaculatory duct obstruction in subfertile males: analysis of 87 patients. *Fertil Steril* 1991; 56 (4), 725-730
82. Dik P, Lock TM, Schrier BP, Zeijlemaker BY, Boon TA. Transurethral marsupialization of a medial prostatic cyst with prostatitis-like symptoms. *J Urol* 1996; 155 (4), 1301-1304.