Bölüm
10

İNFERTİLİTE VE ENDOMETRİOZİS

Eda Adeviye ŞAHİN[1]
Turan ŞAHİN[2]

GİRİŞ

Endometriozis, endometriyuma benzer dokunun (gland ve stroma) uterus dışındaki bölgelerde bulunması ile karakterize (özellikle overleri içeren pelvik alan, ligamentler, peritoneal yüzeylerin yanısıra mesane ve barsaklar da dahil olmak üzere), kadınlarda yaygın, genellikle kronik, inflamatuar bir hastalıktır(1). Yüzeysel periton ve serozal lezyonlardan, overlere (endometrioma) ve >5 mm derinliğinde nodüllere kadar değişen heterojen bir hastalıktır ve genellikle skar ve adezyonlar eşlik eder. Endometriozis, tipik olarak dismenore, disparoni ve infertilite ile ilişkilidir(2). Ancak hastaların % 20-25'i asemptomatik olabilir. Endometriotik dokunun büyümesi östrojene bağımlıdır; buna göre, durum esas olarak menarş ve menopoz arasında ortaya çıkar, ancak hastalık premenarşeal kızlarda da tanımlanmıştır(3) ve menopozdan sonra tekrarlayabilir.

Endometriozis, yüksek nüks oranları ile karakterize edilen bir süreçtir. Etiyoloji ve patogenez belirsizliğini korumaktadır. Tedavinin temel amaçları semptomların hafifletilmesini, mevcut endometriotik implantların çıkarılmasını ve yeni ektopik endometriyal doku odaklarının önlenmesini içerir. Mevcut terapötik yaklaşımlar tam kür sağlayamayabilmektedir; bu nedenle klinisyenler hastalığın klinik semptomlarını yönetmeye odaklanırlar. Tıbbi, cerrahi ve psikolojik tedavilerin spesifik kombinasyonları endometriozisli kadınların yaşam kalitesini iyileştirebilir. Bu tedavilerin faydaları, özellikle kadınların kendi yaşamları için sahip oldukları beklentiler açısından tam olarak kanıtlanmamıştır. Teorik olarak avantajlı olmasına rağmen, bir kombinasyon tıbbi-cerrahi tedavinin fertiliteyi önemli

[1] Malatya Eğitim ve Araştırma Hastanesi Obstetri ve Jinekoloji Kliniği
[2] Sancaktepe Şehit Prof. Dr. İlhan Varank Eğitim ve Araştırma Hastanesi Obstetri ve Jinekoloji Kliniği

pinlerle) ve IUI kullanımı için destekleyici kanıtlar vardır (64, 65). Endometriozis hastaları cerrahi olarak tedavi edildiğinden ve bazı kadınlarda açıklanamayan infertiliteye sahip oldukları ve minimal evre endometriozisi olduğu varsayıldığı için bu çalışmaların çoğu seçim yanlılığına maruz kalmaktadır. Genel olarak, ovulasyon ve IUI halen IVF'e alternatif olarak minimal evre endometriozisi olan kadınlar için uygun bir tedavi seçeneği olarak kabul edilmektedir.

İn vitro fertilizasyon (IVF)

IVF kullanan daha agresif infertilite tedavisi formu, ileri endometriozis ve bozulmuş pelvik anatomisi olan kadınlarda doğurganlığı en üst düzeye çıkarmaktadır.Bir meta-analiz, endometriozisli infertil kadınların IVF ile başarısının önemli ölçüde daha düşük olduğunu göstermiştir (66). Buna daha düşük bir over yanıtı, daha az implantasyon ve genel olarak daha düşük gebelik oranları dahildir. Ek olarak, hastalığın daha ileri bir aşaması daha düşük bir sonuçla ilişkiliydi.

ENDOMETRİOZİSTE GEBELİK SONUÇLARI

Endometriozisli kadınların hastalıksız kadınlara göre daha yüksek olumsuz obstetrik sonuçlara sahip olduğu gösterilmiştir. Büyük bir çalışmada, endometriozisli kadınlarda preeklampsi (OR 1.13,% 95 CI 1.02-1.26), antepartum kanama / plasental komplikasyonlar (OR 1.76,% 95 CI 1.56-1.99) ve sezaryen doğum (OR 1.47 ,% 95 CI 1.40-1.54) daha yüksek oranlara sahipti (67). Bu ilişkilerin endometriozis veya ART tedavisine bağlı olup olmadığı açık değildir.

REFERANSLAR

1. Kennedy S, Bergqvist A, Chapron C, D'Hooghe T, Dunselman G, Greb R, et al. ESHRE guideline for the diagnosis and treatment of endometriosis. Hum Reprod. 2005;20(10):2698-704.
2. Halme J, Hammond MG, Hulka JF, Raj SG, Talbert LM. Retrograde menstruation in healthy women and in patients with endometriosis. Obstet Gynecol. 1984;64(2):151-4.
3. Marsh EE, Laufer MR. Endometriosis in premenarcheal girls who do not have an associated obstructive anomaly. Fertil Steril. 2005;83(3):758-60.
4. Hummelshoj L, Prentice A, Groothuis P. Update on endometriosis. Womens Health (Lond). 2006;2(1):53-6.
5. Giudice LC, Kao LC. Endometriosis. Lancet. 2004;364(9447):1789-99.
6. Simoens S, Hummelshoj L, D'Hooghe T. Endometriosis: cost estimates and methodological perspective. Hum Reprod Update. 2007;13(4):395-404.
7. Bulletti C, Coccia ME, Battistoni S, Borini A. Endometriosis and infertility. J Assist Reprod Genet. 2010;27(8):441-7.
8. Nnoaham KE, Hummelshoj L, Webster P, d'Hooghe T, de Cicco Nardone F, de Cicco Nardone C, et al. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. Fertil Steril. 2011;96(2):366-73 e8.
9. Schuring AN, Dahlhues B, Korte A, Kiesel L, Titze U, Heitkotter B, et al. The endometrial stem cell markers notch-1 and numb are associated with endometriosis. Reprod Biomed Online. 2018;36(3):294-301.

10. Cousins FL, O DF, Gargett CE. Endometrial stem/progenitor cells and their role in the pathogenesis of endometriosis. Best Pract Res Clin Obstet Gynaecol. 2018;50:27-38.
11. Sampson JA. Metastatic or Embolic Endometriosis, due to the Menstrual Dissemination of Endometrial Tissue into the Venous Circulation. Am J Pathol. 1927;3(2):93-110 43.
12. Nunley WC, Jr., Kitchin JD, 3rd. Congenital atresia of the uterine cervix with pelvic endometriosis. Arch Surg. 1980;115(6):757-8.
13. Ferguson BR, Bennington JL, Haber SL. Histochemistry of mucosubstances and histology of mixed mullerian pelvic lymph node glandular inclusions. Evidence for histogenesis by mullerian metaplasia of coelomic epithelium. Obstet Gynecol. 1969;33(5):617-25.
14. Steele RW, Dmowski WP, Marmer DJ. Immunologic aspects of human endometriosis. Am J Reprod Immunol. 1984;6(1):33-6.
15. Oosterlynck DJ, Cornillie FJ, Waer M, Vandeputte M, Koninckx PR. Women with endometriosis show a defect in natural killer activity resulting in a decreased cytotoxicity to autologous endometrium. Fertil Steril. 1991;56(1):45-51.
16. Harada T, Iwabe T, Terakawa N. Role of cytokines in endometriosis. Fertil Steril. 2001;76(1):1-10.
17. Chan RW, Schwab KE, Gargett CE. Clonogenicity of human endometrial epithelial and stromal cells. Biol Reprod. 2004;70(6):1738-50.
18. Taylor HS. Endometrial cells derived from donor stem cells in bone marrow transplant recipients. JAMA. 2004;292(1):81-5.
19. Du H, Taylor HS. Contribution of bone marrow-derived stem cells to endometrium and endometriosis. Stem Cells. 2007;25(8):2082-6.
20. Simpson JL, Elias S, Malinak LR, Buttram VC, Jr. Heritable aspects of endometriosis. I. Genetic studies. Am J Obstet Gynecol. 1980;137(3):327-31.
21. Hadfield RM, Mardon HJ, Barlow DH, Kennedy SH. Endometriosis in monozygotic twins. Fertil Steril. 1997;68(5):941-2.
22. Hadfield RM, Yudkin PL, Coe CL, Scheffler J, Uno H, Barlow DH, et al. Risk factors for endometriosis in the rhesus monkey (Macaca mulatta): a case-control study. Hum Reprod Update. 1997;3(2):109-15.
23. Bedaiwy MA, Falcone T, Mascha EJ, Casper RF. Genetic polymorphism in the fibrinolytic system and endometriosis. Obstet Gynecol. 2006;108(1):162-8.
24. Dinulescu DM, Ince TA, Quade BJ, Shafer SA, Crowley D, Jacks T. Role of K-ras and Pten in the development of mouse models of endometriosis and endometrioid ovarian cancer. Nat Med. 2005;11(1):63-70.
25. Grechukhina O, Petracco R, Popkhadze S, Massasa E, Paranjape T, Chan E, et al. A polymorphism in a let-7 microRNA binding site of KRAS in women with endometriosis. EMBO Mol Med. 2012;4(3):206-17.
26. Practice Committee of the American Society for Reproductive M. Endometriosis and infertility: a committee opinion. Fertil Steril. 2012;98(3):591-8.
27. Bulun SE. Endometriosis. N Engl J Med. 2009;360(3):268-79.
28. Schenken RS, Asch RH, Williams RF, Hodgen GD. Etiology of infertility in monkeys with endometriosis: luteinized unruptured follicles, luteal phase defects, pelvic adhesions, and spontaneous abortions. Fertil Steril. 1984;41(1):122-30.
29. Bedaiwy MA, Falcone T, Sharma RK, Goldberg JM, Attaran M, Nelson DR, et al. Prediction of endometriosis with serum and peritoneal fluid markers: a prospective controlled trial. Hum Reprod. 2002;17(2):426-31.
30. Opoien HK, Fedorcsak P, Polec A, Stensen MH, Abyholm T, Tanbo T. Do endometriomas induce an inflammatory reaction in nearby follicles? Hum Reprod. 2013;28(7):1837-45.
31. Punnonen J, Teisala K, Ranta H, Bennett B, Punnonen R. Increased levels of interleukin-6 and interleukin-10 in the peritoneal fluid of patients with endometriosis. Am J Obstet Gynecol. 1996;174(5):1522-6.

32. Pellicer A, Oliveira N, Ruiz A, Remohi J, Simon C. Exploring the mechanism(s) of endometriosis-related infertility: an analysis of embryo development and implantation in assisted reproduction. Hum Reprod. 1995;10 Suppl 2:91-7.
33. Dmowski WP, Rao R, Scommegna A. The luteinized unruptured follicle syndrome and endometriosis. Fertil Steril. 1980;33(1):30-4.
34. Cahill DJ, Hull MG. Pituitary-ovarian dysfunction and endometriosis. Hum Reprod Update. 2000;6(1):56-66.
35. Kitajima M, Dolmans MM, Donnez O, Masuzaki H, Soares M, Donnez J. Enhanced follicular recruitment and atresia in cortex derived from ovaries with endometriomas. Fertil Steril. 2014;101(4):1031-7.
36. Garrido N, Navarro J, Garcia-Velasco J, Remoh J, Pellice A, Simon C. The endometrium versus embryonic quality in endometriosis-related infertility. Hum Reprod Update. 2002;8(1):95-103.
37. Matorras R, Corcostegui B, Esteban J, Ramon O, Prieto B, Exposito A, et al. Fertility in women with minimal endometriosis compared with normal women was assessed by means of a donor insemination program in unstimulated cycles. Am J Obstet Gynecol. 2010;203(4):345 e1-6.
38. Lessey BA, Castelbaum AJ, Sawin SW, Buck CA, Schinnar R, Bilker W, et al. Aberrant integrin expression in the endometrium of women with endometriosis. J Clin Endocrinol Metab. 1994;79(2):643-9.
39. Bulun SE, Cheng YH, Yin P, Imir G, Utsunomiya H, Attar E, et al. Progesterone resistance in endometriosis: link to failure to metabolize estradiol. Mol Cell Endocrinol. 2006;248(1-2):94-103.
40. Taylor HS, Bagot C, Kardana A, Olive D, Arici A. HOX gene expression is altered in the endometrium of women with endometriosis. Hum Reprod. 1999;14(5):1328-31.
41. Lebovic DI, Mueller MD, Taylor RN. Immunobiology of endometriosis. Fertil Steril. 2001;75(1):1-10.
42. Leyendecker G, Kunz G, Wildt L, Beil D, Deininger H. Uterine hyperperistalsis and dysperistalsis as dysfunctions of the mechanism of rapid sperm transport in patients with endometriosis and infertility. Hum Reprod. 1996;11(7):1542-51.
43. Nisolle M, Donnez J. Peritoneal endometriosis, ovarian endometriosis, and adenomyotic nodules of the rectovaginal septum are three different entities. Fertil Steril. 1997;68(4):585-96.
44. Bazot M, Darai E. Diagnosis of deep endometriosis: clinical examination, ultrasonography, magnetic resonance imaging, and other techniques. Fertil Steril. 2017;108(6):886-94.
45. Falcone T, Flyckt R. Clinical Management of Endometriosis. Obstet Gynecol. 2018;131(3):557-71.
46. Guerriero S, Condous G, van den Bosch T, Valentin L, Leone FP, Van Schoubroeck D, et al. Systematic approach to sonographic evaluation of the pelvis in women with suspected endometriosis, including terms, definitions and measurements: a consensus opinion from the International Deep Endometriosis Analysis (IDEA) group. Ultrasound Obstet Gynecol. 2016;48(3):318-32.
47. Abrao MS, Goncalves MO, Dias JA, Jr., Podgaec S, Chamie LP, Blasbalg R. Comparison between clinical examination, transvaginal sonography and magnetic resonance imaging for the diagnosis of deep endometriosis. Hum Reprod. 2007;22(12):3092-7.
48. Bazot M, Malzy P, Cortez A, Roseau G, Amouyal P, Darai E. Accuracy of transvaginal sonography and rectal endoscopic sonography in the diagnosis of deep infiltrating endometriosis. Ultrasound Obstet Gynecol. 2007;30(7):994-1001.
49. Nisenblat V, Prentice L, Bossuyt PM, Farquhar C, Hull ML, Johnson N. Combination of the non-invasive tests for the diagnosis of endometriosis. Cochrane Database Syst Rev. 2016;7:CD012281.
50. Ozkan S, Murk W, Arici A. Endometriosis and infertility: epidemiology and evidence-based treatments. Ann N Y Acad Sci. 2008;1127:92-100.
51. Berube S, Marcoux S, Langevin M, Maheux R. Fecundity of infertile women with minimal or mild endometriosis and women with unexplained infertility. The Canadian Collaborative Group on Endometriosis. Fertil Steril. 1998;69(6):1034-41.

52. Hughes E, Brown J, Collins JJ, Farquhar C, Fedorkow DM, Vandekerckhove P. Ovulation suppression for endometriosis. Cochrane Database Syst Rev. 2007(3):CD000155.
53. Surrey ES, Silverberg KM, Surrey MW, Schoolcraft WB. Effect of prolonged gonadotropin-releasing hormone agonist therapy on the outcome of in vitro fertilization-embryo transfer in patients with endometriosis. Fertil Steril. 2002;78(4):699-704.
54. Sallam HN, Garcia-Velasco JA, Dias S, Arici A. Long-term pituitary down-regulation before in vitro fertilization (IVF) for women with endometriosis. Cochrane Database Syst Rev. 2006(1):CD004635.
55. Macer ML, Taylor HS. Endometriosis and infertility: a review of the pathogenesis and treatment of endometriosis-associated infertility. Obstet Gynecol Clin North Am. 2012;39(4):535-49.
56. Pundir J, Omanwa K, Kovoor E, Pundir V, Lancaster G, Barton-Smith P. Laparoscopic Excision Versus Ablation for Endometriosis-associated Pain: An Updated Systematic Review and Meta-analysis. J Minim Invasive Gynecol. 2017;24(5):747-56.
57. Marcoux S, Maheux R, Berube S. Laparoscopic surgery in infertile women with minimal or mild endometriosis. Canadian Collaborative Group on Endometriosis. N Engl J Med. 1997;337(4):217-22.
58. Parazzini F. Ablation of lesions or no treatment in minimal-mild endometriosis in infertile women: a randomized trial. Gruppo Italiano per lo Studio dell'Endometriosi. Hum Reprod. 1999;14(5):1332-4.
59. Flyckt R, Kim S, Falcone T. Surgical Management of Endometriosis in Patients with Chronic Pelvic Pain. Semin Reprod Med. 2017;35(1):54-64.
60. Camus E, Poncelet C, Goffinet F, Wainer B, Merlet F, Nisand I, et al. Pregnancy rates after in-vitro fertilization in cases of tubal infertility with and without hydrosalpinx: a meta-analysis of published comparative studies. Hum Reprod. 1999;14(5):1243-9.
61. Hart RJ, Hickey M, Maouris P, Buckett W. Excisional surgery versus ablative surgery for ovarian endometriomata. Cochrane Database Syst Rev. 2008(2):CD004992.
62. Goodman LR, Goldberg JM, Flyckt RL, Gupta M, Harwalker J, Falcone T. Effect of surgery on ovarian reserve in women with endometriomas, endometriosis and controls. Am J Obstet Gynecol. 2016;215(5):589 e1- e6.
63. Chapron C, Vercellini P, Barakat H, Vieira M, Dubuisson JB. Management of ovarian endometriomas. Hum Reprod Update. 2002;8(6):591-7.
64. Deaton JL, Gibson M, Blackmer KM, Nakajima ST, Badger GJ, Brumsted JR. A randomized, controlled trial of clomiphene citrate and intrauterine insemination in couples with unexplained infertility or surgically corrected endometriosis. Fertil Steril. 1990;54(6):1083-8.
65. Taylor HS, Giudice LC, Lessey BA, Abrao MS, Kotarski J, Archer DF, et al. Treatment of Endometriosis-Associated Pain with Elagolix, an Oral GnRH Antagonist. N Engl J Med. 2017;377(1):28-40.
66. Barnhart K, Dunsmoor-Su R, Coutifaris C. Effect of endometriosis on in vitro fertilization. Fertil Steril. 2002;77(6):1148-55.
67. Stephansson O, Kieler H, Granath F, Falconer H. Endometriosis, assisted reproduction technology, and risk of adverse pregnancy outcome. Hum Reprod. 2009;24(9):2341-7.