

EKTOPIK GEBELİK

Deniz DİRİK

Giriş

Ektopik gebelik erken gebelikte karşılaşılan en ciddi komplikasyonlardan biridir⁽¹⁾. Ektopik gebelik, gebelik ürününün endometrial kavite dışında başka bir bölgeye yerleşmesi sonucu oluşur⁽²⁾. En sık %95'ten fazla bir oranla fallop tüpüne yerleşirken; over, abdomen, serviks,uterin kornu ve eski uterin skar da diğer yerleştiği yerler arasındadır. ,Tüm gebeliklerin yaklaşık %1-2 'sini ektopik gebelikler oluşturmalarına rağmen reproduktif yaştaki kadınlarda önemli bir morbidite ve mortalite nedenidir^(3, 4).1991-1999 yılları arasında ABD'de ulusal istatistik verilere göre yapılan bir çalışmada ektopik gebelik mortalite oranı 100.000 ektopik gebelikte 31,9 olarak bulunmuştur. Bu orana bağlı olarak bir kadının canlı doğumdan sonra mortalite riskine göre, ektopik gebelik mortalite riskinin 4,5 kat daha yüksek olduğunu bildirilmiştir⁽⁴⁾. Ayrıca, ektopik gebelikten ve ilgili tedavi prosedürlerinden kaynaklanan komplikasyonlar dışında, ektopik gebelik geçiren kadınlarda daha sonraki gebeliklerinde tekrar ektopik gebelik geçirme riski ve gelecekte infertilite riski daha yüksektir⁽⁵⁾.

Gelişen tanı ve tedavi yöntemlerine bağlı ektopik gebelik mortalite oranı son yıllarda keskin bir şekilde düşmüş olsa da, ektopik gebelik insidansı hala global olarak artmaktadır⁽⁶⁾.1972-1992 yılları arasında insidansında tahmini altı kat artış oldu. Bu artış üreme çağındaki kadınlarda genel olarak 3 nedene bağlanmıştır. Bunlar pelvik inflamatuvar hastalık ve sigara kullanımında artış, yardımcı üreme tekniklerinin yaygın kullanımı ve ektopik gebelik farkındalığının artışıdır⁽⁷⁾.

Risk Faktörleri

Ektopik gebeliğin etiyojisi net olarak tanımlanmamıştır. Genel olarak kabul edilen hipotez, embriyonun fallop tüpünde tutulmasının ve tubal mikro-ortamdaki

Çoklu doz protokolü

En yaygın kullanılan çoklu doz rejimi, 1, 3, 5 ve 7. günlerde MTX (günde 1 mg / kg IM veya IV) ve 2, 4, 6 ve 8. günlerde lökovorin (0.1 mg / kg IM) uygulanmasıdır. HCG seviyeleri 1, 3, 5 ve 7. günlerde ölçülür. Eğer serum hCG'si önceki ölçümünden %15'ten **fazla** düşerse , tedavi durdurulur ve takibe başlanır⁽⁸⁴⁾.

Takip aşaması haftalık hCG ölçümlerinden oluşur. HCG , bir önceki seviyeye göre %15'ten **daha az** düşerse , hastaya ertesi gün ilave bir MTX 1 mg/kg IM doz uygulanır, bunu ertesi gün 0.1 mg/kg lökovorin dozu takip eder . HCG, seviye saptanamayana kadar takip edilir.

Metotreksat tedavisi sırasında alınması gereken önlemler

Hastalar MTX tedavisi sırasında hCG saptanamayana kadar vajinal ilişkidenden kaçınmalı, teorik tubal rüptür riski nedeniyle MTX tedavisinin gözetimi sırasında pelvik muayenelerden kaçınmalı, MTX'in dermatit riskini sınırlamak için güneşe maruz kalmaktan kaçınmalı, Folik asit içeren vitaminlerden kaçınmalı, MTX ile etkileşimi MTX'in renal atılımını azaltabileceği ve toksisite riskini arttırabileceği için steroid olmayan antienflamatuar ilaçlardan (NSAID) kaçınmalıdır⁽⁷²⁾.

KAYNAKLAR

1. Campillo ISSL, Meaney S, O'Donoghue K, et al. Ectopic pregnancy hospitalisations: A national population-based study of rates, management and outcomes. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2018;231:174-179.
2. Rana P, Kazmi I, Singh R, et al. Ectopic pregnancy: a review. *Arch Gynecol Obstet*. 2013;288(4):747-757.
3. Goldner TE, Lawson HW, Xia Z, et al. Surveillance for ectopic pregnancy—United States, 1970–1989. *Morbidity and Mortality Weekly Report: CDC Surveillance Summaries*. 1993;73-85.
4. Creanga AA, Shapiro-Mendoza CK, Bish CL, et al. Trends in ectopic pregnancy mortality in the United States: 1980–2007. *Obstetrics & Gynecology*. 2011;117(4):837-843.
5. Musa J, Daru P, Mutahir J, et al. Ectopic pregnancy in Jos Northern Nigeria: prevalence and impact on subsequent fertility. *Nigerian journal of medicine: journal of the National Association of Resident Doctors of Nigeria*. 2009;18(1):35-38.
6. Shobeiri F, Tehranian N, Nazari MJB. Trend of ectopic pregnancy and its main determinants in Hamadan province, Iran (2000-2010). *BMC research notes*. 2014;7(1):733.
7. Sivalingam VN, Duncan WC, Kirk E, et al. Diagnosis and management of ectopic pregnancy. *J Fam Plann Reprod Health Care*. 2011;37(4):231-240.
8. Shaw J, Dey S, Critchley H, et al. Current knowledge of the aetiology of human tubal ectopic pregnancy. *Human reproduction update*. 2010;16(4):432-444.
9. Li C, Zhao W-H, Zhu Q, et al. Risk factors for ectopic pregnancy: a multi-center case-control study. *BMC pregnancy and childbirth*. 2015;15(1):187.

10. Zhang D, Shi W, Li C, et al. Risk factors for recurrent ectopic pregnancy: a case-control study. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2016;123:82-89.
11. Murray H, Baakdah H, Bardell T, et al. Diagnosis and treatment of ectopic pregnancy. *Cmaj*. 2005;173(8):905-912.
12. Bouyer J, Coste J, Shojaei T, et al. Risk factors for ectopic pregnancy: a comprehensive analysis based on a large case-control, population-based study in France. *American journal of epidemiology*. 2003;157(3):185-194.
13. Diamond MP, Legro RS, Coutifaris C, et al. Letrozole, gonadotropin, or clomiphene for unexplained infertility. *New England Journal of Medicine*. 2015;373(13):1230-1240.
14. Du T, Chen H, Fu R, et al. Comparison of ectopic pregnancy risk among transfers of embryos vitrified on day 3, day 5, and day 6. *Fertility and sterility* 2017;108(1):108-116. e101.
15. Zhang Y-l, Sun J, Su Y-c, et al. Ectopic pregnancy in frozen-thawed embryo transfer: a retrospective analysis of 4,034 cycles and related factors. *Systems biology in reproductive medicine*. 2013;59(1):34-37.
16. Audebert A, Pouly JL, Bonifacie B, et al. Laparoscopic surgery for distal tubal occlusions: lessons learned from a historical series of 434 cases. *Fertility and sterility* 2014;102(4):1203-1208.
17. Malacova E, Kemp A, Hart R, et al. Long-term risk of ectopic pregnancy varies by method of tubal sterilization: a whole-population study. *Fertility and sterility* 2014;101(3):728-734.
18. Sivin IJO, gynecology. Dose-and age-dependent ectopic pregnancy risks with intrauterine contraception. *Obstetrics and gynecology*. 1991;78(2):291-298.
19. Li C, Zhao W-H, Meng C-X, et al. Contraceptive use and the risk of ectopic pregnancy: a multi-center case-control study. *Plos one* 2014;9(12):e115031.
20. Furlong L-A. Ectopic pregnancy risk when contraception fails. A review. *The Journal of reproductive medicine*. 2002;47(11):881-885.
21. Callahan R, Jacobson I, Halpern V, et al. Ectopic pregnancy with use of progestin-only injectables and contraceptive implants: a systematic review. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2015;92(6):514-522.
22. Hoover RN, Hyer M, Pfeiffer RM, et al. Adverse health outcomes in women exposed in utero to diethylstilbestrol. *New England Journal of Medicine*. 2011;365(14):1304-1314.
23. Alataş E, Yildirim B, Öztekin Ö, et al. Laparoscopic management of a primary ectopic ovarian pregnancy and vaginal douching as a possible cause. *Archives of gynecology and obstetrics*. 2008;277(4):363-365.
24. Andersen A-MN, Wohlfahrt J, Christens P, et al. Maternal age and fetal loss: population based register linkage study. *Bmj*. 2000;320(7251):1708-1712.
25. Bouyer J, Coste J, Fernandez H, et al. Sites of ectopic pregnancy: a 10 year population-based study of 1800 cases. *Human reproduction*. 2002;17(12):3224-3230.
26. Bolaji I, Gupta SJU. Medical management of interstitial pregnancy with high serum beta-selective human chorionic gonadotrophin. *Ultrasound*. 2010;18(2):60-67.
27. Yumusak OH, Kusukbas G, Esmer B, et al. Angular pregnancy turning out an intrauterine pregnancy: expectant management of eccentric fundal pregnancies. *J Cases Obstet Gynecol*. 2016;3(3):109-112.

28. Kalidindi M, Shahid A, Odejinmi FJG, et al. Expect the unexpected: the dilemmas in the diagnosis and management of interstitial ectopic pregnancy—case report and literature review. *Gynecology and Minimally Invasive Therapy*. 2016;5(1):35-37.
29. Grindler NM, Ng J, Tocce K, et al. Considerations for management of interstitial ectopic pregnancies: two case reports. *Journal of Medical Case Reports*. 2016;10(1):106.
30. Tulandi T, Al-Jaroudi DJO, Gynecology. Interstitial pregnancy: results generated from the Society of Reproductive Surgeons Registry. *Obstetrics & Gynecology*. 2004;103(1):47-50.
31. Rizk B, Tan SL, Morcos S, et al. Heterotopic pregnancies after in vitro fertilization and embryo transfer. *American journal of obstetrics and gynecology*. 1991;164(1):161-164.
32. Wallach EE, Tal J, Haddad S, et al. Heterotopic pregnancy after ovulation induction and assisted reproductive technologies: a literature review from 1971 to 1993. *Fertility and sterility*. 1996;66(1):1-12.
33. Jeon JH, Hwang YI, Shin IH, et al. The risk factors and pregnancy outcomes of 48 cases of heterotopic pregnancy from a single center. *Journal of Korean medical science*. 2016;31(7):1094-1099.
34. Rotas MA, Haberman S, Levгур MJO, et al. Cesarean scar ectopic pregnancies: etiology, diagnosis, and management. *Obstetrics & Gynecology* 2006;107(6):1373-1381.
35. Petersen KB, Hoffmann E, Larsen CR, et al. Cesarean scar pregnancy: a systematic review of treatment studies. *Fertility and Sterility*. 2016;105(4):958-967.
36. Zhang Q, Xing X, Liu S, et al. Intramural ectopic pregnancy following pelvic adhesion: case report and literature review. *Archives of gynecology and obstetrics* 2019:1-14.
37. Kong L, Mao N, Shi Y, et al. Diagnosis and management of intramural ectopic pregnancy in the second trimester—a case report. *BJR| case reports*. 2017:20160095.
38. Ong C, Su LL, Chia D, et al. Sonographic diagnosis and successful medical management of an intramural ectopic pregnancy. *Journal of Clinical Ultrasound*. 2010;38(6):320-324.
39. Singh S. Diagnosis and management of cervical ectopic pregnancy. *Journal of human reproductive sciences*. 2013;6(4):273.
40. Chrisi C, Stratoudakis G, Zygouris D, et al. Cervical pregnancy: a case report. *Obstet Gynecol Int J*. 2015;14(1):27-29.
41. Kuzmar L, Jordan JJCeleS. Cervical ectopic pregnancy with colic abdominal pain. *Ciencia e Innovación en Salud*. 2017.
42. Sotelo CJTJfNP. Ovarian Ectopic Pregnancy: A Clinical Analysis. *The Journal for Nurse Practitioners*. 2019;15(3):224-227.
43. Comstock C, Huston K, Lee WJO, et al. The ultrasonographic appearance of ovarian ectopic pregnancies. *Obstetrics & Gynecology* 2005;105(1):42-45.
44. Martin JJ, Sessums JK, Martin RW, et al. Abdominal pregnancy: current concepts of management. *Obstetrics and Gynecology*. 1988;71(4):549-557.
45. Delke I, Veridiano NP, Tancer MLJO, et al. Abdominal pregnancy: review of current management and addition of 10 cases. *Obstetrics and gynecology* 1982;60(2):200-204.
46. Dahiya K, Sharma DJJoGS. Advanced abdominal pregnancy: a diagnostic and management dilemma. *Journal of Gynecologic Surgery*. 2007;23(2):69-72.

47. Karaman E, Çetin O, Kolusari A, et al. Primary tubal choriocarcinoma presented as ruptured ectopic pregnancy. *Journal of clinical and diagnostic research: JCDR* 2015;9(9):QD17.
48. Alkatout I, Honemeyer U, Strauss A, et al. Clinical diagnosis and treatment of ectopic pregnancy. *Obstetrical & gynecological survey* 2013;68(8):571-581.
49. Wu G, Yang J, Xu W, et al. Serum beta human chorionic gonadotropin levels on day 12 after in vitro fertilization in predicting final type of clinical pregnancy. *The Journal of reproductive medicine* 2014;59(3-4):161-166.
50. Feng C, Chen ZY, Zhang J, et al. Clinical utility of serum reproductive hormones for the early diagnosis of ectopic pregnancy in the first trimester. *Journal of Obstetrics and Gynaecology Research*. 2013;39(2):528-535.
51. Casanova BC, Sammel MD, Chittams J, et al. Prediction of outcome in women with symptomatic first-trimester pregnancy: focus on intrauterine rather than ectopic gestation. *Journal of Women's Health* 2009;18(2):195-200.
52. Job-Spira N, Fernandez H, Bouyer J, et al. Ruptured tubal ectopic pregnancy: risk factors and reproductive outcome: results of a population-based study in France. *American journal of obstetrics and gynecology*. 1999;180(4):938-944.
53. Stovall TG, Kellerman AL, Ling FW, et al. Emergency department diagnosis of ectopic pregnancy. *Annals of emergency medicine*. 1990;19(10):1098-1103.
54. Daya SJAjoo, gynecology. Human chorionic gonadotropin increase in normal early pregnancy. *American journal of obstetrics and gynecology*. 1987;156(2):286-290.
55. Connolly A, Ryan DH, Stuebe AM, et al. Reevaluation of discriminatory and threshold levels for serum β -hCG in early pregnancy. *Obstetrics & Gynecology* 2013;121(1):65-70.
56. Webster K, Eadon H, Fishburn S, et al. Ectopic pregnancy and miscarriage: diagnosis and initial management: summary of updated NICE guidance. *Bmj*. 2019;367.
57. Dialani V, Levine DJUq. Ectopic pregnancy: a review. *Ultrasound quarterly* 2004;20(3):105-117.
58. Dogra V, Paspulati RM, Bhatt SJUq. First trimester bleeding evaluation. *Ultrasound quarterly*. 2005;21(2):69-85.
59. Doubilet PM, Benson CB, Bourne T, et al. Diagnostic criteria for nonviable pregnancy early in the first trimester. *New England Journal of Medicine* 2013;369(15):1443-1451.
60. Kadar N, Caldwell BV, Romero RJO, et al. A method of screening for ectopic pregnancy and its indications. *Obstetrics and gynecology*. 1981;58(2):162-166.
61. Morse CB, Sammel MD, Shaunik A, et al. Performance of human chorionic gonadotropin curves in women at risk for ectopic pregnancy: exceptions to the rules. *Fertility and sterility*. 2012;97(1):101-106. e102.
62. Kadar N, DeVORE G, Romero RJO, et al. Discriminatory hCG zone: its use in the sonographic evaluation for ectopic pregnancy. *Obstetrics and gynecology* 1981;58(2):156-161.
63. Silva C, Sammel MD, Zhou L, et al. Human chorionic gonadotropin profile for women with ectopic pregnancy. *Obstetrics & Gynecology*. 2006;107(3):605-610.
64. Rotmensch S, Cole LAJTL. False diagnosis and needless therapy of presumed malignant disease in women with false-positive human chorionic gonadotropin concentrations. *The Lancet*. 2000;355(9205):712-715.

65. Zee J, Sammel M, Chung K, et al. Ectopic pregnancy prediction in women with a pregnancy of unknown location: data beyond 48 h are necessary. *Human Reproduction*. 2014;29(3):441-447.
66. Seeber BE, Barnhart KTJO, Gynecology. Suspected ectopic pregnancy. *Obstetrics & Gynecology* 2006;107(2):399-413.
67. Condous G, Kirk E, Lu C, et al. Diagnostic accuracy of varying discriminatory zones for the prediction of ectopic pregnancy in women with a pregnancy of unknown location. *The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology*. 2005;26(7):770-775.
68. Krause HG, Goh JTJA, obstetrics NZjo, et al. Positive Kleihauer result following an ectopic pregnancy. *Australian and New Zealand journal of obstetrics and gynaecology* 1996;36(3):324-325.
69. Van Den Eeden SK, Shan J, Bruce C, et al. Ectopic pregnancy rate and treatment utilization in a large managed care organization. *Obstetrics & Gynecology*. 2005;105(5):1052-1057.
70. Spandorfer SD, Sawin SW, Benjamin I, et al. Postoperative day 1 serum human chorionic gonadotropin level as a predictor of persistent ectopic pregnancy after conservative surgical management. *Fertility and sterility*. 1997;68(3):430-434.
71. Gracia CR, Brown HA, Barnhart KTJF, et al. Prophylactic methotrexate after linear salpingostomy: a decision analysis. *Fertility and sterility*. 2001;76(6):1191-1195.
72. Fertility PCotASfRMJ, sterility. Medical treatment of ectopic pregnancy: a committee opinion. *Fertility and sterility* 2013;100(3):638-644.
73. Kelly H, Harvey D, Moll SJO, et al. A cautionary tale: fatal outcome of methotrexate therapy given for management of ectopic pregnancy. *Obstetrics & Gynecology*. 2006;107(2):439-441.
74. Willner N, Storch S, Tadmor T, et al. Almost a tragedy: severe methotrexate toxicity in a hemodialysis patient treated for ectopic pregnancy. *European journal of clinical pharmacology*. 2014;70(3):261-263.
75. Barnhart KT, Gosman G, Ashby R, et al. The medical management of ectopic pregnancy: a meta-analysis comparing "single dose" and "multidose" regimens. *Obstetrics & Gynecology*. 2003;101(4):778-784.
76. Lipscomb GH, Bran D, McCord ML, et al. Analysis of three hundred fifteen ectopic pregnancies treated with single-dose methotrexate. *American journal of obstetrics and gynecology*. 1998;178(6):1354-1358.
77. Lipscomb GH, editor Medical therapy for ectopic pregnancy. *Seminars in reproductive medicine*; 2007: Copyright© 2007 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New
78. Stovall TG, Ling FW, Gray LA, et al. Methotrexate treatment of unruptured ectopic pregnancy: a report of 100 cases. *Obstetrics and gynecology* 1991;77(5):749-753.
79. Stovall TG, Ling FWJAjoo, gynecology. Single-dose methotrexate: an expanded clinical trial. *American journal of obstetrics and gynecology*. 1993;168(6):1759-1765.
80. Kirk E, Condous G, Van Calster B, et al. A validation of the most commonly used protocol to predict the success of single-dose methotrexate in the treatment of ectopic pregnancy. *Human Reproduction*. 2007;22(3):858-863.
81. Natale A, Candiani M, Barbieri M, et al. Pre-and post-treatment patterns of human chorionic gonadotropin for early detection of persistence after a single dose of met-

- hotrexate for ectopic pregnancy. *European Journal of Obstetrics & Gynecology and reproductive biology*. 2004;117(1):87-92.
82. Saraj AJ, Wilcox JG, Najmabadi S, et al. Resolution of hormonal markers of ectopic gestation: a randomized trial comparing single-dose intramuscular methotrexate with salpingostomy. *Obstetrics & Gynecology*. 1998;92(6):989-994.
83. Gamzu R, Almog B, Levin Y, et al. The ultrasonographic appearance of tubal pregnancy in patients treated with methotrexate. *Human reproduction* 2002;17(10):2585-2587.
84. Stovall TG, Ling FW, Buster JEJF, et al. Outpatient chemotherapy of unruptured ectopic pregnancy. *Fertility and sterility*. 1989;51(3):435-438.