Bölüm 23

TİROİD VE PARATİROİD HASTALIKLARI

Duygu ADIYAMAN[1]

GEBELİKTE TİROİD HASTALIKLARI

Tiroid hastalığı olan gebelerin tanı ve tedavisi gebe olmayan bireylerinkine benzer olmakla birlikte bu süreçte gebeliğe özgü bazı sorunlar da ortaya çıkabilmektedir. Gebelikte tiroid hastalıklarının doğru yönetimi için tiroid fizyolojisinde ve tiroid fonksiyon testlerinde meydana gelen değişikliklerin anlaşılması elzemdir.

Gebelikte Tiroid Adaptasyonu

Normal bir hamilelik sırasında artan metabolik ihtiyaçları karşılamak için tiroid fizyolojisinde tiroid fonksiyon testlerine de yansıyan çeşitli değişiklikler meydana gelir (1). Hamilelik sırasında tiroid fonksiyonundaki başlıca değişiklik serum tiroksin bağlayıcı globulinde (TBG) artıştır. Hamilelikte salgılanan östrojen TBG üretimini ve sinyalizasyonunu artırdığı, TBG klirensinin de azalmasına neden olduğu için serum TBG konsantrasyonları neredeyse iki katına çıkar (2). Bu dönemde serbest tiroid hormonu konsantrasyonlarını korumak için tiroid bezinin tiroksin (T4) ve triiyodotironin (T3) üretimi artmalıdır. TBG fazlalığı hem serum total hem de serbest T4 ve T3 konsantrasyonlarında bir artışa neden olur. Total T4 ve T3 seviyeleri, gebeliğin ilk yarısında yaklaşık %50 artarak gebeliğin 20. Haftasına kadar plato çizer ve 20. Gebelik haftasından sonra tiroid hormonlarının genel üretim hızı gebelik öncesi oranlara geri döner. İkinci bir değişiklik ise tiroid

[1] Op. Dr., Sağlık Bilimleri Üniversitesi Tepecik Eğitim ve Araştırma Hastanesi Perinatoloji Kliniği, duyguagca@gmail.com

Cerrahi

Gebe olmayan hastalar için cerrahi endikasyonları net olarak belirlenmiştir. Cerrahi primer hiperparatiroidizmin tek küratif tedavisidir. Gebeler için serum kalsiyum düzeyi 11 mg/dl altında tutulamayan hastalarda cerrahi yapılması önerilir (98, 99). Ek olarak cerrahi endikasyonu olup yapılan hastaların bebeklerinde medikal tedavi ile yönetilenlere kıyasla daha az neonatal morbidite olduğu da bildirilmiştir (98). Cerrahi tercih edilecek ise ikinci trimester tercih edilmelidir.

Maternal ve Fetal Komplikasyonlar

Her ne kadar gebelikte primer hiperparatiroidizm nadir görülse de ciddi maternal ve fetal komplikasyonlara neden olabilmektedir. Bu komplikasyonlar nefrolitiazis, pankreatit, peptik ülser, kısa QT, maternal aritmiler, konfüzyon, stupor ve komadır (100). Ayrıca birinci ve ikinci trimesterde spontan abort ve ölü doğumlar görülebilir (87, 89, 90). Tedavi almayan primer hiperparatiroidizmli annelerin %80 inde fetal komplikasyonlar görülür (89). Bu komplikasyonlardan en sık görülen fetal hipokalsemidir. Fetal hipokalsemi 3-5 aya kadar uzayabilir ve yeterli kalsiyum ve vitamin D desteği ile yönetilebilir.

SONUÇ

Tiroid ve paratiroid bezi hastalıklarına sahip gebe kadınların yönetimi ve tedavisi gebe olmayan bireylerle paralellik göstermekle birlikte bu kadınlarda gebeliğe özgü bazı maternal ve fetal komplikasyonlar da görülebilmektedir. Hamilelik öncesinde tanı almış hastaların yönetiminde veya hamilelik sırasında bu hastalıkların saptanması halinde olası komplikasyonların önlenmesi esastır. Fetusun korunması da göz önünde bulundurularak tedavi endikasyonları ve terapötik seçenekler klinisyenler tarafından iyi değerlendirilmelidir.

KAYNAKLAR

1. Glinoer D. The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology. Endocrine reviews. 1997;18(3):404-33.
2. Ain KB, Mori Y, Refetoff S. Reduced clearance rate of thyroxine-binding globulin (TBG) with increased sialylation: a mechanism for estrogen-induced elevation of serum TBG concentration. The Journal of clinical endocrinology and metabolism. 1987;65(4):689-96.
3. Ballabio M, Poshychinda M, Ekins RP. Pregnancy-induced changes in thyroid function: role of human chorionic gonadotropin as putative regulator of maternal thyroid. The Journal of clinical endocrinology and metabolism. 1991;73(4):824-31.
4. Burrow GN, Fisher DA, Larsen PR. Maternal and fetal thyroid function. The New England journal of medicine. 1994;331(16):1072-8.

5. TEMD. Türkiye Endokrinoloji ve Metabolizma Derneği Tiroid Hastalıkları Tanı ve Tedavi Kılavuzu Türkiye Klinikleri 2017;157.
6. Alexander EK, Pearce EN, Brent GA, et al. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. Thyroid : official journal of the American Thyroid Association. 2017;27(3):315-89.
7. Leung AM, Pearce EN, Braverman LE. Iodine content of prenatal multivitamins in the United States. The New England journal of medicine. 2009;360(9):939-40.
8. Krassas GE, Poppe K, Glinoer D. Thyroid function and human reproductive health. Endocrine reviews. 2010;31(5):702-55.
9. Lo JC, Rivkees SA, Chandra M, et al. Gestational thyrotoxicosis, antithyroid drug use and neonatal outcomes within an integrated healthcare delivery system. Thyroid : official journal of the American Thyroid Association. 2015;25(6):698-705.
10. ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 37, August 2002. (Replaces Practice Bulletin Number 32, November 2001). Thyroid disease in pregnancy. Obstetrics and gynecology. 2002;100(2):387-96.
11. Casey BM, Dashe JS, Wells CE, et al. Subclinical hyperthyroidism and pregnancy outcomes. Obstetrics and gynecology. 2006;107(2 Pt 1):337-41.
12. Stricker R, Echenard M, Eberhart R, et al. Evaluation of maternal thyroid function during pregnancy: the importance of using gestational age-specific reference intervals. European journal of endocrinology. 2007;157(4):509-14.
13. Dashe JS, Casey BM, Wells CE, et al. Thyroid-stimulating hormone in singleton and twin pregnancy: importance of gestational age-specific reference ranges. Obstetrics and gynecology. 2005;106(4):753-7.
14. Fitzpatrick DL, Russell MA. Diagnosis and management of thyroid disease in pregnancy. Obstetrics and gynecology clinics of North America. 2010;37(2):173-93.
15. Glinoer D, de Nayer P, Bourdoux P, et al. Regulation of maternal thyroid during pregnancy. The Journal of clinical endocrinology and metabolism. 1990;71(2):276-87.
16. Goodwin TM, Montoro M, Mestman JH, et al. The role of chorionic gonadotropin in transient hyperthyroidism of hyperemesis gravidarum. The Journal of clinical endocrinology and metabolism. 1992;75(5):1333-7.
17. Hershman JM. Human chorionic gonadotropin and the thyroid: hyperemesis gravidarum and trophoblastic tumors. Thyroid : official journal of the American Thyroid Association. 1999;9(7):653-7.
18. Kimura M, Amino N, Tamaki H, et al. Gestational thyrotoxicosis and hyperemesis gravidarum: possible role of hCG with higher stimulating activity. Clinical endocrinology. 1993;38(4):345-50.
19. Mortimer RH, Cannell GR, Addison RS, et al. Methimazole and propylthiouracil equally cross the perfused human term placental lobule. The Journal of clinical endocrinology and metabolism. 1997;82(9):3099-102.
20. Momotani N, Noh JY, Ishikawa N, et al. Effects of propylthiouracil and methimazole on fetal thyroid status in mothers with Graves' hyperthyroidism. The Journal of clinical endocrinology and metabolism. 1997;82(11):3633-6.
21. Adali E, Yildizhan R, Kolusari A, et al. The use of plasmapheresis for rapid hormonal control in severe hyperthyroidism caused by a partial molar pregnancy. Archives of gynecology and obstetrics. 2009;279(4):569-71.
22. Azezli A, Bayraktaroglu T, Topuz S, et al. Hyperthyroidism in molar pregnancy: rapid preoperative preparation by plasmapheresis and complete improvement after evacuation. Transfusion and apheresis science : official journal of the World Apheresis Association : official journal of the European Society for Haemapheresis. 2007;36(1):87-9.
23. Lydakis C, Lip GY, Beevers M, et al. Atenolol and fetal growth in pregnancies complicated by hypertension. American journal of hypertension. 1999;12(6):541-7.

24. Lip GY, Beevers M, Churchill D, et al. Effect of atenolol on birth weight. The American journal of cardiology. 1997;79(10):1436-8.
25. Ross DS, Burch HB, Cooper DS, et al. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. Thyroid : official journal of the American Thyroid Association. 2016;26(10):1343-421.
26. Bowman P, Osborne NJ, Sturley R, et al. Carbimazole embryopathy: implications for the choice of antithyroid drugs in pregnancy. QJM : monthly journal of the Association of Physicians. 2012;105(2):189-93.
27. Martínez-Frías ML, Cereijo A, Rodríguez-Pinilla E, et al. Methimazole in animal feed and congenital aplasia cutis. Lancet (London, England). 1992;339(8795):742-3.
28. Foulds N, Walpole I, Elmslie F, et al. Carbimazole embryopathy: an emerging phenotype. American journal of medical genetics Part A. 2005;132a(2):130-5.
29. Wing DA, Millar LK, Koonings PP, et al. A comparison of propylthiouracil versus methimazole in the treatment of hyperthyroidism in pregnancy. American journal of obstetrics and gynecology. 1994;170(1 Pt 1):90-5.
30. Rosenfeld H, Ornoy A, Shechtman S, et al. Pregnancy outcome, thyroid dysfunction and fetal goitre after in utero exposure to propylthiouracil: a controlled cohort study. British journal of clinical pharmacology. 2009;68(4):609-17.
31. Andersen SL, Olsen J, Wu CS, et al. Birth defects after early pregnancy use of antithyroid drugs: a Danish nationwide study. The Journal of clinical endocrinology and metabolism. 2013;98(11):4373-81.
32. Bahn RS, Burch HS, Cooper DS, et al. The Role of Propylthiouracil in the Management of Graves' Disease in Adults: report of a meeting jointly sponsored by the American Thyroid Association and the Food and Drug Administration. Thyroid : official journal of the American Thyroid Association. 2009;19(7):673-4.
33. Kuy S, Roman SA, Desai R, et al. Outcomes following thyroid and parathyroid surgery in pregnant women. Archives of surgery (Chicago, Ill : 1960). 2009;144(5):399-406; discussion
34. Stoffer SS, Hamburger JI. Inadvertent 131I therapy for hyperthyroidism in the first trimester of pregnancy. Journal of nuclear medicine : official publication, Society of Nuclear Medicine. 1976;17(02):146-9.
35. Kim HO, Lee K, Lee SM, et al. Association Between Pregnancy Outcomes and Radioactive Iodine Treatment After Thyroidectomy Among Women With Thyroid Cancer. JAMA internal medicine. 2020;180(1):54-61.
36. Davis LE, Lucas MJ, Hankins GD, et al. Thyrotoxicosis complicating pregnancy. American journal of obstetrics and gynecology. 1989;160(1):63-70.
37. Sheffield JS, Cunningham FG. Thyrotoxicosis and heart failure that complicate pregnancy. American journal of obstetrics and gynecology. 2004;190(1):211-7.
38. Phoojaroenchanachai M, Sriussadaporn S, Peerapatdit T, et al. Effect of maternal hyperthyroidism during late pregnancy on the risk of neonatal low birth weight. Clinical endocrinology. 2001;54(3):365-70.
39. Millar LK, Wing DA, Leung AS, et al. Low birth weight and preeclampsia in pregnancies complicated by hyperthyroidism. Obstetrics and gynecology. 1994;84(6):946-9.
40. Zimmerman D. Fetal and neonatal hyperthyroidism. Thyroid : official journal of the American Thyroid Association. 1999;9(7):727-33.
41. Luton D, Le Gac I, Vuillard E, et al. Management of Graves' disease during pregnancy: the key role of fetal thyroid gland monitoring. The Journal of clinical endocrinology and metabolism. 2005;90(11):6093-8.
42. Peleg D, Cada S, Peleg A, et al. The relationship between maternal serum thyroid-stimulating immunoglobulin and fetal and neonatal thyrotoxicosis. Obstetrics and gynecology. 2002;99(6):1040-3.

43. Polak M, Le Gac I, Vuillard E, et al. Fetal and neonatal thyroid function in relation to maternal Graves' disease. Best practice & research Clinical endocrinology & metabolism. 2004;18(2):289-302.
44. Amino N, Tanizawa O, Mori H, et al. Aggravation of thyrotoxicosis in early pregnancy and after delivery in Graves' disease. The Journal of clinical endocrinology and metabolism. 1982;55(1):108-12.
45. Allan WC, Haddow JE, Palomaki GE, et al. Maternal thyroid deficiency and pregnancy complications: implications for population screening. Journal of medical screening. 2000;7(3):127-30.
46. Casey BM, Dashe JS, Spong CY, et al. Perinatal significance of isolated maternal hypothyroxinemia identified in the first half of pregnancy. Obstetrics and gynecology. 2007;109(5):1129-35.
47. Liu H, Shan Z, Li C, et al. Maternal subclinical hypothyroidism, thyroid autoimmunity, and the risk of miscarriage: a prospective cohort study. Thyroid : official journal of the American Thyroid Association. 2014;24(11):1642-9.
48. LaFranchi SH, Haddow JE, Hollowell JG. Is thyroid inadequacy during gestation a risk factor for adverse pregnancy and developmental outcomes? Thyroid : official journal of the American Thyroid Association. 2005;15(1):60-71.
49. Stagnaro-Green A, Chen X, Bogden JD, et al. The thyroid and pregnancy: a novel risk factor for very preterm delivery. Thyroid : official journal of the American Thyroid Association. 2005;15(4):351-7.
50. Männistö T, Mendola P, Grewal J, et al. Thyroid diseases and adverse pregnancy outcomes in a contemporary US cohort. The Journal of clinical endocrinology and metabolism. 2013;98(7):2725-33.
51. Idris I, Srinivasan R, Simm A, et al. Maternal hypothyroidism in early and late gestation: effects on neonatal and obstetric outcome. Clinical endocrinology. 2005;63(5):560-5.
52. Willoughby KA, McAndrews MP, Rovet JF. Effects of maternal hypothyroidism on offspring hippocampus and memory. Thyroid : official journal of the American Thyroid Association. 2014;24(3):576-84.
53. Casey BM, Dashe JS, Wells CE, et al. Subclinical hypothyroidism and pregnancy outcomes. Obstetrics and gynecology. 2005;105(2):239-45.
54. Wilson KL, Casey BM, McIntire DD, et al. Subclinical thyroid disease and the incidence of hypertension in pregnancy. Obstetrics and gynecology. 2012;119(2 Pt 1):315-20.
55. Korevaar TI, Schalekamp-Timmermans S, de Rijke YB, et al. Hypothyroxinemia and TPO-antibody positivity are risk factors for premature delivery: the generation R study. The Journal of clinical endocrinology and metabolism. 2013;98(11):4382-90.
56. Nelson SM, Haig C, McConnachie A, et al. Maternal thyroid function and child educational attainment: prospective cohort study. BMJ (Clinical research ed). 2018;360:k452.
57. Li Y, Shan Z, Teng W, et al. Abnormalities of maternal thyroid function during pregnancy affect neuropsychological development of their children at 25-30 months. Clinical endocrinology. 2010;72(6):825-9.
58. Fan X, Wu L. The impact of thyroid abnormalities during pregnancy on subsequent neuropsychological development of the offspring: a meta-analysis. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2016;29(24):3971-6.
59. Nazarpour S, Ramezani Tehrani F, Simbar M, et al. Effects of levothyroxine treatment on pregnancy outcomes in pregnant women with autoimmune thyroid disease. European journal of endocrinology. 2017;176(2):253-65.
60. Negro R, Schwartz A, Gismondi R, et al. Universal screening versus case finding for detection and treatment of thyroid hormonal dysfunction during pregnancy. The Journal of clinical endocrinology and metabolism. 2010;95(4):1699-707.

61. Casey BM, Thom EA, Peaceman AM, et al. Treatment of Subclinical Hypothyroidism or Hypothyroxinemia in Pregnancy. The New England journal of medicine. 2017;376(9):815-25.
62. Lazarus JH, Bestwick JP, Channon S, et al. Antenatal thyroid screening and childhood cognitive function. The New England journal of medicine. 2012;366(6):493-501.
63. Zhou Q, Wang C, Xu H, et al. Impact of Preconception Treatment Initiation for Hypothyroidism on Neurocognitive Function in Children. The Journal of clinical endocrinology and metabolism. 2020;105(11).
64. Kooistra L, Crawford S, van Baar AL, et al. Neonatal effects of maternal hypothyroxinemia during early pregnancy. Pediatrics. 2006;117(1):161-7.
65. Henrichs J, Bongers-Schokking JJ, Schenk JJ, et al. Maternal thyroid function during early pregnancy and cognitive functioning in early childhood: the generation R study. The Journal of clinical endocrinology and metabolism. 2010;95(9):4227-34.
66. Başkanlığı TCSBTHSKKvÜSD. Doğum Öncesi Bakım Yönetim Rehberi. 2014;924.
67. De Groot L, Abalovich M, Alexander EK, et al. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. The Journal of clinical endocrinology and metabolism. 2012;97(8):2543-65.
68. Abalovich M, Gutierrez S, Alcaraz G, et al. Overt and subclinical hypothyroidism complicating pregnancy. Thyroid : official journal of the American Thyroid Association. 2002;12(1):63-8.
69. Vadiveloo T, Mires GJ, Donnan PT, et al. Thyroid testing in pregnant women with thyroid dysfunction in Tayside, Scotland: the thyroid epidemiology, audit and research study (TEARS). Clinical endocrinology. 2013;78(3):466-71.
70. Kovacs CS. Calcium and bone metabolism in pregnancy and lactation. The Journal of clinical endocrinology and metabolism. 2001;86(6):2344-8.
71. Khan AA, Clarke B, Rejnmark L, et al. MANAGEMENT OF ENDOCRINE DISEASE: Hypoparathyroidism in pregnancy: review and evidence-based recommendations for management. European journal of endocrinology. 2019;180(2):R37-r44.
72. Turner M, Barré PE, Benjamin A, et al. Does the maternal kidney contribute to the increased circulating 1,25-dihydroxyvitamin D concentrations during pregnancy? Mineral and electrolyte metabolism. 1988;14(4):246-52.
73. Stevenson JC, Hillyard CJ, MacIntyre I, et al. A physiological role for calcitonin: protection of the maternal skeleton. Lancet (London, England). 1979;2(8146):769-70.
74. Stevenson JC, Abeyasekera G, Hillyard CJ, et al. Calcitonin and the calcium-regulating hormones in postmenopausal women: effect of oestrogens. Lancet (London, England). 1981;1(8222):693-5.
75. Shoback D. Clinical practice. Hypoparathyroidism. The New England journal of medicine. 2008;359(4):391-403.
76. Bilezikian JP, Khan A, Potts JT, Jr., et al. Hypoparathyroidism in the adult: epidemiology, diagnosis, pathophysiology, target-organ involvement, treatment, and challenges for future research. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research. 2011;26(10):2317-37.
77. Hatswell BL, Allan CA, Teng J, et al. Management of hypoparathyroidism in pregnancy and lactation - A report of 10 cases. Bone reports. 2015;3:15-9.
78. Almaghamsi A, Almalki MH, Buhary BM. Hypocalcemia in Pregnancy: A Clinical Review Update. Oman medical journal. 2018;33(6):453-62.
79. Cardot-Bauters C. Hypoparathyroidism and pregnancy. Annales d'endocrinologie. 2016;77(2):172-5.
80. Shah KH, Bhat S, Shetty S, et al. Hypoparathyroidism in pregnancy. BMJ case reports. 2015;2015.
81. Yeh MW, Ituarte PH, Zhou HC, et al. Incidence and prevalence of primary hyperparathyroidism in a racially mixed population. The Journal of clinical endocrinology and metabolism. 2013;98(3):1122-9.

82. Kort KC, Schiller HJ, Numann PJ. Hyperparathyroidism and pregnancy. American journal of surgery. 1999;177(1):66-8.
83. Walker MD, Silverberg SJ. Primary hyperparathyroidism. Nature reviews Endocrinology. 2018;14(2):115-25.
84. Silva BC, Cusano NE, Bilezikian JP. Primary hyperparathyroidism. Best practice & research Clinical endocrinology & metabolism. 2018:101247.
85. Perrier ND. Asymptomatic hyperparathyroidism: a medical misnomer? Surgery. 2005;137(2):127-31.
86. Trombetti A, Christ ER, Henzen C, et al. Clinical presentation and management of patients with primary hyperparathyroidism of the Swiss Primary Hyperparathyroidism Cohort: a focus on neuro-behavioral and cognitive symptoms. Journal of endocrinological investigation. 2016;39(5):567-76.
87. Malekar-Raikar S, Sinnott BP. Primary hyperparathyroidism in pregnancy-a rare cause of life-threatening hypercalcemia: case report and literature review. Case reports in endocrinology. 2011;2011:520516.
88. Marcocci C, Cetani F. Clinical practice. Primary hyperparathyroidism. The New England journal of medicine. 2011;365(25):2389-97.
89. Dochez V, Ducarme G. Primary hyperparathyroidism during pregnancy. Archives of gynecology and obstetrics. 2015;291(2):259-63.
90. Norman J, Politz D, Politz L. Hyperparathyroidism during pregnancy and the effect of rising calcium on pregnancy loss: a call for earlier intervention. Clinical endocrinology. 2009;71(1):104-9.
91. Olesen C, de Vries CS, Thrane N, et al. Effect of diuretics on fetal growth: A drug effect or confounding by indication? Pooled Danish and Scottish cohort data. British journal of clinical pharmacology. 2001;51(2):153-7.
92. Krysiak R, Wilk M, Okopien B. Recurrent pancreatitis induced by hyperparathyroidism in pregnancy. Archives of gynecology and obstetrics. 2011;284(3):531-4.
93. Levy S, Fayez I, Taguchi N, et al. Pregnancy outcome following in utero exposure to bisphosphonates. Bone. 2009;44(3):428-30.
94. Bashir M, Mokhtar M, Baagar K, et al. A CASE OF HYPERPARATHYROIDISM TREATED WITH CINACALCET DURING PREGNANCY. AACE clinical case reports. 2019;5(1):e40-e3.
95. Edling KL, Korenman SG, Janzen C, et al. A pregnant dilemma: primary hyperparathyroidism due to parathyromatosis in pregnancy. Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists. 2014;20(2):e14-7.
96. Vera L, Oddo S, Di Iorgi N, et al. Primary hyperparathyroidism in pregnancy treated with cinacalcet: a case report and review of the literature. Journal of medical case reports. 2016;10(1):361.
97. Diaz-Soto G, Linglart A, Sénat MV, et al. Primary hyperparathyroidism in pregnancy. Endocrine. 2013;44(3):591-7.
98. Kelly TR. Primary hyperparathyroidism during pregnancy. Surgery. 1991;110(6):1028-33; discussion 33-4.
99. Kamenický P, Lecoq AL, Chanson P. Primary hyperparathyroidism in pregnancy. Annales d'endocrinologie. 2016;77(2):169-71.
100. McCarthy A, Howarth S, Khoo S, et al. Management of primary hyperparathyroidism in pregnancy: a case series. Endocrinology, diabetes & metabolism case reports. 2019;2019.