

Bölüm 3

MENSTRÜEL SIKLUS FİZYOLOJİSİ

İbrahim KALE¹

GİRİŞ

Puberteden başlayıp menopoz kadar her ay düzenli olarak devam eden menstrüel siklus parakrin ve otokrin faktörler ile hormonlar tarafından sıkı bir şekilde kontrol edilmektedir. Hipotalamus, hipofiz, overler ve uterus arasındaki bu sıkı etkileşim neticesinde binlerce primordial folikül içinden tek bir olgun oosit gelişip ovule olmakta ve buna endometriumdaki siklik değişiklikler eşlik etmektedir. Menstrüel siklus kabaca foliküler faz, ovulasyon ve luteal fazdan oluşmaktadır. Bu bölümde menstrüel siklustaki dinamik değişiklikler overler ve endometrium için ayrı ayrı değerlendirilecektir.

HİPOTALAMO - HİPOFİZER AKS

Hipotalamus, üçüncü ventrikülün altında, optik kiazmanın ve hipofiz bezinin üstünde yerleşmiştir. Hipotalamus üst kortikal merkezden gelen uyarıların, periferik endokrin organlardan gelen hormonal geri bildirimlerin ve çevresel faktörlerin etkisiyle endokrin sistemin kordinasyonunu sağlayan temel merkezdir. Hipotalamusun ön hipofizle direkt nöronal bağlantısı yoktur fakat hipotalamusta bulunan nöronların bir bölümü median eminens sonlanır. Median eminens superior hipofiz arterlerinden oluşan kapiller damar ağı tarafından beslenir. Bu kapiller damar ağı hipofiz sapı etrafındaki portal damarlara açılır ve bu damarlar da ön hipofizin etrafında yoğun bir kılcal damar ağı oluşturur. Median eminens sonlanan hipotalamik nöronlardan salgılanan hormonlar bu özel portal kan akımı sayesinde periferik kana karışmadan önce yüksek konsantrasyonda hipofizdeki hedef hücrelerine ulaşır. Hipotalamustan pulsatil olarak salgılanan hormonların etkisini göstermesinde bu özel portal kan akımının önemi büyüktür. Ön

¹ Uzman Doktor, Ümraniye Eğitim ve Araştırma Hastanesi, dribakale@hotmail.com

polimorfonükleer lökositler ve monositler sızmaya başlar. Endometrial bezler ve stromal doku açığa çıkan prostaglandinler, sitokinler ve lizozomal enzimlerin etkisi ile yıkılmaya başlar.

Anahtar Kelimeler: menstrüel siklus, ovulasyon.

REFERANSLAR

1. Knobil E. On the control of gonadotropin secretion in the rhesus monkey. *Recent Prog Horm Res.* 1974;30(0):1-46.
2. Clayton RN, Catt KJ. Gonadotropin-releasing hormone receptors: characterization, physiological regulation, and relationship to reproductive function. *Endocr Rev.* 1981 Spring;2(2):186-209.
3. Yen SS, Quigley ME, Reid RL, et al. Neuroendocrinology of opioid peptides and their role in the control of gonadotropin and prolactin secretion. *Am J Obstet Gynecol.* 1985 Jun 15;152(4):485-93.
4. Reame N, Sauder SE, Kelch RP, et al. Pulsatile gonadotropin secretion during the human menstrual cycle: evidence for altered frequency of gonadotropin-releasing hormone secretion. *J Clin Endocrinol Metab.* 1984 Aug;59(2):328-37.
5. Speroff, L., Fritz, M.A. (2007) *Klinik Jinekolojik Endokrinoloji ve İnfertilite.* (Ahmet ERK, Serdar GÜNALP, Çev Ed.). Ankara: Güneş Tıp Kitabevleri.
6. Baker TG. A quantitative and cytological study of germ cells in human ovaries. *Proc R Soc Lond B Biol Sci.* 1963 Oct 22;158:417-33.
7. Peters H, Byskov AG, Grinstead J. Follicular growth in fetal and prepubertal ovaries of humans and other primates. *Clin Endocrinol Metab.* 1978 Nov;7(3):469-85.
8. Trombly DJ, Woodruff TK, Mayo KE. Roles for transforming growth factor beta superfamily proteins in early folliculogenesis. *Semin Reprod Med.* 2009 Jan;27(1):14-23. doi: 10.1055/s-0028-1108006. Epub 2009 Feb 5.
9. Albertini DF, Anderson E. The appearance and structure of intercellular connections during the ontogeny of the rabbit ovarian follicle with particular reference to gap junctions. *J Cell Biol.* 1974 Oct;63(1):234-50.
10. Granot I, Dekel N. Developmental expression and regulation of the gap junction protein and transcript in rat ovaries. *Mol Reprod Dev.* 1997 Jul;47(3):231-9.
11. Granot I, Dekel N. The ovarian gap junction protein connexin43: regulation by gonadotropins. *Trends Endocrinol Metab.* 2002 Sep;13(7):310-3.
12. Nixon B, Aitken RJ, McLaughlin EA. New insights into the molecular mechanisms of sperm-egg interaction. *Cell Mol Life Sci.* 2007 Jul;64(14):1805-23.
13. Oktay K, Briggs D, Gosden RG. Ontogeny of follicle-stimulating hormone receptor gene expression in isolated human ovarian follicles. *J Clin Endocrinol Metab.* 1997 Nov;82(11):3748-51.
14. Erickson GF. An analysis of follicle development and ovum maturation, *Seminars Reprod Endocrinol.* 1986; 4:233.
15. Kobayashi M, Nakano R, Ooshima A. Immunohistochemical localization of pituitary gonadotrophins and gonadal steroids confirms the 'two-cell, two-gonadotrophin' hypothesis of steroidogenesis in the human ovary. *J Endocrinol.* 1990 Sep;126(3):483-8.
16. Hild-Petito S, West NB, Brenner RM, et al. Localization of androgen receptor in the follicle and corpus luteum of the primate ovary during the menstrual cycle. *Biol Reprod.* 1991 Mar;44(3):561-8.
17. McNatty KP, Makris A, Reinhold VN, et al. Metabolism of androstenedione by human ovarian tissues in vitro with particular reference to reductase and aromatase activity. *Steroids.* 1979 Oct;34(4):429-43.
18. Hillier SG, van den Boogaard AM, Reichert LE Jr, et al. Intraovarian sex steroid hormone interactions and the regulation of follicular maturation: aromatization of androgens by human granulosa cells in vitro. *J Clin Endocrinol Metab.* 1980 Apr;50(4):640-7.

19. Erickson GF, Magoffin DA, Dyer CA, et al. The ovarian androgen producing cells: a review of structure/function relationships. *Endocr Rev.* 1985 Summer;6(3):371-99.
20. Eppig JJ, Chesnel F, Hirao Y, et al. Oocyte control of granulosa cell development: how and why. *Hum Reprod.* 1997 Nov;12(11 Suppl):127-32.
21. Asimakopoulou B, Köster F, Felberbaum R, et al. Cytokine and hormonal profile in blood serum and follicular fluids during ovarian stimulation with the multidose antagonist or the long agonist protocol. *Hum Reprod.* 2006 Dec;21(12):3091-5. Epub 2006 Sep 27.
22. Goodman AL, Hodgen GD. The ovarian triad of the primate menstrual cycle. *Recent Prog Horm Res.* 1983;39:1-73.
23. Montgomery Rice V, Limback SD, Roby KF, et al. Differential responses of granulosa cells from small and large follicles to follicle stimulating hormone (FSH) during the menstrual cycle and acyclicity: effects of tumour necrosis factor-alpha. *Hum Reprod.* 1998 May;13(5):1285-91.
24. Durlinger AL, Gruijters MJ, Kramer P, et al. Anti-Müllerian hormone inhibits initiation of primordial follicle growth in the mouse ovary. *Endocrinology.* 2002 Mar;143(3):1076-84.
25. Durlinger AL, Visser JA, Themmen AP. Regulation of ovarian function: the role of anti-Müllerian hormone. *Reproduction.* 2002 Nov;124(5):601-9.
26. Zeleznik AJ, Schuler HM, Reichert LE Jr. Gonadotropin-binding sites in the rhesus monkey ovary: role of the vasculature in the selective distribution of human chorionic gonadotropin to the preovulatory follicle. *Endocrinology.* 1981 Aug;109(2):356-62.
27. Ravindranath N, Little-Ihrig L, Phillips HS, et al. Vascular endothelial growth factor messenger ribonucleic acid expression in the primate ovary. *Endocrinology.* 1992 Jul;131(1):254-60.
28. Richards JS, Jahnsen T, Hedin L, et al. Ovarian follicular development: from physiology to molecular biology. *Recent Prog Horm Res.* 1987;43:231-76.
29. Filicori M, Cognigni GE, Ciampaglia W. Effects of LH on oocyte yield and developmental competence. *Hum Reprod.* 2003 Jun;18(6):1357-8.
30. McLachlan RI, Robertson DM, Healy DL, et al. Circulating immunoreactive inhibin levels during the normal human menstrual cycle. *J Clin Endocrinol Metab.* 1987 Nov;65(5):954-61.
31. Groome NP, Illingworth PJ, O'Brien M, et al. Measurement of dimeric inhibin B throughout the human menstrual cycle. *J Clin Endocrinol Metab.* 1996 Apr;81(4):1401-5.
32. Welt CK¹, Smith ZA, Pauler DK, Hall JE. Differential regulation of inhibin A and inhibin B by luteinizing hormone, follicle-stimulating hormone, and stage of follicle development. *J Clin Endocrinol Metab.* 2001 Jun;86(6):2531-7.
33. Blumenfeld Z. Response of human fetal pituitary cells to activin, inhibin, hypophysiotropic and neuroregulatory factors in vitro. *Early Pregnancy.* 2001 Jan;5(1):41-2.
34. Norwitz ER, Xu S, Jeong KH, et al. Activin A augments GnRH-mediated transcriptional activation of the mouse GnRH receptor gene. *Endocrinology.* 2002 Mar;143(3):985-97.
35. Bilezikjian LM, Corrigan AZ, Blount AL, et al. Pituitary follistatin and inhibin subunit messenger ribonucleic acid levels are differentially regulated by local and hormonal factors. *Endocrinology.* 1996 Oct;137(10):4277-84.
36. Kaiser UB, Lee BL, Carroll RS, et al. Follistatin gene expression in the pituitary: localization in gonadotropes and folliculostellate cells in diestrous rats. *Endocrinology.* 1992 May;130(5):3048-56.
37. Besecke LM, Guendner MJ, Sluss PA, et al. Pituitary follistatin regulates activin-mediated production of follicle-stimulating hormone during the rat estrous cycle. *Endocrinology.* 1997 Jul;138(7):2841-8.
38. Pauerstein CJ, Eddy CA, Croxatto HD. Temporal relationships of estrogen, progesterone, and luteinizing hormone levels to ovulation in women and infrahuman primates. *Am J Obstet Gynecol.* 1978 Apr 15;130(8):876-86.
39. Young JR, Jaffe RB. Strength-duration characteristics of estrogen effects on gonadotropin response to gonadotropin-releasing hormone in women. II. Effects of varying concentrations of estradiol. *J Clin Endocrinol Metab.* 1976 Mar;42(3):432-42.
40. Hoff JD, Quigley ME, Yen SS. Hormonal dynamics at midcycle: a reevaluation. *J Clin Endocrinol Metab.* 1983 Oct;57(4):792-6.

41. Zelinski-Wooten MB, Hutchison JS, Chandrasekher YA, et al. Administration of human luteinizing hormone (hLH) to macaques after follicular development: further titration of LH surge requirements for ovulatory changes in primate follicles. *J Clin Endocrinol Metab.* 1992 Aug;75(2):502-7.
42. World Health Organization, Task Force on Methods for the Determination of the Fertile Period, Special Programme of Research, Development and Research Training in Human Reproduction. Temporal relationships between ovulation and defined changes in the concentration of plasma estradiol-17 beta, luteinizing hormone, follicle-stimulating hormone, and progesterone. *Am J Obstet Gynecol.* 1980 Oct 15;138(4):383-90.
43. Yong EL, Baird DT, Yates R, et al. Hormonal regulation of the growth and steroidogenic function of human granulosa cells. *J Clin Endocrinol Metab.* 1992 Apr;74(4):842-9.
44. Tedeschi C, Hazum E, Kokia E, et al. Endothelin-1 as a luteinization inhibitor: inhibition of rat granulosa cell progesterone accumulation via selective modulation of key steroidogenic steps affecting both progesterone formation and degradation. *Endocrinology.* 1992 Nov;131(5):2476-8.
45. Brannian JD, Woodruff TK, Mather JP, et al. Activin-A inhibits progesterone production by macaque luteal cells in culture. *J Clin Endocrinol Metab.* 1992 Sep;75(3):756-61.
46. Hoffman, B.L., Schorge, J.O., Schaffer, J.I., Halvorson, L.M., Bradshaw K.D., Cunningham F.G. (2015). *Williams Jinekoloji.* (Gökhan YILDIRIM Çev. Ed.). İstanbul: Nobel Tıp Kitapevleri.
47. Judd HL, Yen SS. Serum androstenedione and testosterone levels during the menstrual cycle. *J Clin Endocrinol Metab.* 1973 Mar;36(3):475-81.
48. Beers WH. Follicular plasminogen and plasminogen activator and the effect of plasmin on ovarian follicle wall. *Cell.* 1975 Nov;6(3):379-86.
49. Lumsden MA, Kelly RW, Templeton AA, et al. Changes in the concentration of prostaglandins in preovulatory human follicles after administration of hCG. *J Reprod Fertil.* 1986 May;77(1):119-24.
50. Espey LL, Tanaka N, Adams RF, et al. Ovarian hydroxyeicosatetraenoic acids compared with prostanoids and steroids during ovulation in rats. *Am J Physiol.* 1991 Feb;260(2 Pt 1):E163-9.
51. Miyazaki T, Dharmarajan AM, Atlas SJ, et al. Do prostaglandins lead to ovulation in the rabbit by stimulating proteolytic enzyme activity? *Fertil Steril.* 1991 Jun;55(6):1183-8.
52. Pall M, Fridén BE, Brännström M. Induction of delayed follicular rupture in the human by the selective COX-2 inhibitor rofecoxib: a randomized double-blind study. *Hum Reprod.* 2001 Jul;16(7):1323-8.
53. Anasti JN, Kalantaridou SN, Kimzey LM, et al. Human follicle fluid vascular endothelial growth factor concentrations are correlated with luteinization in spontaneously developing follicles. *Hum Reprod.* 1998 May;13(5):1144-7.
54. Smith SK, Lenton EA, Cooke ID. Plasma gonadotrophin and ovarian steroid concentrations in women with menstrual cycles with a short luteal phase. *J Reprod Fertil.* 1985 Nov;75(2):363-8.
55. McLachlan RI, Cohen NL, Vale WW, et al. The importance of luteinizing hormone in the control of inhibin and progesterone secretion by the human corpus luteum. *J Clin Endocrinol Metab.* 1989 Jun;68(6):1078-85.
56. Schipper I, de Jong FH, Fauser BC. Lack of correlation between maximum early follicular phase serum follicle stimulating hormone concentrations and menstrual cycle characteristics in women under the age of 35 years. *Hum Reprod.* 1998 Jun;13(6):1442-8.
57. Welt CK, Pagan YL, Smith PC, et al. Control of follicle-stimulating hormone by estradiol and the inhibins: critical role of estradiol at the hypothalamus during the luteal-follicular transition. *J Clin Endocrinol Metab.* 2003 Apr;88(4):1766-71.
58. Jia XC, Kessel B, Yen SS, et al. Serum bioactive follicle-stimulating hormone during the human menstrual cycle and in hyper- and hypogonadotropic states: application of a sensitive granulosa cell aromatase bioassay. *J Clin Endocrinol Metab.* 1986 Jun;62(6):1243-9.
59. Tabibzadeh S. The signals and molecular pathways involved in human menstruation, a unique process of tissue destruction and remodeling. *Mol Hum Reprod.* 1996 Feb;2(2):77-92.

60. Casey ML, Hemsell DL, MacDonald PC, et al. NAD⁺-dependent 15-hydroxyprostaglandin dehydrogenase activity in human endometrium. *Prostaglandins*. 1980 Jan;19(1):115-22.
61. Treloar AE, Boynton RE, Behn BG, et al. Variation of the human menstrual cycle through reproductive life. *Int J Fertil*. 1967 Jan-Mar;12(1 Pt 2):77-126.
62. Ludwig H, Spornitz UM. Microarchitecture of the human endometrium by scanning electron microscopy: menstrual desquamation and remodeling. *Ann N Y Acad Sci*. 1991;622:28-46.
63. Lessey BA, Killam AP, Metzger DA, et al. Immunohistochemical analysis of human uterine estrogen and progesterone receptors throughout the menstrual cycle. *J Clin Endocrinol Metab*. 1988 Aug;67(2):334-40.
64. Beato M. Gene regulation by steroid hormones. *Cell*. 1989 Feb 10;56(3):335-44.
65. Tabibzadeh S. Proliferative activity of lymphoid cells in human endometrium throughout the menstrual cycle. *J Clin Endocrinol Metab*. 1990 Feb;70(2):437-43.