

BÖLÜM 46

OVER HİPERSTİMÜLASYON SENDROMUNUN PATOGENEZİ, KLİNİK BELİRTİLERİ, TANI, ÖNLEME VE YÖNETİMİ

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Giriş

Over hiperstimülasyon sendromu (OHSS), yumurtalıkların yardımıyla üreme tedavileri (veya nadiren folikül uyarıcı hormon [FSH] reseptöründeki mutasyonlar) nedeniyle iatrojenik olarak aşırı uyarıldığında ortaya çıkan serumun intravasküler boşluktan üçüncü boşluğa kaymasıyla sonuçlanır. Şiddetli formuna OHSS denilmekte inme ve ekstremitelerde perfüzyon kaybı dahil venöz veya arteriyel tromboembolik olaylara neden olabileceğinden hayatı tehdit eden bir durumdur.

OHSS, yardımıyla üreme tedavileri (YÜT) için kontrollü over hiperstimülasyonunun (KOH) en ciddi komplikasyonudur. Abdominal distansiyon ve rahatsızlık, büyümüş, genişlemiş overler, assit ve artmış vasküler geçirgenliğin diğer komplikasyonlarını içeren geniş bir belirti ve semptom yelpazesidir [1, 2]. OHSS'nin patofizyolojisi tam olarak anlaşılamamıştır, ancak üçüncü boşluğa sıvı kaybıyla sonuçlanan kılcal geçirgenliğin artması ana özelliğidir. Duyarlı hastada, son foliküller olgunlaşma ve ovülasyonun tetiklenmesi için insan koryonik gonadotropin (hCG) uygulaması, OHSS için önemli bir uyarıcıdır ve yumurtalıkta vasküler endotelial büyüme faktörünün (VEGF)

aşırı ekspresyonuna, vazoaaktif-anjiyojenik maddelerin salınmasının artmasına neden olur.

OHSS, genç, sağlıklı hastaları etkileyen iyatrojenik ve potansiyel olarak yaşamı tehdit eden bir durumdur. Ek olarak, işten yoksunluk, yatak istirahati veya hastaneye yatış ve ağır vakaların yoğun tıbbi yönetimi nedeniyle OHSS ile ilişkili önemli bir ekonomik yük oluşturmaktadır.

OHSS'nin iki klinik formu vardır: erken başlangıç formu (hCG uygulamasından sonraki ilk sekiz günde meydana gelir) ve geç başlangıç formu (hCG uygulamasından dokuz gün veya daha uzun süre sonra ortaya çıkan, gebeliğe bağlı hCG üretim) [3].

Etiyoloji

OHSS sıklığı, klinik ortama (örn. Ovulasyon indüksiyonu / over stimülasyonu ve zamanlı cinsel ilişki, intrauterin inseminasyona veya in vitro fertilizasyon [IVF]) ve OHSS için kullanılan sınıflandırma kriterlerine (tablo 1) göre değişmektedir. OHSS'nin en şiddetli biçimi nadiren, tedavi gören genç kadınlarda potansiyel olarak ölümcül bir sonuçla karşılaşılabilen iyatrojenik bir komplikasyondur.

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OHSS gebeliklerinin daha yüksek oranda düşük ve daha sonra gebelik diyabeti ve gebeliğe bağlı hipertansiyon gibi komplikasyonlara sahip olduğunu göstermektedir [121]. Öte yandan OHSS sendromu gelişmemiş IVF kontrol hastalarına kıyasla OHSS gelişen kadınlarda ikinci ve üçüncü trimesterde artmış fetal ve maternal morbidite göstermemiştir [122].

Sonuç

Over hiperstimülasyon sendromu (OHSS), yumurtalıkların yardımıyla üreme tedavileri sonrası iatrojenik olarak gelişen ve hayatı tehdit eden bir klinik durumdur. Tedavi öncesi uygun değerlendirme ve tedavinin bireyselleştirilmesi ile siklusların transvajinal ultrasonografi (TVUSG) ve estradiol ile yakın takibi gerekmektedir. Klinik OHSS durumunun erken tanısı ve hasta eğitimi ile beraber derneklerin takip ve tedavi planlarının göz önünde bulundurulması ve gelişebilecek komplikasyonları öngürme ve önleme stratejilerinin uygulanması gerekmektedir. OHSS gebeliklerinin daha yüksek oranda düşük ve daha sonra gebelik diyabeti ve gebeliğe bağlı hipertansiyon gibi komplikasyonlara sahip olmakla beraber ikinci ve üçüncü trimesterde artmış fetal ve maternal morbidite gösterilmemiştir.

KAYNAKALR

- Golan A, Ron-el R, Herman A, et al. Ovarian hyperstimulation syndrome: an update review. *Obstet Gynecol Surv* 1989; 44:430.
- Whelan JG 3rd, Vlahos NF. The ovarian hyperstimulation syndrome. *Fertil Steril* 2000; 73:883.
- Lyons CA, Wheeler CA, Frishman GN, et al. Early and late presentation of the ovarian hyperstimulation syndrome: two distinct entities with different risk factors. *Hum Reprod* 1994; 9:792.
- Schenker JG, Weinstein D. Ovarian hyperstimulation syndrome: a current survey. *Fertil Steril* 1978; 30:255.
- Delvigne A, Rozenberg S. Epidemiology and prevention of ovarian hyperstimulation syndrome (OHSS): a review. *Hum Reprod Update* 2002; 8:559.
- Papanikolaou EG, Tournaye H, Verpoest W, et al. Early and late ovarian hyperstimulation syndrome: early pregnancy outcome and profile. *Hum Reprod* 2005; 20:636.
- Abramov Y, Elchalal U, Schenker JG. Severe OHSS: An 'epidemic' of severe OHSS: a price we have to pay? *Hum Reprod* 1999; 14:2181.
- Cunha-Filho JS, Samama M, Fanchin R, et al. Clinical and laboratory evaluation of hospitalized patients with severe ovarian hyperstimulation syndrome. *Reprod Biomed Online* 2003; 6:448.
- Binder H, Dittrich R, Einhaus F, et al. Update on ovarian hyperstimulation syndrome: Part 1--Incidence and pathogenesis. *Int J Fertil Womens Med* 2007; 52:11.
- Rizk B, Smitz J. Ovarian hyperstimulation syndrome after superovulation using GnRH agonists for IVF and related procedures. *Hum Reprod* 1992; 7:320.
- Mozes M, Bogokowsky H, Antebi E, et al. Thromboembolic phenomena after ovarian stimulation with human gonadotrophins. *Lancet* 1965; 2:1213.
- Roberts WG, Palade GE. Neovascutature induced by vascular endothelial growth factor is fenestrated. *Cancer Res* 1997; 57:765.
- Schenker JG. Prevention and treatment of ovarian hyperstimulation. *Hum Reprod* 1993; 8:653.
- Aboulghar MA, Mansour RT. Ovarian hyperstimulation syndrome: classifications and critical analysis of preventive measures. *Hum Reprod Update* 2003; 9:275.
- Soares SR, Gómez R, Simón C, et al. Targeting the vascular endothelial growth factor system to prevent ovarian hyperstimulation syndrome. *Hum Reprod Update* 2008; 14:321.
- Yen SS, Llerena O, Little B, Pearson OH. Disappearance rates of endogenous luteinizing hormone and chorionic gonadotropin in man. *J Clin Endocrinol Metab* 1968; 28:1763.
- McClure N, Healy DL, Rogers PA, et al. Vascular endothelial growth factor as capillary permeability agent in ovarian hyperstimulation syndrome. *Lancet* 1994; 344:235.
- Kamat BR, Brown LF, Manseau EJ, et al. Expression of vascular permeability factor/vascular endothelial growth factor by human granulosa and theca lutein cells. Role in corpus luteum development. *Am J Pathol* 1995; 146:157.
- Yan Z, Weich HA, Bernart W, et al. Vascular endothelial growth factor (VEGF) messenger ribonucleic acid (mRNA) expression in luteinized human granulosa cells in vitro. *J Clin Endocrinol Metab* 1993; 77:1723.
- Neulen J, Yan Z, Raczek S, et al. Human chorionic gonadotropin-dependent expression of vascular endothelial growth factor/vascular permeability factor in human granulosa cells: importance in ovarian hyperstimulation syndrome. *J Clin Endocrinol Metab* 1995; 80:1967.
- Wang TH, Horng SG, Chang CL, et al. Human chorionic gonadotropin-induced ovarian hyperstimulation syndrome is associated with up-regulation of vascular endothelial growth factor. *J Clin Endocrinol Metab* 2002; 87:3300.
- Yamamoto S, Konishi I, Tsuruta Y, et al. Expression of vascular endothelial growth factor (VEGF) during folliculogenesis and corpus luteum formation in the human ovary. *Gynecol Endocrinol* 1997; 11:371.
- Pellicer A, Albert C, Mercader A, et al. The pathogenesis of ovarian hyperstimulation syndrome: in vivo studies investigating the role of interleukin-1beta, inter-



- leukin-6, and vascular endothelial growth factor. *Fertil Steril* 1999; 71:482.
24. Chae HD, Park EJ, Kim SH, et al. Ovarian hyperstimulation syndrome complicating a spontaneous singleton pregnancy: a case report. *J Assist Reprod Genet* 2001; 18:120.
 25. Smits G, Olatunbosun O, Delbaere A, et al. Ovarian hyperstimulation syndrome due to a mutation in the follicle-stimulating hormone receptor. *N Engl J Med* 2003; 349:760.
 26. Vasseur C, Rodien P, Beau I, et al. A chorionic gonadotropin-sensitive mutation in the follicle-stimulating hormone receptor as a cause of familial gestational spontaneous ovarian hyperstimulation syndrome. *N Engl J Med* 2003; 349:753.
 27. Montanelli L, Delbaere A, Di Carlo C, et al. A mutation in the follicle-stimulating hormone receptor as a cause of familial spontaneous ovarian hyperstimulation syndrome. *J Clin Endocrinol Metab* 2004; 89:1255.
 28. Abir R, Fisch B. Invited commentary: a single nucleotide polymorphism in BMP15 is associated with high response to controlled ovarian hyperstimulation. *Reprod Biomed Online* 2011; 23:77.
 29. Hanevik HI, Hilmarsen HT, Skjelbred CF, et al. A single nucleotide polymorphism in BMP15 is associated with high response to ovarian stimulation. *Reprod Biomed Online* 2011; 23:97.
 30. Morón FJ, de Castro F, Royo JL, et al. Bone morphogenetic protein 15 (BMP15) alleles predict over-response to recombinant follicle stimulation hormone and iatrogenic ovarian hyperstimulation syndrome (OHSS). *Pharmacogenet Genomics* 2006; 16:485.
 31. Cappa F, Pasqua C, Tobia M, Ventura T. [Ascites and hydrothorax due to endogenous hyperstimulation of H. C. G. in a case of hydatidiform mole destruens with secondary irreversible kidney insufficiency due to disseminated intravascular coagulation]. *Riv Ital Ginecol* 1976; 56:363.
 32. Guvenal F, Guvenal T, Timuroglu Y, et al. Spontaneous ovarian hyperstimulation-like reaction caused by primary hypothyroidism. *Acta Obstet Gynecol Scand* 2006; 85:124.
 33. Borna S, Nasery A. Spontaneous ovarian hyperstimulation in a pregnant woman with hypothyroidism. *Fertil Steril* 2007; 88:705. e1.
 34. Miras AD, Mogford JT, Wright J, et al. Ovarian hyperstimulation from ectopic hypersecretion of follicle stimulating hormone. *Lancet* 2015; 385:392.
 35. Practice Committee of American Society for Reproductive Medicine. Ovarian hyperstimulation syndrome. *Fertil Steril* 2008; 90:S188.
 36. Tummon I, Gavrilova-Jordan L, Allemand MC, Session D. Polycystic ovaries and ovarian hyperstimulation syndrome: a systematic review*. *Acta Obstet Gynecol Scand* 2005; 84:611.
 37. Ocal P, Sahmay S, Cetin M, et al. Serum anti-Müllerian hormone and antral follicle count as predictive markers of OHSS in ART cycles. *J Assist Reprod Genet* 2011; 28:1197.
 38. Navot D, Bergh PA, Laufer N. Ovarian hyperstimulation syndrome in novel reproductive technologies: prevention and treatment. *Fertil Steril* 1992; 58:249.
 39. Enskog A, Henriksson M, Unander M, et al. Prospective study of the clinical and laboratory parameters of patients in whom ovarian hyperstimulation syndrome developed during controlled ovarian hyperstimulation for in vitro fertilization. *Fertil Steril* 1999; 71:808.
 40. Delvigne A. Symposium: Update on prediction and management of OHSS. *Epidemiology of OHSS. Reprod Biomed Online* 2009; 19:8.
 41. Lewis CG, Warnes GM, Wang XJ, Matthews CD. Failure of body mass index or body weight to influence markedly the response to ovarian hyperstimulation in normal cycling women. *Fertil Steril* 1990; 53:1097.
 42. Delvigne A, Rozenberg S. Review of clinical course and treatment of ovarian hyperstimulation syndrome (OHSS). *Hum Reprod Update* 2003; 9:77.
 43. Abramov Y, Elchalal U, Schenker JG. Pulmonary manifestations of severe ovarian hyperstimulation syndrome: a multicenter study. *Fertil Steril* 1999; 71:645.
 44. Fábregues F, Balasch J, Ginès P, et al. Ascites and liver test abnormalities during severe ovarian hyperstimulation syndrome. *Am J Gastroenterol* 1999; 94:994.
 45. Elchalal U, Schenker JG. The pathophysiology of ovarian hyperstimulation syndrome--views and ideas. *Hum Reprod* 1997; 12:1129.
 46. Practice Committee of the American Society for Reproductive Medicine. Ovarian hyperstimulation syndrome. *Fertil Steril* 2003; 80:1309.
 47. Grossman LC, Michalakakis KG, Browne H, et al. The pathophysiology of ovarian hyperstimulation syndrome: an unrecognized compartment syndrome. *Fertil Steril* 2010; 94:1392.
 48. Abramov Y, Elchalal U, Schenker JG. Febrile morbidity in severe and critical ovarian hyperstimulation syndrome: a multicentre study. *Hum Reprod* 1998; 13:3128.
 49. Humaidan P, Nelson SM, Devroey P, et al. Ovarian hyperstimulation syndrome: review and new classification criteria for reporting in clinical trials. *Hum Reprod* 2016; 31:1997.
 50. Mashiach S, Bider D, Moran O, et al. Adnexal torsion of hyperstimulated ovaries in pregnancies after gonadotropin therapy. *Fertil Steril* 1990; 53:76.
 51. Aboulghar MA, Mansour RT, Serour GI, Amin YM. Moderate ovarian hyperstimulation syndrome complicated by deep cerebrovascular thrombosis. *Hum Reprod* 1998; 13:2088.
 52. Stewart JA, Hamilton PJ, Murdoch AP. Thromboembolic disease associated with ovarian stimulation and assisted conception techniques. *Hum Reprod* 1997; 12:2167.
 53. Cluoroe AD, Synek BJ. A fatal case of ovarian hyperstimulation syndrome with cerebral infarction. *Pathology* 1995; 27:344.
 54. Phillips LL, Gladstone W, vande Wiele R. Studies of the coagulation and fibrinolytic systems in hyperstimulation syndrome after administration of human gonadotropins. *J Reprod Med* 1975; 14:138.
 55. Tang OS, Ng EH, Wai Cheng P, Chung Ho P. Cortical vein thrombosis misinterpreted as intracranial haemorrhage.



- rhage in severe ovarian hyperstimulation syndrome: case report. *Hum Reprod* 2000; 15:1913.
56. Arya R, Shehata HA, Patel RK, et al. Internal jugular vein thrombosis after assisted conception therapy. *Br J Haematol* 2001; 115:153.
57. Dulitzky M, Cohen SB, Inbal A, et al. Increased prevalence of thrombophilia among women with severe ovarian hyperstimulation syndrome. *Fertil Steril* 2002; 77:463.
58. Ovarian Stimulation TEGGO, Bosch E, Broer S, et al. ESHRE guideline: ovarian stimulation for IVF/ICSI†. *Hum Reprod Open* 2020; 2020:hoaa009.
59. Fauser BC, Van Heusden AM. Manipulation of human ovarian function: physiological concepts and clinical consequences. *Endocr Rev* 1997; 18:71.
60. Homburg R, Insler V. Ovulation induction in perspective. *Hum Reprod Update* 2002; 8:449.
61. Olivennes F, Howies CM, Borini A, et al. Individualizing FSH dose for assisted reproduction using a novel algorithm: the CONSORT study. *Reprod Biomed Online* 2011; 22 Suppl 1:S73.
62. Bayram N, van Wely M, Vandekerckhove P, et al. Pulsatile luteinising hormone releasing hormone for ovulation induction in subfertility associated with polycystic ovary syndrome. *Cochrane Database Syst Rev* 2000; :CD000412.
63. Daya Salim, Gunby Joanne L. Recombinant versus urinary follicle stimulating hormone for ovarian stimulation in assisted reproduction cycles. *Cochrane Database of Systematic Reviews*. In: The Cochrane Library, Issue 3, Art. No. CD002810. DOI: 0. 1002/14651858. CD002810. pub4
64. Westergaard Lars W, Bossuyt Patrick MM, Van der Veen Fulco, van Wely Madelon. Human menopausal gonadotropin versus recombinant follicle stimulation hormone for ovarian stimulation in assisted reproductive cycles. *Cochrane Database of Systematic Reviews*. In: The Cochrane Library, Issue 11, Art. No. CD003973.
65. Kahnberg A, Enskog A, Brännström M, et al. Prediction of ovarian hyperstimulation syndrome in women undergoing in vitro fertilization. *Acta Obstet Gynecol Scand* 2009; 88:1373.
66. D'Angelo A, Davies R, Salah E, et al. Value of the serum estradiol level for preventing ovarian hyperstimulation syndrome: a retrospective case control study. *Fertil Steril* 2004; 81:332.
67. Al-Inany HG, Abou-Setta AM, Aboulghar M. Gonadotrophin-releasing hormone antagonists for assisted conception: a Cochrane review. *Reprod Biomed Online* 2007; 14:640.
68. Lin H, Li Y, Li L, et al. Is a GnRH antagonist protocol better in PCOS patients? A meta-analysis of RCTs. *PLoS One* 2014; 9:e91796.
69. Delvigne A, Rozenberg S. A qualitative systematic review of coasting, a procedure to avoid ovarian hyperstimulation syndrome in IVF patients. *Hum Reprod Update* 2002; 8:291.
70. D'Angelo A, Brown J, Amso NN. Coasting (withholding gonadotrophins) for preventing ovarian hyperstimulation syndrome. *Cochrane Database Syst Rev* 2011; :CD002811.
71. Mansour R, Aboulghar M, Serour G, et al. Criteria of a successful coasting protocol for the prevention of severe ovarian hyperstimulation syndrome. *Hum Reprod* 2005; 20:3167.
72. Levinsohn-Tavor O, Friedler S, Schachter M, et al. Coasting-what is the best formula? *Hum Reprod* 2003; 18:937.
73. Rizk B, Aboulghar M. Modern management of ovarian hyperstimulation syndrome. *Hum Reprod* 1991; 6:1082.
74. Tang T, Glanville J, Orsi N, et al. The use of metformin for women with PCOS undergoing IVF treatment. *Hum Reprod* 2006; 21:1416.
75. Khattab S, Fotouh IA, Mohees IA, et al. Use of metformin for prevention of ovarian hyperstimulation syndrome: a novel approach. *Reprod Biomed Online* 2006; 13:194.
76. Tso LO, Costello MF, Albuquerque LE, et al. Metformin treatment before and during IVF or ICSI in women with polycystic ovary syndrome. *Cochrane Database Syst Rev* 2014; :CD006105.
77. Palomba S, Falbo A, La Sala GB. Effects of metformin in women with polycystic ovary syndrome treated with gonadotrophins for in vitro fertilisation and intracytoplasmic sperm injection cycles: a systematic review and meta-analysis of randomised controlled trials. *BJOG* 2013; 120:267.
78. van der Linden M, Buckingham K, Farquhar C, et al. Luteal phase support for assisted reproduction cycles. *Cochrane Database Syst Rev* 2011; :CD009154.
79. Yen SS, Llerena O, Little B, Pearson OH. Disappearance rates of endogenous luteinizing hormone and chorionic gonadotropin in man. *J Clin Endocrinol Metab* 1968; 28:1763.
80. Agrawal R, Conway G, Sladkevicius P, et al. Serum vascular endothelial growth factor and Doppler blood flow velocities in in vitro fertilization: relevance to ovarian hyperstimulation syndrome and polycystic ovaries. *Fertil Steril* 1998; 70:651.
81. Pellicer A, Albert C, Mercader A, et al. The pathogenesis of ovarian hyperstimulation syndrome: in vivo studies investigating the role of interleukin-1beta, interleukin-6, and vascular endothelial growth factor. *Fertil Steril* 1999; 71:482.
82. Schmidt DW, Maier DB, Nulsen JC, Benadiva CA. Reducing the dose of human chorionic gonadotropin in high responders does not affect the outcomes of in vitro fertilization. *Fertil Steril* 2004; 82:841.
83. Kolibianakis EM, Papanikolaou EG, Tournaye H, et al. Triggering final oocyte maturation using different doses of human chorionic gonadotropin: a randomized pilot study in patients with polycystic ovary syndrome treated with gonadotropin-releasing hormone antagonists and recombinant follicle-stimulating hormone. *Fertil Steril* 2007; 88:1382.
84. Tsoumpou I, Muglu J, Gelbaya TA, Nardo LG. Symposium: Update on prediction and management of OHSS. Optimal dose of HCG for final oocyte maturation in IVF cycles: absence of evidence? *Reprod Biomed Online* 2009; 19:52.



85. Youssef MA, Al-Inany HG, Aboulghar M, et al. Recombinant versus urinary human chorionic gonadotrophin for final oocyte maturation triggering in IVF and ICSI cycles. *Cochrane Database Syst Rev* 2011; :CD003719.
86. Griesinger G, Diedrich K, Devroey P, Kolibianakis EM. GnRH agonist for triggering final oocyte maturation in the GnRH antagonist ovarian hyperstimulation protocol: a systematic review and meta-analysis. *Hum Reprod Update* 2006; 12:159.
87. Acevedo B, Gomez-Palomares JL, Ricciarelli E, Hernández ER. Triggering ovulation with gonadotropin-releasing hormone agonists does not compromise embryo implantation rates. *Fertil Steril* 2006; 86:1682.
88. Babayof R, Margalioth EJ, Huleihel M, et al. Serum inhibin A, VEGF and TNF α levels after triggering oocyte maturation with GnRH agonist compared with HCG in women with polycystic ovaries undergoing IVF treatment: a prospective randomized trial. *Hum Reprod* 2006; 21:1260.
89. Engmann L, Siano L, Schmidt D, et al. GnRH agonist to induce oocyte maturation during IVF in patients at high risk of OHSS. *Reprod Biomed Online* 2006; 13:639.
90. Youssef MA, Van der Veen F, Al-Inany HG, et al. Gonadotropin-releasing hormone agonist versus HCG for oocyte triggering in antagonist-assisted reproductive technology. *Cochrane Database Syst Rev* 2014; :CD008046.
91. Corbett S, Shmorgun D, Claman P, et al. The prevention of ovarian hyperstimulation syndrome. *J Obstet Gynaecol Can* 2014; 36:1024.
92. Grøndahl C. Oocyte maturation. Basic and clinical aspects of in vitro maturation (IVM) with special emphasis of the role of FF-MAS. *Dan Med Bull* 2008; 55:1.
93. Das M, Son WY, Buckett W, et al. In-vitro maturation versus IVF with GnRH antagonist for women with polycystic ovary syndrome: treatment outcome and rates of ovarian hyperstimulation syndrome. *Reprod Biomed Online* 2014; 29:545.
94. Shavit T, Ellenbogen A, Michaeli M, et al. In-vitro maturation of oocytes vs in-vitro fertilization with a gonadotropin-releasing hormone antagonist for women with polycystic ovarian syndrome: can superiority be defined? *Eur J Obstet Gynecol Reprod Biol* 2014; 179:46.
95. Pattinson HA, Hignett M, Dunphy BC, Fleetham JA. Outcome of thaw embryo transfer after cryopreservation of all embryos in patients at risk of ovarian hyperstimulation syndrome. *Fertil Steril* 1994; 62:1192.
96. Tiitinen A, Husa LM, Tulppala M, et al. The effect of cryopreservation in prevention of ovarian hyperstimulation syndrome. *Br J Obstet Gynaecol* 1995; 102:326.
97. Queenan JT Jr, Veeck LL, Toner JP, et al. Cryopreservation of all prezygotes in patients at risk of severe hyperstimulation does not eliminate the syndrome, but the chances of pregnancy are excellent with subsequent frozen-thaw transfers. *Hum Reprod* 1997; 12:1573.
98. D'Angelo A, Amso N. Embryo freezing for preventing ovarian hyperstimulation syndrome. *Cochrane Database Syst Rev* 2007; :CD002806.
99. Chen ZJ, Shi Y, Sun Y, et al. Fresh versus Frozen Embryos for Infertility in the Polycystic Ovary Syndrome. *N Engl J Med* 2016; 375:523.
100. Youssef MA, Al-Inany HG, Evers JL, Aboulghar M. Intra-venous fluids for the prevention of severe ovarian hyperstimulation syndrome. *Cochrane Database Syst Rev* 2011; :CD001302.
101. Venetis CA, Kolibianakis EM, Toulis KA, et al. Intravenous albumin administration for the prevention of severe ovarian hyperstimulation syndrome: a systematic review and metaanalysis. *Fertil Steril* 2011; 95:188.
102. Jee BC, Suh CS, Kim YB, et al. Administration of intravenous albumin around the time of oocyte retrieval reduces pregnancy rate without preventing ovarian hyperstimulation syndrome: a systematic review and meta-analysis. *Gynecol Obstet Invest* 2010; 70:47.
103. Ferraretti AP, Gianaroli L, Diotallevi L, et al. Dopamine treatment for severe ovarian hyperstimulation syndrome. *Hum Reprod* 1992; 7:180.
104. Tsunoda T, Shibahara H, Hirano Y, et al. Treatment for ovarian hyperstimulation syndrome using an oral dopamine prodrug, docarpamine. *Gynecol Endocrinol* 2003; 17:281.
105. Manno M, Tomei F, Marchesan E, Adamo V. Cabergoline: a safe, easy, cheap, and effective drug for prevention/treatment of ovarian hyperstimulation syndrome? *Eur J Obstet Gynecol Reprod Biol* 2005; 122:127.
106. Alvarez C, Martí-Bonmatí L, Novella-Maestre E, et al. Dopamine agonist cabergoline reduces hemoconcentration and ascites in hyperstimulated women undergoing assisted reproduction. *J Clin Endocrinol Metab* 2007; 92:2931.
107. Alvarez C, Alonso-Muriel I, García G, et al. Implantation is apparently unaffected by the dopamine agonist Cabergoline when administered to prevent ovarian hyperstimulation syndrome in women undergoing assisted reproduction treatment: a pilot study. *Hum Reprod* 2007; 22:3210.
108. Carizza C, Abdelmassih V, Abdelmassih S, et al. Cabergoline reduces the early onset of ovarian hyperstimulation syndrome: a prospective randomized study. *Reprod Biomed Online* 2008; 17:751.
109. Tang H, Hunter T, Hu Y, et al. Cabergoline for preventing ovarian hyperstimulation syndrome. *Cochrane Database Syst Rev* 2012; :CD008605.
110. Moini A, Zafarani F, Haddadian S, et al. Effect of low-dose aspirin therapy on implantation rate in women undergoing in-vitro fertilization cycles. *Saudi Med J* 2007; 28:732.
111. Várnagy A, Bódis J, Mánfai Z, et al. Low-dose aspirin therapy to prevent ovarian hyperstimulation syndrome. *Fertil Steril* 2010; 93:2281.
112. Kabukçu, C. (2019). Ovaryan Hiperstimülasyon Sendromu (OHSS). İ. Veysel Fenkçi, Ümit Çavuş, (Temel Kadın Hastalıkları ve Doğum Bilgisi, (s1049-1057). Ankara; Akademisyen Kitapevi
113. Practice Committee of American Society for Reproductive Medicine. Ovarian hyperstimulation syndrome. *Fertil Steril* 2008; 90:S188.
114. Levin I, Almog B, Avni A, et al. Effect of paracentesis of ascitic fluids on urinary output and blood indices in pa-



- tients with severe ovarian hyperstimulation syndrome. *Fertil Steril* 2002; 77:986.
115. Maslovitz S, Jaffa A, Eytan O, et al. Renal blood flow alteration after paracentesis in women with ovarian hyperstimulation. *Obstet Gynecol* 2004; 104:321.
116. Manno M, Tomei F, Marchesan E, Adamo V. Cabergoline: a safe, easy, cheap, and effective drug for prevention/treatment of ovarian hyperstimulation syndrome? *Eur J Obstet Gynecol Reprod Biol* 2005; 122:127.
117. Rollene NL, Amols MH, Hudson SBA, Coddington CC. Treatment of ovarian hyperstimulation syndrome using a dopamine agonist and gonadotropin releasing hormone antagonist: a case series. *Fertil Steril* 2009; 92:1169. e15.
118. Tang H, Mourad S, Zhai SD, Hart RJ. Dopamine agonists for preventing ovarian hyperstimulation syndrome. *Cochrane Database Syst Rev* 2016; 11:CD008605.
119. Busso CE, Garcia-Velasco JA, Gomez R, et al. Ovarian hyperstimulation syndrome. In: *Infertility and assisted reproduction*, Rizk B, Garcia-Velasco JA, Sallam HM, Makrigiannakis A (Eds), Cambridge University Press, Cambridge, UK 2008. p. 243.
120. Nouri K, Tempfer CB, Lenart C, et al. Predictive factors for recovery time in patients suffering from severe OHSS. *Reprod Biol Endocrinol* 2014; 12:59.
121. Abramov Y, Elchalal U, Schenker JG. Obstetric outcome of in vitro fertilized pregnancies complicated by severe ovarian hyperstimulation syndrome: a multicenter study. *Fertil Steril* 1998; 70:1070.
122. Mathur RS, Jenkins JM. Is ovarian hyperstimulation syndrome associated with a poor obstetric outcome? *BJOG* 2000; 107:943.
123. Wisner A, Levron J, Kreizer D, et al. Outcome of pregnancies complicated by severe ovarian hyperstimulation syndrome (OHSS): a follow-up beyond the second trimester. *Hum Reprod* 2005; 20:910.