

BÖLÜM 27

Obstrüktif Uyku Apne Sendromunda Genel Önlemler ve Medikal Tedavi



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GİRİŞ

Obstrüktif Uyku Apne Sendromu (OUAS), sık görülen ve ciddi sistemik komplikasyonlara yol açan, multidisipliner yaklaşım gerektiren bir hastalıktır. OUAS hastalarının tedavisinde hedef, semptom ve bulguları ortadan kaldırmak, oksijen desatürasyonunu düzeltmek ve uyku kalitesini iyileştirmektir. En etkili tedavi yöntemi pozitif hava yolu basıncı (Positive Airway Pressure- PAP) uygulamasıdır. PAP tedavisi dışında, ağız içi araç, cerrahi tedavi, genel önlemler ve medikal tedavi seçenekleri uygulanmaktadır (Tablo 1) (1,2). Üçüncü Amerikan Uyku Klavuzu (ICD-3) ve ulusal uyku rehberleri eşliğinde OUAS'ın tedavisinde, temel yaklaşım OUAS ağırlığına göre belirlenmektedir. OUAS ağırlığına bakılmaksızın her hastada öncelikle genel önlemleri içerir tedavi yöntemleri uygulanmalıdır (2).

GENEL ÖNLEMLER

Davranışsal değişiklikler ve hasta eğitimi

Davranış terapileri, OUAS tanısı alan ve değiştirilebilir risk faktörleri olan tüm hastalarda önerilmelidir. Yaşam tarzı önerileri hastaya göre bireysel olarak ele alınmalı, uygulanacak tedavinin başarı oranını değerlendirip hastanın onayı alınarak uygulanmalıdır. Hastalara tedavi edilmediği takdirde oluşabilecek risk ve komplikasyonlar anlatılmalı, tedavinin önemi vurgulanmalıdır. OUAS hastalarında sık görülen gündüz aşırı uykululuk hali, trafik ve iş kazalarına dave-

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uykululuğun diğer olası nedenleri ekarte edildikten sonra, kendi cihazı ile yapılan polisomnografide solunumsal olayların elimine edildiği kesin olarak gösterilmişse, PAP cihazı ile birlikte stimulan ilaçlar düşünülmelidir (81).

Modafinil ve r-izomeri olan armodafinil, narkolepsi ve vardiyalı çalışmaya bağlı uyku bozukluğunun yanı sıra OUAS'ta optimal PAP tedavisine rağmen devam eden rezidü uyku halinin tedavisinde de FDA kurumu tarafından onaylanmıştır (82). OUAS'lı hastalarda rezidüel uyku halinin tedavisinde CPAP ve modafinil beraber kullanımının, tek başına CPAP kullanan hastalara göre Çoklu Uyku Latans Testi (Multiple Sleep Latency Test-MSLT) değerlerinin anlamlı derecede düzeldiği gösterilmiştir (83). Yapılan geniş metaanalizlerde modafinil/armodafinil tedavisinin Epworth skorunu yaklaşık 2.2 puan düşürdüğü, uyanıklığı Sürdürme Testi (Maintenance of Wakefulness Test-MWT) ile 3 dakika iyileştirme sağladığı gösterilmiştir (84). Uzun dönem etkinlik açısından yapılan çalışmalarda bir yıl boyunca modafinil kullanan hastalarda gündüz aşırı uyku hali gelişmediği ve yaşam kalitesinin yüksek olduğu gösterilmiş, armodafinil ile yapılan çalışmalarda da benzer sonuçlar elde edilmiştir (85).

KAYNAKLAR

1. Köktürk O, Ulukavak Çiftçi T. Obstrüktif uyku apne sendromu. Genel önlemler ve medikal tedavi. *Tüberküloz ve Toraks Dergisi* 2002;50:119-24.
2. American Academy of Sleep Medicine. International classification of sleep disorders. 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2014.
3. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med* 2002;165:1217-39.
4. Randerath W.J., Verbraecken J., Andreas S., et al. Non-CPAP therapies in obstructive sleep apnoea. *Eur Respir J* 2011;37: 1000-28
5. Jehan, S., Zizi, F., Pandi-Perumal, S. R., Wall, S., Auguste, E., Myers, A. K., ... & McFarlane, S. I. (2017). Obstructive sleep apnea and obesity: implications for public health. *Sleep medicine and disorders: international journal*, 1(4).
6. Köktürk O. Obstrüktif uyku apne sendromu epidemiyolojisi. *Tüberküloz ve Toraks* 1998; 46(2)193-201.
7. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. *JAMA*. 2000;284(23):3015-3021.
8. Köktürk O, Köktürk N. Obstrüktif uyku apne sendromu fizyopatolojisi. *Tüberküloz ve Toraks Dergisi* 1998; 46: 288-300.
9. Senaratna CV, English DR, Currier D, Perret JL, Lowe A, et al. Sleep apnoea in Australian men: disease burden, co-morbidities, and correlates from the Australian longitudinal study on male health. *BMC Public Health*. 2016;16(Suppl 3):1029.
10. Ko GT, Chan JC, Chan AW, Wong PT, Hui SS, et al. Association between sleeping hours, working hours and obesity in Hong Kong Chinese: the 'better health for better Hong Kong' health promotion campaign. *Int J Obes (Lond)* 2007;31(2):254-260.
11. Baron KG, Reid KJ, Kim T, Van Horn L, Attarian H, et al. Circadian timing and alignment in healthy adults: associations with BMI, body fat, caloric intake and physical activity. *Int J Obes (Lond)* 2016;41(2):203-209.

12. Chaput JP, Després JP, Bouchard C, Tremblay A. Short sleep duration is associated with reduced leptin levels and increased adiposity: results from the Quebec family study. *Obesity (Silver Spring)* 2007;15(1):253–261.
13. Cummings DE, Foster KE. Ghrelin-leptin tango in body-weight regulation. *Gastroenterology*. 2003;124(5):1532–1535.
14. Schwartz MW, Morton GJ. Obesity: keeping hunger at bay. *Nature*. 2002;418(6898):595–597.
15. Taheri S, Lin L, Austin D, Young T, Mignot E. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. *PLoS Med*. 2004;1(3):e62.
16. Vgontzas AN, Lin HM, Papaliaga M, Calhoun S, Vela-Bueno A, et al. Short sleep duration and obesity: the role of emotional stress and sleep disturbances. *Int J Obes (Lond)* 2008;32(5):801–809.
17. Gangwisch JE, Malaspina D, Boden-Albala B, Heymsfield SB. Inadequate sleep as a risk factor for obesity: analyses of the NHANES I. *Sleep*. 2005;28(10):1289.
18. Kohatsu ND, Tsai R, Young T, Vangilder R, Burmeister LF. Sleep duration and body mass index in a rural population. *Arch Intern Med*. 2006;166(16):1701–1705.
19. Montserrat JM, Ballester E, Hernandez L. Overview of management options for snoring and sleep apnea. *Eur Respir Mon (Respiratory Disorders During Sleep)* 1998; 3: 144-78.
20. Sanders MH. Medical therapy for obstructive sleep apnea-hypopnea syndrome. In: Kryger MH, Roth T, Dement WC (eds). *Principles and Practice of Sleep Medicine*. Philadelphia: WB Saunders Company, 2000: 879-93
21. Johansson K, Neovius M, Lagerros YT, Harlid R, Rössner S, Granath F, et al. Effect of a very low energy diet on moderate and severe obstructive sleep apnoea in obese men: a randomised controlled trial. *BMJ* 2009; 339: b4609.
22. Fernandes JF, Araújo Lda S, Kaiser SE, Sanjuliani AF, Klein MR. The effects of moderate energy restriction on apnoea severity and CVD risk factors in obese patients with obstructive sleep apnoea. *Br J Nutr* 2015; 114: 2022-31
23. Santos FL, Esteves SS, da Costa Pereira A, Yancy WS Jr, Nunes JP. Systematic review and meta-analysis of clinical trials of the effects of low carbohydrate diets on cardiovascular risk factors. *Obes Rev* 2012; 13: 1048-66
24. Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, Greenberg I, et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *N Engl J Med* 2008; 359: 229-41.
25. Papandreou C, Schiza SE, Bouloukaki I, Hatzis CM, Kafatos AG, Sifakias NM, et al. Effect of Mediterranean diet versus prudent diet combined with physical activity on OSAS: a randomized trial. *Eur Respir J* 2012; 39: 1398-404
26. Peppard PE, Young T. Exercise and sleep-disordered breathing: an association independent of body habitus. *Sleep*. 2004;27:480–484.
27. Quan SF, O'Connor GT, Quan JS, et al. Association of physical activity with sleep-disordered breathing. *Sleep Breath*. 2007;11:149–157.
28. Kline CE, Crowley EP, Ewing GB, et al. The effect of exercise training on obstructive sleep apnea and sleep quality: a randomized controlled trial. *Sleep*. 2011;34:1631–1640.
29. Mendelson M, Lyons OD, Yadollahi A, et al. Effects of exercise training on sleep apnoea in patients with coronary artery disease: a randomised trial. *Eur Respir J*. 2016;48:142–150.
30. Ross R, Dagnone D, Jones PJ, et al. Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men. A randomized, controlled trial *Ann Intern Med*. 2000; 133 :92–103.
31. Giannopoulou I, Ploutz-Snyder LL, Carhart R, et al. Exercise is required for visceral fat loss in postmenopausal women with type 2 diabetes *J Clin Endocrinol Metab*. 2005; 90 :1511–1518.
32. Tsutsumi W, Miyazaki S, Itasaka Y, Togawa K. Influence of alcohol on respiratory disturbance during sleep. *Psychiatry Clin Neurosci* 2000; 54: 332-3.
33. Issa FG, Sullivan CE. Alcohol, snoring and sleep apnea. *J Neurol Neurosurg Psychiatry* 1982; 45: 353-9.

34. Mittleman MM, Dawson A, Henriksen SJ, Sobers M, Bloom FE. Bedtime ethanol increases resistance of upper airways and produces sleep apneas in asymptomatic snorers. *Alcohol Clin Exp Res* 1988; 12: 801-5.
35. Stelmach-Mardas M, Mardas M, Iqbal K, Kostrzewska M, Piorunek T. Dietary and cardio-metabolic risk factors in patients with Obstructive Sleep Apnea: cross-sectional study. *PeerJ* 2017; 5: e3259.
36. Jeong JI, Kim HY, Hong SD, Ryu G, Kim SJ, Lee KE, et al. Upper Airway Variation and Frequent Alcohol Consumption Can Affect Compliance With Continuous Positive Airway Pressure. *Clinical and Experimental Otorhinolaryngology* 2016; 9: 346-51.
37. Hadar T, Yaniv E, Shvili Y, Koren R, Shvero J. Histopathological changes of the nasal mucosa induced by smoking. *Inhal Toxicol* 2009; 21: 1119.
38. Kashyap R, Hock LM, Bowman TJ. Higher prevalence of smoking in patients diagnosed as having obstructive sleep apnea. *Sleep Breath* 2001; 5: 167-72.
39. Kim KS, Kim JH, Park SY, Won HR, Lee HJ, Yang HS, Kim HJ. Smoking induces oropharyngeal narrowing and increases the severity of obstructive sleep apnea syndrome. *J Clin Sleep Med* 2012; 8: 367-74.
40. Chung F, Memtsoudis SG, Ramachandran SK, et al. Society of Anesthesia and Sleep Medicine Guidelines on Preoperative Screening and Assessment of Adult Patients With Obstructive Sleep Apnea. *Anesth Analg* 2016; 123: 452-73.
41. Hillman DR, Chung F. Anaesthetic management of sleep-disordered breathing in adults. *Respirology* 2017; 22: 230-9.
42. Ravesloot MJ, van Maanen JP, Dun L, de Vries N. The undervalued potential of positional therapy in position-dependent snoring and obstructive sleep apnea-a review of the literature. *Sleep Breath*. 2013;17(1):39-49.
43. Richard W, Kox D, den Herder C, Laman M, van Tinteren H, de Vries N. The role of sleep position in obstructive sleep apnea syndrome. *Eur Arch Otorhinolaryngol*. 2006;263(10):946-950.
44. Cartwright RD. Effect of sleep position on sleep apnea severity. *Sleep*. 1984;7(2):110-114.
45. Oksenberg A, Silverberg DS, Arons E, Radwan H. Positional vs nonpositional obstructive sleep apnea patients: anthropomorphic, nocturnal polysomnographic, and multiple sleep latency test data. *Chest*. 1997;112(3):629-639.
46. Marklund M, Persson M, Franklin KA. Treatment success with a mandibular advancement device is related to supine-dependent sleep apnea. *Chest*. 1998;114(6):1630-1635.
47. Oksenberg A, Gadoth N. Are we missing a simple treatment for most adult sleep apnea patients? The avoidance of the supine sleep position. *J Sleep Res*. 2014;23(2):204-210.
48. Lee CH, Kim DK, Kim SY, Rhee CS, Won TB. Changes in site of obstruction in obstructive sleep apnea patients according to sleep position: a DISE study. *Laryngoscope* 2015; 125: 248-54.
49. Ravesloot MJ, Frank MH, van Maanen JP, Verhagen EA, de Lange J, de Vries N. Positional OSA part 2: retrospective cohort analysis with a new classification system (APOC) *Sleep Breath*. 2016;20(2):881-888.
50. Mador MJ, Kufel TJ, Magalang UJ, Rajesh SK, Watwe V, Grant BJ. Prevalence of positional sleep apnea in patients undergoing polysomnography. *Chest*. 2005;128(4):2130-2137.
51. Mo JH, Lee CH, Rhee CS, Yoon IY, Kim JW. Positional dependency in Asian patients with obstructive sleep apnea and its implication for hypertension. *Arch Otolaryngol Head Neck Surg*. 2011;137(8):786-790.
52. Itasaka Y, Miyazaki S, Ishikawa K, Togawa K. The influence of sleep position and obesity on sleep apnea. *Psychiatry Clin Neurosci*. 2000;54(3):340-341.
53. Morong S, Benoist LB, Ravesloot MJ, Laman DM, de Vries N. The effect of weight loss on OSA severity and position dependence in the bariatric population. *Sleep Breath*. 2014;18(4):851-856.

54. Oksenberg A, Dynia A, Nasser K, Gadoth N. Obstructive sleep apnoea in adults: body postures and weight changes interactions. *J Sleep Res.* 2012;21(4):402-409.
55. Calik W. Treatments for obstructive sleep apnea. *J Clin Outcomes Manag* 2016; 23: 181-92.
56. Ravesloot MJL, White D, Heinzer R, Oksenberg A, Pépin JL. Efficacy of the New Generation of Devices for Positional Therapy for Patients With Positional Obstructive Sleep Apnea: A Systematic Review of the Literature and Meta-Analysis. *J Clin Sleep Med.* 2017;13(6):813-824. Published 2017 Jun 15. doi:10.5664/jcsm.6622
57. Eijsvogel MM, Ubbink R, Dekker J, Oppersma E, de Jongh FH, van der Palen J, et al. Sleep position trainer versus tennis ball technique in positional obstructive sleep apnea syndrome. *J Clin Sleep Med* 2015; 11: 139-47
58. Köktürk O. Obstrüktif uyku apne sendromu sonuçları. *Tüberküloz ve Toraks Dergisi* 2000; 48: 273-89.
59. Guilleminault C, Stoohs R, Clerk A, Cetel M, Maistros P. A cause of excessive daytime sleepiness. The upper airway resistance syndrome. *Chest* 1993;104:781-7.
60. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993;328:1230-5.
61. Punjabi NM, Ahmed MM, Polotsky VY, Beamer BA, O'Donnell CP. Sleep-disordered breathing, glucose intolerance, and insulin resistance. *Respir Physiol Neurobiol* 2003;136:167-78.
62. Kapur VK, Koepsell TD, de Maine J, et al. Association of hypothyroidism and obstructive sleep apnea. *Am J Respir Crit Care Med* 1998; 158: 1379-85.
63. Hedner J, Grote L, Zou D. Pharmacological treatment of sleep apnea: current situation and future strategies. *Sleep Med Rev* 2008;12:33-47.
64. Smith I, Lasserson TJ, Wright J. Drug therapy for obstructive sleep apnoea in adults. *Cochrane Database Syst Rev* 2006;2:CD003002
65. Qureshi A, Lee-Chiong TL. Medical treatment of obstructive sleep apnea. *Semin Respir Crit Care Med* 2005;26:96-108.
66. Prasad B, Radulovacki M, Olopade C, Herdegen JJ, Logan T, Carley DW. Prospective trial of efficacy and safety of ondansetron and fluoxetine in patients with obstructive sleep apnea syndrome. *Sleep* 2010; 33: 982-9
67. Mason M, Welsh EJ, Smith I. Drug therapy for obstructive sleep apnoea in adults. *Cochrane Database Syst Rev* 2013; CD003002.
68. Hudgel DW. Treatment of obstructive sleep apnea. *Chest* 1996; 109: 1347-58.
69. Lorimier PH, Scholliers ML, Sanna A, Sergysels R. Traitement medical du syndrome d'apnees du sommeil. *Rev Mal Resp* 1990; 7: 467-74.
70. Liu HM, Chiang IJ, Kuo KN, Liou CM, Chen C. The effect of acetazolamide on sleep apnea at high altitude: a systematic review and meta-analysis. *Ther Adv Respir Dis* 2017; 11: 20-9.
71. Standards of Practice Committee of the American Academy of Sleep Medicine, Morgenthaler T. I., Kapen S., et al. Practice parameters for the medical therapy of obstructive sleep apnea. *Sleep.* 2006;29(8):1031-1035. doi: 10.1093/sleep/29.8.1031.
72. Tingting X., Danming Y., Xin C. Non-surgical treatment of obstructive sleep apnea syndrome. *European Archives of Oto-Rhino-Laryngology.* 2018;275(2):335-346. doi: 10.1007/s00405-017-4818-y.
73. Brouillette R. T., Manoukian J. J., Ducharme F. M., et al. Efficacy of fluticasone nasal spray for pediatric obstructive sleep apnea. *The Journal of Pediatrics.* 2001;138(6):838-844. doi: 10.1067/mpd.2001.114474.
74. Kheirandish-Gozal L., Gozal D. Intranasal budesonide treatment for children with mild obstructive sleep apnea syndrome. *Pediatrics.* 2008;122(1):e149-e155. doi: 10.1542/peds.2007-3398.

75. Chadha N. K., Zhang L., Mendoza-Sassi R. A., César J. A. Using nasal steroids to treat nasal obstruction caused by adenoid hypertrophy: does it work? *Otolaryngology-Head and Neck Surgery*. 2009;140(2):139–147. doi: 10.1016/j.otohns.2008.11.008.
76. Goldbart A. D., Goldman J. L., Veling M. C., Gozal D. Leukotriene modifier therapy for mild sleep-disordered breathing in children. *American Journal of Respiratory and Critical Care Medicine*. 2005;172(3):364–370. doi: 10.1164/rccm.200408-1064OC.
77. Goldbart A. D., Greenberg-Dotan S., Tal A. Montelukast for children with obstructive sleep apnea: a double-blind, placebo-controlled study. *Pediatrics*. 2012;130(3):e575–e580. doi: 10.1542/peds.2012-0310.
78. Wang B., Liang J. The effect of montelukast on mild persistent OSA after adenotonsillectomy in children: a preliminary study. *Otolaryngology and Head and Neck Surgery*. 2017;156(5):952–954. doi: 10.1177/0194599817696501.
79. Kheirandish-Gozal L., Bhattacharjee R., Bandla H. P. R., Gozal D. Antiinflammatory therapy outcomes for mild OSA in children. *Chest*. 2014;146(1):88–95. doi: 10.1378/chest.13-2288.
80. Pépin JL, Viot-Blanc V, Escourrou P, Racineux JL, Sapene M, Lévy P, et al. Prevalence of residual excessive sleepiness in CPAP-treated sleep apnoea patients: the French multicentre study. *Eur Respir J* 2009; 33: 1062e7.
81. Karadağ M. Moderatör. CPAP Tedavisine Persistan Uykululuk, Değerlendirme ve Tedavi. Santamaria J, Iranzo A, Montserrat JM, Pablo J. Persistent sleepiness in CPAP treated obstructive sleep apnea patients: Evaluation and treatment. *Sleep Medicine Reviews* 2007: 195-207. <http://gogus-hast-tuberkuloz.uludag.edu.tr/literatur6.pdf>
82. Kumar R. Approved and investigational uses of modafinil: an evidence-based review. *Drugs* 2008; 68: 1803-39.
83. Pack AI, Black JE, Schwartz JR, et al. Modafinil as adjunct therapy for daytime sleepiness in obstructive sleep apnea. *Am J Respir Crit Care Med* 2001; 164:1675–81.
84. Chapman JL, Vakulin A, Hedner J, Yee BJ, Marshall NS. Modafinil/ armodafinil in obstructive sleep apnoea: a systematic review and meta-analysis. *Eur Respir J* 2016; 47: 1420-8.
85. Boethel CD, Al-Sadi A, Barker JA. Residual Sleepiness in Obstructive Sleep Apnea Differential Diagnosis, Evaluation, and Possible Causes. *Sleep Med Clin* 2013; 8: 571–82