

BÖLÜM 35

Obstrüktif Uyku Sendromunda Alternatif ve Yeni Geliştirilen Tedaviler



Aslıhan Banu ER¹

GİRİŞ

Obstrüktif uyku apne sendromu (OSAS), toplumda her geçen gün sıklığı artan kardiyovasküler sistem başta olmak üzere ve tüm sistemleri etkileyen, mortalite ve morbiditenin arttığı, mesleki ve sosyal yaşamda kısıtlayıcı sonuçlara sebep olan uykuda solunum bozukluğudur (1,2). OSAS üst solunum yolunda gerek anatomik yapının anormal seyrine bağlı, gerekse uykuda anormal nöromusküler yanıtla bağlı olarak gerçekleşmektedir.

OSAS tedavisinde temelde kilo verme, ağız içi araç kullanımı ve cerrahi yöntemler olsa da, sürekli pozitif hava yolu basınç (CPAP) tedavisi altın standart yöntem olarak yer almaktadır. Her ne kadar altın standart yöntem olsa da, uzun dönemde hastanın uyum problemlerinin artmasıyla alternatif ve yeni tedavi arayışına geçilmiştir. Bu yaklaşımda özellikle üst hava yolu yapısı, arousal eşiği, kas yanıtı ve loop gain gibi kişiselleştirilmiş tedaviye yönelik tedaviler ve gündüz aşırı uykululuk hali, uykusuzluk gibi semptomlara yönelik tedaviler ve komorbiditele-re bağlı sonuca yönelik tedaviler ön plana çıkmaktadır.

Primer tedavide kullanılan CPAP tedavisine ek olarak kullanılan bilevel pozitif hava yolu basıncı (BiPAP) ve pozitif ototitrasyon hava yolu basıncı (APAP) tedavilerine ayrı başlıkta anlatılacağı için değinilmeyecektir. Ancak tanısal yöntem olarak taşınabilir uyku kayıt sistemlerinin bulunması; hem hastaya ulaşımı kolaylaşmış, hem de personel ihtiyacını ve maliyetleri azaltmıştır. Ayrıca primer tedavide alternatif olarak kullanılan pozitif ekspiratuar hava yolu basıncı (EPAP)

¹ Uzm. Dr., Uşak Üniversitesi Eğitim ve Araştırma Hastanesi Göğüs Hastalıkları Kliniği,
aslihanbanu@gmail.com

olmaları sebebiyle kullanılmamaktadır. Metilfenidatın, psikostimulan etkisi olsa da OSAS'da kullanımı önerilmemektedir.

2. Sempatomimetik Olmayan Ajanlar: Kafein, teobromin, almitrin, doksapram, leptazol, niketamid gibi ilaçlar tanımlansa da halen çalışmalar devam etmektedir. Henüz kafein haricinde kullanımı önerilmemektedir.

3. Hipnotikler: Orta derecede kronik obstrüktif akciğer hastalığı olan hastalarda yeni çift oreksin reseptör antagonisti olan daridorexant ajanının, gece solunum fonksiyonu ve uyku üzerindeki etkisini araştıran çalışmalarla uyku parametrelerinin düzeldiği tespit edilmiştir (48).

SONUÇ

OSAS sıklığının artması, komorbiditelerinin fazlalığı, tanışsal merkezlerin yetersizliği ve tedavi uyumundaki güçlükler nedeniyle; yeni ve alternatif tanı- tedavi yöntemlerin bulunması için çokça çalışmanın yapılması gerekmektedir.

KAYNAKLAR

1. Patil SP, Winocur E, Buenaver L, Smith MT. Medical and Device Treatment for Obstructive Sleep Apnea: Alternative, Adjunctive, and Complementary Therapies. In: Principles and Practice of Sleep Medicine. Kryger M, Roth T, Dement WC. 6th ed. Philadelphia: Elsevier, Inc.: 2017: 1139-54.
2. Baptista PM, Costantino A, Moffa A, Rinaldi V, Casale M. Hypoglossal Nerve Stimulation in the Treatment of Obstructive Sleep Apnea: Patient Selection and New Perspectives. *Nature and Science of Sleep* 2020;12: 151-9.
3. Wu H, Yuan X, Zhan X, Li L, Wei Y. A review of EPAP nasal device therapy for obstructive sleep apnea. *Sleep Breath* 2015; 19: 769-74.
4. Colrain IM, Brooks S, Black J. A pilot evaluation of a nasal expiratory resistance device for the treatment of obstructive sleep apnea. *J Clin Sleep Med* 2008; 4: 426-33.
5. Walsh JK, Griffin KS, Forst EH, Ahmed HH, Eisenstein RD, Curry DT, et al. A convenient expiratory positive airway pressure nasal device for the treatment of sleep apnea in patients non-adherent with continuous positive airway pressure. *Sleep Med* 2011; 12: 147-52.
6. Sakamoto Y, Furuhashi A, Komori E, et al. The most effective amount of forward movement for oral appliances for obstructive sleep apnea: A systematic review. *Int J Environ Res Public Health* 2019; 16(18): 1-11.
7. Opsahl UL, Berge M, Lehmann S, Bjorvatn B, Opsahl P, Johansson A. Acoustic pharyngometry - A new method to facilitate oral appliance therapy. *J Oral Rehabil*. 2021 May;48(5):601-613. doi: 10.1111/joor.13134. Epub 2020 Dec 28. PMID: 33314265; PMCID: PMC8246767.
8. Ben Salah G, Abbes K, Abdelmoula C, Naji B, Masmoudi M, Abdelmoula MH, Turki M. An efficient design for real-time obstructive sleep apnea OSA detection through esophageal pressure Pes signal. *Biomed Tech (Berl)*. 2021 May;66(5):473-487. doi: 10.1515/bmt-2020-0207. PMID: 33951763.
9. Wong AM, Barnes HN, Joosten SA, et al. The effect of surgical weight loss on obstructive sleep apnoea: A systematic review and meta-analysis. *Sleep Medicine Reviews* 2018; 42: 85-99.

10. Omobomi O, Quan SF. Positional therapy in the management of positional obstructive sleep apnea-a review of the current literature. *Sleep Breath* 2018; 22: 297-304.
11. Bignold JJ, Deans-Costi G, Goldsworthy MR, et al. Poor longterm patient compliance with the tennis ball technique for treating positional obstructive sleep apnea. *J Clin Sleep Med* 2009; 5: 428-30.
12. Berry RB, Kryger MH, Massie CA. A novel nasal expiratory positive airway pressure (EPAP) device for the treatment of obstructive sleep apnea: A randomized controlled trial. *SLEEP* 2011; 34 (4): 479-85.
13. Oliven A, Odeh M, Gavriely N. Effect of hypercapnia on upper airway resistance and collapsibility in anesthetized dogs. *Respir Physiol* 1989; 75: 29-38.
14. Lo YL, Jordan AS, Malhotra A, et al. Genioglossal muscle response to CO₂ stimulation during NREM sleep. *Sleep* 2006; 29: 470-7.
15. Farid-Moayer M, Siegel LC, Black J. Oral pressure therapy for treatment of obstructive sleep apnea: Clinical feasibility. *Nat Sci Sleep* 2013; 5: 53-9.
16. Colrain IM, Black J, Siegel LC, et al. A multicenter evaluation of oral pressure therapy for the treatment of obstructive sleep apnea. *Sleep Med* 2013; 14: 830-7.
17. McGinley BM, Patil SP, Kirkness JP, et al. A nasal cannula can be used to treat obstructive sleep apnea. *Am J Respir Crit Care Med* 2007; 176: 194-200.
18. Yenigun A, Tugrul S, Dogan R, Aksoy F, Ozturan O. A feasibility study in the treatment of obstructive sleep apnea syndrome and snoring: Nasopharyngeal stent. *Am J Otolaryngol*. 2020 Nov-Dec;41(6):102460. doi: 10.1016/j.amjoto.2020.102460. Epub 2020 Mar 16. PMID: 32247706.
19. Japatti SR, Chourasia N, Siddegowda CY, Shriram P, Yajurvedi R, Beawerwala T. Sagittal Genioplasty: New Techniques. *J Maxillofac Oral Surg*. 2020 Dec;19(4):638-641. doi: 10.1007/s12663-019-01313-x. Epub 2019 Dec 20. PMID: 33071514; PMCID: PMC7524966.
20. Iannella G, Lechien JR, Perrone T, Meccariello G, Cammaroto G, Cannavicci A, Burgio L, Maniaci A, Cocuzza S, Di Luca M, Stilo G, De Vito A, Magliulo G, Greco A, de Vincentiis M, Ralli M, Pelucchi S, Ciorba A, Vicini C. Barbed reposition pharyngoplasty (BRP) in obstructive sleep apnea treatment: State of the art. *Am J Otolaryngol*. 2021 Sep 1;43(1):103197. doi: 10.1016/j.amjoto.2021.103197. Epub ahead of print. PMID: 34492427.
21. Wang Z, Liang H, Wang J, Zang Y, Xu H, Lan K, He M, Yan W, Cao D, Yan M, Zhang Z. [Investigation on new paradigm of clinical physiological monitoring by using wearable devices]. *Sheng Wu Yi Xue Gong Cheng Xue Za Zhi*. 2021 Aug 25;38(4):753-763. Chinese. doi: 10.7507/1001-5515.202010021. PMID: 34459176.
22. Oliven A, Odeh M, Schnall RP. Improved upper airway patency elicited by electrical stimulation of the hypoglossus nerves. *Respiration* 1996; 63: 213-6.
23. Soose RJ, Gillespie MB. Upper airway stimulation therapy: A novel approach to managing obstructive sleep apnea. *Laryngoscope* 2016; 126 (Suppl 7): 5-8.
24. Costantino A, Rinaldi V, Moffa A, et al. Hypoglossal nerve stimulation long-term clinical outcomes: A systematic review and meta-analysis. *Sleep Breath*. 2019doi:10.1007/s11325-019-01923-2.
25. Strohl MM, Yamauchi M, Peng Z, Strohl KP. Insights since FDA approval of hypoglossal nerve stimulation for the treatment of obstructive sleep apnea. *Curr Sleep Med Rep* 2017; 3: 133-41.
26. Murtaza G, Turagam MK, Akella K, Madoukh B, Sharma SP, Gopinathannair R, Lakkireddy D. Pacing therapies for sleep apnea and cardiovascular outcomes: A systematic review. *J Interv Card Electrophysiol*. 2021 Jun;61(1):11-17. doi: 10.1007/s10840-020-00760-8. Epub 2020 May 22. PMID: 32445012.
27. Tingting X, Danming Y, Xin C. Non-surgical treatment of obstructive sleep apnea syndrome. *Eur Arch Otorhinolaryngol* 2018; 275(2): 335–346.

28. Kent DT, Zealear D, Schwartz AR. Ansa Cervicalis Stimulation: A New Direction in Neurostimulation for OSA. *Chest*. 2021 Mar;159(3):1212-1221. doi: 10.1016/j.chest.2020.10.010. Epub 2020 Oct 14. PMID: 33065104; PMCID: PMC8097630.
29. Sideris AW, Wallace G, Lam ME, Kitipornchai L, Lewis R, Jones A, Jeiranikhameneh A, Beirne S, Hingley L, Mackay S. Smart polymer implants as an emerging technology for treating airway collapse in obstructive sleep apnea: a pilot (proof of concept) study. *J Clin Sleep Med*. 2021 Feb 1;17(2):315-324. doi: 10.5664/jcsm.8946. PMID: 33118930; PMCID: PMC7853238.
30. Camacho M, Cortal V, Abdullatif J, et al. Myofunctional therapy to treat obstructive sleep apnea: A systematic review and meta-analysis. *Sleep* 2015; 38: 669-75.
31. Puhan MA, Suarez A, Lo Cascio C, et al. Didgeridoo playing as alternative treatment for obstructive sleep apnoea syndrome: Randomised controlled trial. *BMJ* 2006; 332: 266-70.
32. Lin CM, Huang YS, Guilleminault C. Pharmacotherapy of obstructive sleep apnea. *Expert Opin Pharmacother* 2012; 13: 841-57.
33. Hedner J, Kraiczi H, Peker Y, et al. Reduction of sleep-disordered breathing after physostigmine. *Am J Respir Crit Care Med* 2003; 168: 1246-51.
34. Susky-Soranos L, Moraes W, Guilleminault C, et al. Beneficial effect of donepezil on obstructive sleep apnea: A double blind placebo controlled Clinical trial. *Sleep medicine* 2012; 13: 290-96.
35. Freire AO, Sugai GC, Chrispin FS, et al. Treatment of moderate obstructive sleep apnea syndrome with acupuncture: A randomised, placebo-controlled pilot trial. *Sleep Med* 2007; 8: 43-50.
36. Ko J, Baik J, Lee S, Lee S. Intraoral acupuncture treatment for obstructive sleep apnoea with snoring: a case series. *Acupunct Med*. 2021 Oct;39(5):529-532. doi: 10.1177/0964528420987852. Epub 2021 Feb 14. PMID: 33583194.
37. Cardinali DP, Brown GM, Pandi-Perumal SR. Chronotherapy. *Handb Clin Neurol*. 2021;179:357-370. doi: 10.1016/B978-0-12-819975-6.00023-6. PMID: 34225975.
38. Delord V, Khirani S, Ramirez A, Joseph EL, Gambier C, Belson M, Gajan F, Fauroux B. Medical hypnosis as a tool to acclimatize children to noninvasive positive pressure ventilation: a pilot study. *Chest*. 2013 Jul;144(1):87-91. doi: 10.1378/chest.12-2259. PMID: 23392731.
39. Khirani S, Kadlub N, Delord V, Picard A, Fauroux B. Nocturnal mouthpiece ventilation and medical hypnosis to treat severe obstructive sleep apnea in a child with cherubism. *Pediatr Pulmonol*. 2013 Sep;48(9):927-9. doi: 10.1002/ppul.22686. Epub 2012 Nov 5. PMID: 23129383.
40. Tingting X, Danming Y, Xin C. Non-surgical treatment of obstructive sleep apnea syndrome. *Eur Arch Otorhinolaryngol* 2018; 275(2): 335-346.
41. Acar M, Cingi C, Sakallioğlu O, et al. The effects of mometasone furoate and desloratadine in obstructive sleep apnea syndrome patients with allergic rhinitis. *Am J Rhinol Allergy* 2013; 27(4): 113-116.
42. Murphy PB, Davidson C, Hind MD, Simonds A, Williams AJ, Hopkinson NS, et al. Volume targeted versus pressure support non-invasive ventilation in patients with super obesity and chronic respiratory failure: a randomised controlled trial. *Thorax* 2012; 67: 727-34.
43. Anttalainen U, Saarela T, Vahlberg T, Polo O. Short-term medroxyprogesterone acetate in postmenopausal women with sleep-disordered breathing: a placebo-controlled, randomized, double-blind, parallel-group study. *Menopause*. 2014; 21: 361-8.
44. Jaffuel D, Nogue E, Berdague P, Galinier M, Fournier P, Dupuis M, Georger F, Cadars MP, Ricci JE, Plouvier N, Picard F, Puel V, Mallet JP, Suehs CM, Molinari N, Bourdin A, Roubille F. Sacubitril-valsartan initiation in chronic heart failure patients impacts sleep apnea: the ENT-RESTO-SAS study. *ESC Heart Fail*. 2021 Aug;8(4):2513-2526. doi: 10.1002/eihf.2.13455. Epub 2021 Jun 8. PMID: 34102018; PMCID: PMC8318447.

45. Messineo L, Carter SG, Taranto-Montemurro L, Chiang A, Vakulin A, Adams RJ, Carberry JC, Eckert DJ. Addition of zolpidem to combination therapy with atomoxetine-oxybutynin increases sleep efficiency and the respiratory arousal threshold in obstructive sleep apnoea: A randomized trial. *Respirology*. 2021 Sep;26(9):878-886. doi: 10.1111/resp.14110. Epub 2021 Jun 23. PMID: 34164887.
46. Darwish M, Kirby M, D'Andrea DM, et al. Pharmacokinetics of armodafinil and modafinil after single and multiple doses in patients with excessive sleepiness associated with treated obstructive sleep apnea: A randomized, open-label, crossover study. *Clin Ther* 2010; 32: 2074-87.
47. Black JE, Hirshkowitz M. Modafinil for treatment of residual excessive sleepiness in nasal continuous positive airway pressure-treated obstructive sleep apnea/hypopnea syndrome. *Sleep* 2005; 28: 464-71
48. Boof ML, Dingemanse J, Brunke M, Esselmann A, Heymer P, Kestermann O, Lederer K, Fietze I, Ufer M. Effect of the novel dual orexin receptor antagonist daridorexant on night-time respiratory function and sleep in patients with moderate chronic obstructive pulmonary disease. *J Sleep Res*. 2021 Aug;30(4):e13248. doi: 10.1111/jsr.13248. Epub 2021 Jan 8. PMID: 33417730.