

Bölüm 3

EPİLEPSİ MEDİKAL TEDAVİSİNDE GÜNCEL YAKLAŞIMLAR

Aslı AKYOL GÜRSES¹

GİRİŞ

Epilepsi, 24 saatten daha uzun aralıkla tekrarlayan iki veya daha fazla tetiklenmemiş epilepsi nöbeti ile karakterize durumdur.¹ Yaşam boyu prevalansı 1000'de 7.6 ve yıllık kümülatif insidansı 100000'de 67.77 olarak bildirilmektedir.² Popülasyonun %0.5 ila %1'ini etkilediği tahmin edilen epilepsi; Dünya Sağlık Örgütü'nün 2010'da gerçekleştirilen 'hastalıkların getirdiği küresel yük' çalışmasında; dünya çapında yeti yitimine ayarlanmış yaşam yılı (DALY) bakımından ikinci en sık yük getiren nörolojik hastalık olarak sıralanmıştır.^{3,4,5} Yaşam kalitesini oldukça kısıtlayan ve hem bireysel, hem de toplumsal açıdan önemli sosyal ve ekonomik yük getiren bu hastalığın doğru yönetimi ve tedavisi, nöroloji pratiğinde her daim güncelliğini koruyan bir konu olmaya devam edecektir.

Bu bölümde epilepsi medikal tedavisinde güncel yaklaşımlardan, antiepileptik ilaçlardan ve kısaca tedavi rehberlerinden bahsedilecektir.

EPİLEPSİDE MEDİKAL TEDAVİ

Başarılı bir epilepsi tedavisinde temel prensipler; epilepsi tanısının doğru konulması, nöbet ve sendromların doğru sınıflanması ve bu sınıflamaya uygun, doğru antiepileptiğin seçilmesi; tedaviye monoterapiyle ve düşük dozla başlanması, gerekirse doz artımına gidilmesi; klinik-elektrofizyolojik yanıtın ve yan etkilerin monitorizasyonu ile düzenli kullanımın sağlanmasıdır. Yeterli süre klinik nöbetlerin ve epileptik deşarjların supresyonu ile ilaç kesiminin düşünülmesi mümkündür.⁶

İlaç seçiminde; etkinlik, doz sıklığı ve ilaç etkileşimi gibi farmakokinetik özelliklerin yanında; hastanın yaşı ve komorbid durumları gibi hastayla ilişkili özellikler de göz önünde bulundurulmalıdır.

¹ Aslı Akyol Gürses, Gazi Üniversitesi Tıp Fakültesi Nöroloji Anabilim Dalı, Klinik Nörofizyoloji Bilim Dalı, akyol1984@yahoo.com

kaybetmeden cerrahiye uygunluk açısından değerlendirilmek üzere yönlendirilmelidir. Ketojenik diyet ve nörostimulasyon metodları ise, dirençli epilepside kullanılabilir palyatif tedavi yaklaşımlarıdır.

KAYNAKLAR

1. Fisher RS, Acevedo C, Arzimanoglou A, et al. ILAE official report: a practical clinical definition of epilepsy. *Epilepsia*. 2014 55(4):475-82 doi: 10.1111/epi.12550
2. Fiest KM, Sauro KM, Wiebe S, et al. Prevalence and incidence of epilepsy: A systematic review and meta-analysis of international studies. *Neurology*. 2017;88(3):296-303. doi: 10.1212/WNL.0000000000004206.
3. Keränen T, Riekkinen P. Severe epilepsy: diagnostic and epidemiological aspects. *Acta Neurol Scand Suppl*. 1988;117:7-14. doi: 10.1111/j.1600-0404.1988.tb07997.x.
4. Diaz-Arrastia R, Agostini MA, Van Ness PC. Evolving treatment strategies for epilepsy. *JAMA*. 2002;287(22):2917-20. doi: 10.1001/jama.287.22.2917.
5. Murray CJ, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2197-223. doi: 10.1016/S0140-6736(12)61689-4.
6. Bora İH. Epilepside tedavi ilkeleri ve tedavi yaklaşımları. Bora İH, Yeni SN, Gürses C, editörler. *Epilepsi içinde (s.639-670) 2. Baskı. İstanbul: Nobel Tıp Kitabevleri*
7. Brodie MJ, Barry SJ, Bamagous GA, et al. Patterns of treatment response in newly diagnosed epilepsy. *Neurology*. 2012;78(20):1548-54. doi:10.1212/WNL.0b013e3182563b19.
8. Kwan P, Arzimanoglou A, Berg AT, et al. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. *Epilepsia*. 2010;51(6):1069-77 doi:10.1111/j.1528-1167.2009.02397.x.
9. Bilir E, Yıldırım İ. Epilepsi Cerrahisi Tedavi Endikasyonları ve Skalp Yöntemiyle Temporal Lob Epilepsilerinde Cerrahi Hasta Hazırlık Protokolü. *Türkiye Klinikleri Nöroloji Epilepsi Özel Sayısı* 2012;5(1):113-119
10. Ferrie CD. Idiopathic generalized epilepsies imitating focal epilepsies. *Epilepsia*. 2005;46 Suppl 9:91-5. doi: 10.1111/j.1528-1167.2005.00319.x.
11. Thomas P, Valton L, Genton P. Absence and myoclonic status epilepticus precipitated by antiepileptic drugs in idiopathic generalized epilepsy. *Brain*. 2006;129(Pt 5):1281-92. doi:10.1093/brain/awl047
12. Das AM, Ramamoorthy L, Narayan SK, et al. Barriers of drug adherence among patients with epilepsy: in tertiary care hospital, South India. *J Caring Sci*. 2018; 7(4): 177-181 doi:10.15171/jcs.2018.027
13. Gurumurthy R, Chanda K, Sarma GRK. An evaluation of factors affecting adherence to antiepileptic drugs in patients with epilepsy: a cross-sectional study. *Singapore Med J* 2017;58(2): 98-102 doi: 10.11622/smedj.2016022
14. Shope JT. Compliance in children and adults: review of studies. *Epilepsy Res*. 1988;29(Suppl 1):23-47.
15. Anderson GD, Kim H, Warner MH. Impact of taking antiepileptic drugs at school in group of children and adolescents. *Epilepsy Behav*. 2000;1:17-21. doi: 10.1006/ebeh.2000.0027
16. Doughty J, Baker GA, Jacoby A, et al. Compliance and satisfaction with switching from an immediate-release to sustained-release formulation of valproate in people with epilepsy. *Epilepsy Behav*. 2003;4(6):710-6. doi: 10.1016/j.yebch.2003.08.013.
17. Asadi-Pooya AA, Sperling MR. Epidemiology of psychogenic nonepileptic seizures. *Epilepsy Behav*. 2015; 46:60-65. 10.1016/j.yebch.2015.03.015.
18. Benbadis SR, Allen Hauser W. An estimate of the prevalence of psychogenic non-epileptic seizures. *Seizure*. 2000 Jun;9(4):280-1. doi: 10.1053/seiz.2000.0409.

19. Saygı S. Epileptik Olmayan Psikojenik Nöbetler. Bora İH, Yeni SN, Gürses C, editörler. Epilepsi içinde (s.567-572) 2. Baskı. İstanbul: Nobel Tıp Kitabevleri
20. Aicardi J. Clinical approach to the management of intractable epilepsy. *Dev Med Child Neurol*. 1988 Aug;30(4):429-40. doi: 10.1111/j.1469-8749.1988.tb04769.x.
21. Kwan P, Brodie MJ. Early identification of refractory epilepsy. *N Engl J Med*. 2000;342(5):314-9. doi: 10.1056/NEJM200002033420503
22. Brodie M, Sills GJ. Combining antiepileptic drugs-Rational polytherapy? *Seizure*. 2011;20:369-375 doi: 10.1016/j.seizure.2011.01.004.
23. Perucca P, Scheffer IE, Kiley M. The management of epilepsy in children and adults. *Med J Aust*. 2018;208(5):226-233.
24. Chadwick D. Epilepsy. *J Neurol Neurosurg Psychiatry*. 1994 Mar;57(3):264-77. doi:10.1136/jnnp.57.3.264.
25. Toydemir HE, Özkara Ç. Dirençli epilepsilere yaklaşım. *Türkiye Klinikleri Nöroloji Epilepsi Özel Sayısı* 2012;5(1):102-106
26. Cascino GD, Shorbrugh FW, Trenerry MR, et al. Extratemporal resections and lesionectomies for partial epilepsy: complications and surgical outcome. *Epilepsia* 1994;35(5):1085-90 doi: 10.1111/j.1528-1157.1994.tb02559.x.
27. Bek S. Epilepside cerrahi dışı yöntemlerle tedavi (Nörostimulasyon). Bora İH, editor. Epilepside Tedavi içinde. 1. Baskı Ankara: Türkiye Klinikleri; 2019; p:69-73.
28. Englot DJ, Chang EF, Auguste KI. Vagus nerve stimulation for epilepsy: a meta-analysis of efficacy and predictors of response. *J Neurosurg* 2011;115:1248-1255. doi: 10.3171/2011.7.JNS11977
29. Bilir E, Leventoğlu A. Tedaviye Dirençli Epilepsiler. Bora İH, Yeni SN, Gürses C, editörler. Epilepsi içinde (s.749-760) 2. Baskı. İstanbul: Nobel Tıp Kitabevleri
30. Berkovic SF. Treatment with anti-epileptic drugs. *Aust Fam Physician*. 2005 Dec;34(12):1017-20.
31. Bourgeois BFD. (2011) Phenobarbital and Primidone. InWyllie E. (Ed.) *Treatment of Epilepsy: Principles and Practice* (5th ed. pp. 648-656) Lippincott Williams & Wilkins: Philadelphia
32. Eşkazan EE, Onat F. Antiepileptik İlaçlar. Bora İH, Yeni SN, Gürses C, editörler. Epilepsi içinde (s.671-699) 2. Baskı. İstanbul: Nobel Tıp Kitabevleri
33. Morita DA, Glauser TA. Phenytoin and Fosphenytoin InWyllie E. (Ed.) *Treatment of Epilepsy: Principles and Practice* (5th ed. pp. 630-648) Lippincott Williams & Wilkins: Philadelphia
34. Baier W, Beck U, Dooze H, et al. Cerebellar atrophy following diphenylhydantoin intoxication. *Neuropediatrics*. 1984;15(2):76-81. doi: 10.1055/s-2008-1052345.
35. Ochoa JG, Kilgo WA. The Role of Benzodiazepines in the Treatment of Epilepsy. *Curr Treat Options Neurol*. 2016;18(4):18. doi: 10.1007/s11940-016-0401-x.
36. Greenfield LJ, Rosenberg HKJ, Tietz EI. Benzodiazepines. InWyllie E. (Ed.) *Treatment of Epilepsy: Principles and Practice* (5th ed. pp. 668-689) Lippincott Williams & Wilkins: Philadelphia
37. Jensen HS, Nichol K, Lee D et al. Clobazam and its active metabolite Ndesmethylclobazam display significantly greater affinities for α_2 - versus α_1 -GABA(A)- receptor complexes. *PLoS ONE*. 2014;9(2):e88456. doi: 10.1371/journal.pone.0088456.
38. Ng YT, Conry JA, Drummond R, et al. OV-1012 Study Investigators. Randomized, phase III study results of clobazam in Lennox-Gastaut syndrome. *Neurology*. 2011;77(15):1473-81. doi:10.1212/WNL.0b013e318232de76.
39. Davies JA. Mechanisms of action of antiepileptic drugs. *Seizure* 1995;4:267-271 doi:10.1016/s1059-1311(95)80003-4.
40. Bourgeois BF. Important pharmacokinetic properties of antiepileptic drugs. *Epilepsia* 1995;36 Suppl 5:S1-7. doi: 10.1111/j.1528-1157.1995.tb06004.x.
41. Gierbolini J, Giarratano M, Benbadis SR. Carbamazepine-related antiepileptic drugs for the treatment of epilepsy - a comparative review. *Expert Opin Pharmacother*. 2016;17(7):885-8. doi:10.1517/14656566.2016.1168399.
42. Schlienger RG, Shear NH. Antiepileptic drug hypersensitivity syndrome. *Epilepsia*. 1998;39 Suppl 7:S3-7. doi: 10.1111/j.1528-1157.1998.tb01678.x.

43. McCormack M, Alfirevic A, Bourgeois S, et al. HLA-A*3101 and carbamazepine-induced hypersensitivity reactions in Europeans. *N Engl J Med.* 2011 Mar 24;364(12):1134-43. doi: 10.1056/NEJMoa1013297
44. Birnbaum AK, Marino SE, Bourgeois BFD. Valproate. In Wyllie E. (Ed.) *Treatment of Epilepsy: Principles and Practice* (5th ed. pp. 622-629) Lippincott Williams & Wilkins: Philadelphia
45. Pisani F, Fazio A, Oteri G, et al. Sodium valproate and valpromide: differential interactions with carbamazepine in epileptic patients. *Epilepsia.* 1986 Sep-Oct;27(5):548-52. doi: 10.1111/j.1528-1157.1986.tb03582.x
46. Jentink J, Loane MA, Dolk H, et al. Valproic acid monotherapy in pregnancy and major congenital malformations. *N Engl J Med.* 2010 Jun 10;362(23):2185-93. doi: 10.1056/NEJMoa0907328.
47. Verma A, Hirano M, Moraes CT. (2008) Mitokondrial Hastalıklar. In Bradley WG, Daroff RB, Fenichel GM, Jankovic J (Eds.) Tan E, Özdamar SE (Çev Ed.) *Neurology in Clinical Practice* (Tan E, Özdamar SE, Çev Ed.) (5th ed. pp 1786-1796) Ankara: Veri Medikal Yayıncılık
48. Perucca E, Gram L, Avanzini G, et al. Antiepileptic drugs as a cause of worsening seizures. *Epilepsia.* 1998;39:5-17. doi:10.1111/j.1528-1157.1998.tb01268.x
49. Maguire MJ, Hemming K, Wild JM, et al. Prevalence of visual field loss following exposure to vigabatrin therapy: a systematic review. *Epilepsia* 2010;51:2423-2431. doi:10.1111/j.1528-1167.2010.02772.x
50. Kanner AM, Ashman E, Gloss D, et al. Practice guideline update summary: Efficacy and tolerability of the new antiepileptic drugs II: Treatment-resistant epilepsy: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology.* 2018;91(24):1117. doi: 0.1212/WNL.0000000000006636.
51. Abou-Khalil B. New Generation Antiepileptic Drugs. In: Azar MZ ed. *Epilepsy Board Review.* New York: Springer; 2017. p.225-33.
52. Dunner DL. Safety and tolerability of emerging pharmacological treatments for bipolar disorder. *Bipolar Disord* 2005;7:307-25. doi: 10.1111/j.1399-5618.2005.00235.x.
53. Bloom R, Amber KT. Identifying the incidence of rash, Stevens-Johnson syndrome and toxic epidermal necrolysis in patients taking lamotrigine: a systematic review of 122 randomized controlled trials. *An Bras Dermatol.* 2017 Jan-Feb;92(1):139-141. doi: 10.1590/abd1806-4841.20175070.
54. French J, Smith M, Faught E, Brown L. Practice advisory: The use of felbamate in the treatment of patients with intractable epilepsy: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology.* 1999;52(8):1540-5. doi: 10.1212/wnl.52.8.1540.
55. Wilner A, Raymond K, Pollard R. Topiramate and metabolic acidosis. *Epilepsia.* 1999; 40:792-795. doi: 10.1111/j.1528-1157.1999.tb00781.x.
56. LaRoche SM, Helmers SL. The new antiepileptic drugs: scientific review. *JAMA.* 2004 Feb 4;291(5):605-14. doi: 10.1001/jama.291.5.605.
57. Eckardt KM, Steinhoff BJ. Nonconvulsive status epilepticus in two patients receiving tiagabine treatment. *Epilepsia.* 1998;39:671-674. doi: 10.1111/j.1528-1157.1998.tb01438.x.
58. Knake S, Hamer HM, Schomburg U, et al. Tiagabine-induced absence status in idiopathic generalized epilepsy. *Seizure.* 1999;8:314-317. doi: 10.1053/seiz.1999.0303.
59. Guerreiro C AM, Guerreiro MM. Carbamazepine and Oxcarbazepine. In Wyllie E. (Ed.) *Treatment of Epilepsy: Principles and Practice* (5th ed. pp. 614-621) Lippincott Williams & Wilkins: Philadelphia
60. Van Parys JAP, Meinardi H. Survey of 260 epileptic patients treated with oxcarbazepine on named-patient basis. *Epilepsy Res.* 1994;19:79-85. doi:10.1016/0920-1211(94)90091-4.
61. Doelken MT, Hammen T, Bogner W, et al. Alterations of intracerebral γ -aminobutyric acid (GABA) levels by titration with levetiracetam in patients with focal epilepsies. *Epilepsia.* 2010 Aug;51(8):1477-82. doi: 10.1111/j.1528-1167.2010.02544.x.

62. Welty TE. Zonisamide. In Wyllie E. (Ed.) *Treatment of Epilepsy: Principles and Practice* (5th ed. pp. 723-730) Lippincott Williams & Wilkins: Philadelphia
63. Kubota M, Nishi-Nagase M, Sakakihara Y, et al. Zonisamide-induced urinary lithiasis in patients with intractable epilepsy. *Brain Dev.* 2000;22:230-233. doi: 10.1016/s0387-7604(00)00118-2.
64. Krauss G, Darnley S. Rufinamide. In Wyllie E. (Ed.) *Treatment of Epilepsy: Principles and Practice* (5th ed. pp. 753-757) Lippincott Williams & Wilkins: Philadelphia
65. Wheless, J.W., Conry, J., Krauss, G., et al. Safety and tolerability of rufinamide in children with epilepsy: A pooled analysis of 7 clinical studies. *J Child Neurol* 2209; 24:1520-1525. doi:10.1177/0883073809350508.
66. Beydoun A, D'Souza J, Hebert D, et al. Lacosamide: pharmacology, mechanisms of action and pooled efficacy and safety data in partial-onset seizures. *Expert Rev Neurother.* 2009;9(1):33-42. doi: 10.1586/14737175.9.1.33.
67. Wilson SM, Khanna R. Specific binding of lacosamide to collapsin response mediator protein 2 (CRMP2) and direct impairment of its canonical function: Implications for the therapeutic potential of lacosamide. *Mol Neurobiol.* 2015;51(2):599-609. doi:10.1007/s12035-014-8775-9.
68. Biton V. Lacosamide for the treatment of diabetic neuropathic pain. *Expert Rev Neurother.* 2008 Nov;8(11):1649-60. doi: 10.1586/14737175.8.11.1649.
69. Soares-da-Silva P, Pires N, Bonifacio MJ, et al. Eslicarbazepine acetate for the treatment of focal epilepsy: an update on its proposed mechanisms of action. *Pharmacol Res Perspect.* 2015;3(2):e00124. doi: 10.1002/prp2.124.
70. Becker AJ, Pitsch J, Sochivko D, et al. Transcriptional upregulation of Cav3.2 mediates epileptogenesis in the pilocarpine model of epilepsy. *J Neurosci.* 2008;28(49):13341-53. doi: 10.1523/JNEUROSCI.1421-08.2008.
71. Galiana GL, Gauthier AC, Mattson RH. Eslicarbazepine Acetate: A New Improvement on a Classic Drug Family for the Treatment of Partial-Onset Seizures. *Drugs R D.* 2017 Sep;17(3):329-339. doi: 10.1007/s40268-017-0197-5.
72. Treven, M, Keing X, Assadpour E, et al. The anticonvulsant retigabine is a subtype selective modulator of GABAA receptors. *Epilepsia* 56, 647-657 (2015). doi: 10.1111/epi.12950.
73. Bialer M, Johannessen SI, Levy RH, et al. Progress report on new antiepileptic drugs: a summary of the Ninth Eilat Conference (EILAT IX). *Epilepsy Res.* 2009 Jan;83(1):1-43. doi:10.1016/j.epilepsyres.2008.09.005.
74. Frampton JE. Perampanel: A review in drug-resistant epilepsy. *Drugs.* 2015 Sep; 75(14):1657-68. doi: 10.1007/s40265-015-0465-z.
75. Sargentini-Maier ML, Rolan P, Connell J, et al. The pharmacokinetics, CNS pharmacodynamics and adverse event profile of brivaracetam after single increasing oral doses in healthy males. *Br J Clin Pharmacol.* 2007;63(6):680-688. doi:10.1111/j.1365- 2125.2006.02829.x
76. Sargentini-Maier ML, Espié P, Coquette A, et al. Pharmacokinetics and metabolism of 14C-brivaracetam, a novel SV2A ligand, in healthy subjects. *Drug Metab Dispos.* 2008;36 (1):36-45. doi:10.1124/dmd.107.017129
77. Bialer M, Johannessen SI, Levy RH, Perucca E, et al. HS. Progress report on new antiepileptic drugs: a summary of the tenth Eilat Conference (EILATX). *Epilepsy Res.* 2010;92(2-3):89-124. doi:10.1016/j.epilepsyres.2010.09.001
78. Stockis A, Sargentini-Maier ML, Horsmans Y. Brivaracetam disposition in mild to severe hepatic impairment. *J Clin Pharmacol.* 2013;53 (6):633-641. doi:10.1002/jcph.82
79. Feyissa AM. Brivaracetam in the treatment of epilepsy: a review of clinical trial data. *Neuropsychiatr Dis Treat.* 2019;15:2587-2600. doi: 10.2147/NDT.S143548.
80. Gazzola DM, Delanty N, French JA. Newer antiepileptic drugs. In Wyllie E. (Ed.) *Treatment of Epilepsy: Principles and Practice* (5th ed. p.776) Lippincott Williams & Wilkins: Philadelphia
81. Frampton JE. Stiripentol: A review in Dravet Syndrome. *Drugs.* 2019 Nov;79(16):1785-1796. doi: 10.1007/s40265-019-01204-y.

82. European Medicines Agency. Stiripentol (Diacomit): EU summary of product characteristics. 2018. (05.08.20 tarihinde https://www.ema.europa.eu/documents/product-information/diacomit-epar-product-information_en.pdf adresinden ulaşılmıştır)
83. Reddy DS, Golub VM. The Pharmacological Basis of Cannabis Therapy for Epilepsy. *J Pharmacol Exp Ther*. 2016 Apr;357(1):45-55. doi: 10.1124/jpet.115.230151.
84. Ibeas Bih C, Chen T, Nunn AV, et al. Molecular Targets of Cannabidiol in Neurological Disorders. *Neurotherapeutics*. 2015 Oct;12(4):699-730. doi: 10.1007/s13311-015-0377-3.
85. Sylantsev S, Jensen TP, Ross RA, et al. Cannabinoid- and lysophosphatidylinositol- sensitive receptor GPR55 boosts neurotransmitter release at central synapses. *Proc Natl Acad Sci USA* 2013; 110:5193–5198. doi: 10.1073/pnas.1211204110.
86. Geoffrey AL, Pollack SF, Bruno PL, et al. Drug-drug interaction between clobazam and cannabidiol in children with refractory epilepsy. *Epilepsia*. 2015 Aug;56(8):1246-51. doi:10.1111/epi.13060
87. Thiele EA, Marsh ED, French JA, et al. Cannabidiol in patients with seizures associated with Lennox- Gastaut syndrome (GWPCARE4): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet*. 2018;391(10125):1085–1096. doi: 10.1016/S0140-6736(18)30136-3.
88. French JA, Lawson JA, Yapici Z, et al. Ikeda H, Polster T, Nabbout R et al. Adjunctive everolimus therapy for treatment-resistant focal-onset seizures associated with tuberous sclerosis (EXIST-3): a phase 3, randomised, double-blind, placebo-controlled study. *Lancet*. 2016;388(10056):2153-2163.
89. Glauser T, Ben-Menachem E, Bourgeois B, et al. IILAE treatment guidelines: evidence-based analysis of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. *Epilepsia*. 2006 Jul;47(7):1094-120. doi: 10.1111/j.1528-1167.2006.00585.x.
90. Glauser T, Ben-Menachem E, Bourgeois B, et al.; ILAE Subcommittee on AED Guidelines Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. *Epilepsia*. 2013 Mar;54(3):551-63. doi: 10.1111/epi.12074. Epub 2013 Jan 25
91. Türk Nöroloji Derneği (2007). Epilepsi Rehberi. (05.08.2020 tarihinde <https://www.noroloji.org.tr/TNDDData/Uploads/files/epilepsi.pdf> adresinden ulaşılmıştır).
92. Türk Nöroloji Derneği (2015). Epilepsi Çalışma Grubu Tanı ve Tedavi Rehberi (05.08.20 tarihinde <https://www.noroloji.org.tr/TNDDData/Uploads/files/Epilepsi%202015%20Güncellenmiş.pdf> adresinden ulaşılmıştır.)