BÖLÜM 7

MİGREN ATAKLARININ AKUT TEDAVİSİ

Özlem ERANIL TERİM[1]

GİRİŞ

Migren hastalığı, Antik Yunan döneminde 'hemi-crania' yani 'yarım baş ağrısı' olarak adlandırılmıştır(1). Çok eski tarihlerden beri migren hastalığı bilinmesine rağmen sebepleri ve özellikle tedavi seçenekleri hala günümüz tıbbının yoğun olarak ilgi gösterdiği, araştırdığı alanlardır, çünkü dünya genelinde migren hastalığı her 10 insandan 1'inde görülmektedir (%11,6) ve kadınlarda prevelansı %13,8, erkeklerde ise % 6,9'dur(2). Migren, 15-49 yaşlarındaki hem kadın hem erkeklerde özürlülüğe neden olan hastalıklar içinde 3. sırada yer alır (3).

Migren ağrısı genellikle başın yarı kısmında, zonklayıcı, orta-ağır şiddettedir. Beraberinde foto ve fonofobi ile bulantı, kusma olabilmektedir. Tedavi edilmeyen bir migren atağı 4 ile 72 saat arasında sürmektedir(4). Bu yüzden ideal migren tedavisi, migren atağını en kısa sürede, hastanın tamamen ağrısını sonlandıracak, ağrının tekrar etmemesini sağlayacak ve ilaç yan etkileri ortaya çıkmayacak şekilde olmalıdır. Fakat maalesef bütün hastaları kapsayacak böyle bir 'ideal' tedavi yoktur. Akut migren tedavisi hem hastanın ağrısının kontrol altına alınıp sosyal ve iş hayatının sağlıklı sürdürülmesi, hem de epizodik migrenin kronik migrene dönüşme riskinin azaltılması

[1] Uzm. Dr., Dr. Özlem Terim Nöroloji Kliniği, info@ozlemterim.com

Triptanların ilk trimesterde kullanımları ile fetal malformasyon ve gebelik sürecinde herhangi olumsuz bir etkisi görülmemiştir. Fakat 2. ve 3. trimesterde sumatriptan kullanımında atonik uterus ve doğum esnasında kanamada artış olabileceği görülmüştür (69). Diğer triptanlarla ilgili gebelikteki çalışmalar oldukça kısıtlıdır. Eğer gebelikteki migren ağrısı hastanın günlük yaşamını oldukça kötü etkiliyorsa veya dehidratasyona varacak kadar sıvı alımını engelliyorsa sumatriptan kullanılabilir (11).

EMZİRME DÖNEMİNDE AKUT MİGREN TEDAVİSİ

Emzirme döneminde asetaminofen, metoklopramid, domperidon, proklorperazin ve dimenhidrinat kullanımı güvenlidir(70). NSAİİlar içerisinde ise ibuprofen tercihi önceliklidir. ASA analjezik dozunda kullanımı önerilmemektedir. Bebeğe geçişi düşük bulunduğu için sumatriptan, diklofenak ve ketalorak kullanımında sakınca görülmemektedir (71). Eğer morfin kullanımı zorunlu kalındıysa kullanılabilir olduğu belirtilmiş ama annede sedasyon yarattıysa sütünün sağılıp atılması tavsiye edilmektedir. Metabolizma hızı farklılıkları sebebiyle kodein kullanımı ise önerilmemektedir (72).

SONUÇ

Dünyada milyonlarca kişiyi etkileyen, günlük hayatlarında ağır özürlülüğe sebep olan migren hastalığının patofizyolojisi açıklık kazandıkça triptanlar, gepantlar, ditanlar gibi farmakolojik ve stimülasyon tedavileri gibi non-famakolojik migrene özel tedavi seçenekleri gündeme gelmiştir. Migrene özel tedavi seçenekleri oluştukça ilaç güvenliği yan etkiler açısından artmaktadır. Memnuniyetle belirtmeliyim ki çok yakın gelecekte bizi migren akut tedavisinde çok daha güçlü kılacak yeni ajanlar beklemektedir.

KAYNAKLAR

1. Rose FC. The history of the migraine trust. J Headache Pain. 2006;7(2):109–15.
2. Woldeamanuel YW, Cowan RP. Migraine affects 1 in 10 people worldwide featuring recent rise: A systematic review and meta-analysis of community-based studies involving 6 million participants. J Neurol Sci [Internet]. 2017;372:307–15. Available from: http://dx.doi.org/10.1016/j.jns.2016.11.071
3. Steiner TJ, Stovner LJ, Vos T. GBD 2015: migraine is the third cause of disability in under 50s. J Headache Pain [Internet]. 2016;17(1):0–3. Available from: http://dx.doi.org/10.1186/s10194-016-0699-5
4. Road C. The International Classification of Headache Disorders , 3rd edition (beta version). 2013;33(9):629–808.

5. Tepper SJ. Acute Treatment of Migraine. Vol. 37, Neurologic Clinics. W.B. Saunders; 2019. p. 727–42.
6. Ong JJY, De Felice M. Migraine Treatment: Current Acute Medications and Their Potential Mechanisms of Action. Vol. 15, Neurotherapeutics. Springer Science and Business Media Deutschland GmbH; 2018. p. 274–90.
7. Becker WJ. Acute Migraine Treatment. :953–72.
8. Derry S, Ra M. Paracetamol (acetaminophen) with or without an antiemetic for acute migraine headaches in adults (Review). 2013;(6).
9. Rabbie R, Derry S, Ra M. Ibuprofen with or without an antiemetic for acute migraine headaches in adults (Review). 2013;(4).
10. Suthisisang C, Poolsup N, Kittikulsuth W, Pudchakan P, Wiwatpanich P. Efficacy of low-dose ibuprofen in acute migraine treatment: Systematic review and meta-analysis. Ann Pharmacother. 2007;41(11):1782–91.
11. Becker WJ. Acute Migraine Treatment in Adults. 2015;778–93.
12. Lipton RB, Grosberg B, Singer RP, Pearlman SH, Sorrentino J V, Quiring JN, et al. Efficacy and tolerability of a new powdered formulation of diclofenac potassium for oral solution for the acute treatment of migraine : Results from the International Migraine Pain Assessment Clinical Trial (IMPACT). 2010;30(11):1336–45.
13. Suthisisang CC, Poolsup N, Suksomboon N, Lertpipopmetha V, Tepwitukgid B. Meta-Analysis of the Efficacy and Safety of Naproxen Sodium. 2010;808–18.
14. Diener HC, Pfaffenrath V, Pageler L, Peil H, Aicher B. The fixed combination of acetylsalicylic acid , paracetamol and caffeine is more effective than single substances and dual combination for the treatment of headache : a multicentre , group study. 2005;(2):776–87.
15. Study P, Goldstein J, Silberstein SD, Saper JR, Ryan RE, Lipton RB. Acetaminophen , Aspirin , and Caffeine in Combination Versus Ibuprofen for Acute Migraine : Results From a. 2006;444–53.
16. Vanderpluym JH, Halker Singh RB, Urtecho M, Morrow AS, Nayfeh T, Torres Roldan VD, et al. Acute Treatments for Episodic Migraine in Adults: A Systematic Review and Meta-analysis. Vol. 325, JAMA - Journal of the American Medical Association. American Medical Association; 2021. p. 2357–69.
17. Diener HC, Montagna P, Gács G, Lyczak P, Schumann G, Zöller B, et al. Efficacy and tolerability of diclofenac potassium sachets in migraine: A randomized, double-blind, cross-over study in comparison with diclofenac potassium tablets and placebo. Cephalalgia. 2006;26(5):537–47.
18. Brandes JLJ, Kudrow D, Stark SR, Carroll CPO, Adelman JU, Donnell FJO, et al. Sumatriptan-naproxen for acute treatment of migraine. JAMA J … [Internet]. 2007;297(13):1443–54. Available from: http://jama.ama-assn.org/content/297/13/1443.short%5Cnhttp://jama.ama-assn.org/content/297/13/1443.abstract
19. Villalón* CM, VanDenBrink AM. 5-HT -like receptor agonists and the pathophysiologyof migraine. Mini-Reviews Med Chem [Internet]. 2017;17(11):928–38. Available from: https://0-ac-els--cdn-com.pugwash.lib.warwick.ac.uk/0165614789902381/1-s2.0-0165614789902381-main.pdf?_tid=736e0a7a-e4f8-11e7-9f1f-00000aab0f6c&acdnat=1513714320_32e1ef77415c072a9a6503c18faec54b
20. Ahn AH, Basbaum AI. Where do triptans act in the treatment of migraine? Pain. 2005;115(1–2):1–4.
21. Lipton RB, Bigal ME, Goadsby PJ. Double-blind clinical trials of oral triptans vs other clas-

ses of acute migraine medication - A review. Cephalalgia. 2004;24(5):321–32.
22. Rapoport AM, Tepper SJ, Sheftell FD, Kung E, Bigal ME. Which triptan for which patient? Neurol Sci. 2006;27(SUPPL. 2):123–9.
23. Thorlund K, Mills EJ, Wu P, Ramos E, Chatterjee A, Druyts E, et al. Comparative efficacy of triptans for the abortive treatment of migraine: A multiple treatment comparison meta-analysis. Cephalalgia. 2014;34(4):258–67.
24. Rapoport AM, Tepper SJ, Bigal ME, Sheftell FD. The Triptan Formulations. CNS Drugs. 2003;17(6):431–47.
25. Dodick D, Lipton RB, Martin V, Papademetriou V, Rosamond W, VanDenBrink AM, et al. Consensus statement: Cardiovascular safety profile of triptans (5-HT 1B/1D agonists) in the acute treatment of migraine. Headache. 2004;44(5):414–25.
26. Gillman PK. Triptans, serotonin agonists, and serotonin syndrome (serotonin toxicity): A review: Review article. Headache. 2010;50(2):264–72.
27. Evans RW, Tepper SJ, Shapiro RE, Sun-Edelstein C, Tietjen GE. The FDA alert on serotonin syndrome with use of triptans combined with selective serotonin reuptake inhibitors or selective serotonin-norepinephrine reuptake inhibitors: American headache society position paper. Headache. 2010;50(6):1089–99.
28. Tullo V, Valguarnera F, Barbanti P, Cortelli P, Sette G, Allais G, et al. Comparison of frovatriptan plus dexketoprofen (25â€‰mg or 37.5â€‰mg) with frovatriptan alone in the treatment of migraine attacks with or without aura: A randomized study. Cephalalgia. 2014;34(6):434–45.
29. Masterson CG, Durham PL. DHE repression of ATP-mediated sensitization of trigeminal ganglion neurons. Headache. 2010;50(9):1424–39.
30. Nagy AJ, Gandhi S, Bhola R, Goadsby PJ. Intravenous dihydroergotamine for inpatient management of refractory primary headaches. Neurology. 2011;77(20):1827–32.
31. Marmura MJ, Silberstein SD, Schwedt TJ. The acute treatment of migraine in adults: The american headache society evidence assessment of migraine pharmacotherapies. Headache. 2015 Jan 1;55(1):3–20.
32. Shrewsbury SB, Cook RO, Taylor G, Edwards C, Ramadan NM. Safety and pharmacokinetics of dihydroergotamine mesylate administered via a novel (Tempo™) inhaler. Headache. 2008;48(3):355–67.
33. Mayans L, Willing A. Acute Migraine Headache: Treatment Strategies. Am Fam Physician. 2018;15;97(4):243-251.
34. Tfelt-Hansen P, Saxena PR, Dahlöf C, Pascual J, Láinez M, Henry P, et al. Ergotamine in the acute treatment of migraine. A review and European consensus. Brain. 2000;123(1):9–18.
35. Cameron C, Kelly S, Hsieh SC, Murphy M, Chen L, Kotb A, et al. Triptans in the Acute Treatment of Migraine: A Systematic Review and Network Meta-Analysis. Headache. 2015;55(S4):221–35.
36. Silberstein SD, Freitag FG, Rozen TD, Kudrow DB, Hewitt DJ, Jordan DM, et al. Tramadol/acetaminophen for the treatment of acute migraine pain: Findings of a randomized, placebo-controlled trial. Headache. 2005;45(10):1317–27.
37. Silberstein SD, Edlund W. Practice parameter: Evidence-based guidelines for migraine headache (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2000;55(6):754–62.
38. Derosier F, Sheftell F, Silberstein S, Cady R, Ruoff G, Krishen A, et al. Sumatriptan-naproxen and butalbital: A double-blind, placebo-controlled crossover study. Headache. 2012;52(4):530–43.

39. Ho TW, Rodgers A, Bigal ME. Impact of recent prior opioid use on rizatriptan efficacy. A post hoc pooled analysis. Headache. 2009;49(3):395–403.
40. Barbanti P, Fofi L, Aurilia C, Egeo G. Dopaminergic symptoms in migraine. Neurol Sci. 2013;34(SUPPL. 1):235–8.
41. Colman I, Brown MD, Innes GD, Grafstein E, Roberts TE, Rowe BH. Parenteral metoclopramide for acute migraine: Meta-analysis of randomised controlled trials. Br Med J. 2004;329(7479):1369–72.
42. MacGregor EA, Wilkinson M, Bancroft K. Domperidone plus paracetamol in the treatment of migraine. Cephalalgia. 1993;13(2):124–7.
43. Donaldson D, Sundermann R, Jackson R, Bastani A. Intravenous dexamethasone vs placebo as adjunctive therapy to reduce the recurrence rate of acute migraine headaches: a multicenter, double-blinded, placebo-controlled randomized clinical trial. Am J Emerg Med. 2008;26(2):124–30.
44. Rowe BH, Colman I, Edmonds ML, Blitz S, Walker A, Wiens S. Randomized controlled trial of intravenous dexamethasone to prevent relapse in acute migraine headache. Headache. 2008;48(3):333–40.
45. Kelley NE, Tepper DE. Rescue therapy for acute migraine, part 3: Opioids, NSAIDs, steroids, and post-discharge medications. Headache. 2012;52(3):467–82.
46. Friedman BW, Greenwald P, Bania TC, Esses D, Hochberg M, Solorzano C, et al. Randomized trial of IV dexamethasone for acute migraine in the emergency department. Neurology. 2007;69(22):2038–44.
47. Scott LJ. Rimegepant: First Approval. Drugs [Internet]. 2020;80(7):741–6. Available from: https://doi.org/10.1007/s40265-020-01301-3
48. Negro A, Martelletti P. Gepants for the treatment of migraine. Expert Opin Investig Drugs [Internet]. 2019;28(6):555–67. Available from: https://doi.org/10.1080/13543784.2019.1618830
49. Lipton RB, Dodick DW, Ailani J, Lu K, Finnegan M, Szegedi A, et al. Effect of ubrogepant vs placebo on pain and the most bothersome associated symptom in the acute treatment of migraine: The achieve ii randomized clinical trial. JAMA - J Am Med Assoc. 2019;322(19):1887–98.
50. Lamb YN. Lasmiditan: First Approval. Drugs [Internet]. 2019;79(18):1989–96. Available from: https://doi.org/10.1007/s40265-019-01225-7
51. Clemow DB, Johnson KW, Hochstetler HM, Ossipov MH, Hake AM, Blumenfeld AM. Lasmiditan mechanism of action-review of a selective 5-HT 1F agonist The Journal of Headache and Pain. 2020;3:1–13. Available from: http://creativecommons.org/licenses/by/4.0/.TheCreativeCommonsPublicDomainDedicationwaiver%0Ahttp://creativecommons.org/publicdomain/zero/1.0/
52. Macone AE, Perloff MD. Lasmiditan: Its Development and Potential Use. Clin Pharmacol Drug Dev. 2020;9(3):292–6.
53. Doty EG, Krege JH, Pohl G, Case M, Dowsett SA, Tepper SJ. Pain Freedom at 2 to 8 Hours With Lasmiditan: A Comparison With Rimegepant and Ubrogepant. Headache. 2020;60(8):1793–6.
54. Szkutnik-Fiedler D. Pharmacokinetics, pharmacodynamics and drug–drug interactions of new anti-migraine drugs—Lasmiditan, gepants, and calcitonin-gene-related peptide (CGRP) receptor monoclonal antibodies. Vol. 12, Pharmaceutics. MDPI AG; 2020. p. 1–22.
55. Tassorelli C, Grazzi L, De Tommaso M, Pierangeli G, Martelletti P, Rainero I, et al. Nonin-

vasive vagus nerve stimulation as acute therapy for migraine: The randomized PRESTO study. Neurology. 2018;91(4):e364–73.
56. Diener HC, Bussone G, De Liano H, Eikermann A, Englert R, Floeter T, et al. Placebo-controlled comparison of effervescent acetylsalicylic acid, sumatriptan and ibuprofen in the treatment of migraine attacks. Cephalalgia. 2004;24(11):947–54.
57. Lipton RB, Stewart WF, Stone AM, Láinez MJA, Sawyer JPC. Stratified Care vs Step Care Strategies for Migraine. Jama. 2000;284(20):2599.
58. Ahrens SP, Farmer M V., Williams DL, Willoughby E, Jiang K, Block GA, et al. Efficacy and safety of rizatriptan wafer for the acute treatment of migraine. Cephalalgia. 1999;19(5):525–30.
59. Geraud G, Compagnon A, Rossi A. Zolmitriptan versus a combination of acetylsalicylic acid and metoclopramide in the acute oral treatment of migraine: A double-blind, randomised, three-attack study. Eur Neurol. 2002;47(2):88–98.
60. Doggrell SA, Hancox JC. Cardiac safety concerns for domperidone, an antiemetic and prokinetic, and galactogogue medicine. Expert Opin Drug Saf. 2014;13(1):131–8.
61. Khan RB. Migraine-type headaches in children receiving chemotherapy and ondansetron. J Child Neurol. 2002;17(11):857–8.
62. Jones EB, Gonzalez ER, Boggs JG, Grillo JA, Elswick RK. Safety and Efficacy of Rectal Prochlorperazine for the Treatment of Migraine in the Emergency Department. Ann Emerg Med. 1994;24(2):237–41.
63. Ferrari MD, James MH, Pilgrim A, Ashford E, Bates D, Anderson BA, et al. Oral sumatriptan: Effect of a second dose, and incidence and treatment of headache recurrences. Cephalalgia. 1994;14(5):330–8.
64. Géraud G, Keywood C, Senard JM. Migraine headache recurrence: Relationship to clinical, pharmacological, and pharmacokinetic properties of triptans. Headache. 2003;43(4):376–88.
65. Tepper SJ, Donnan GA, Dowson AJ, Bomhof MAM, Elkind A, Meloche J, et al. A long-term study to maximise migraine relief with zolmitriptan. Curr Med Res Opin. 1999;15(4):254–71.
66. Olesen J, Diener HC, Schoenen J, Hettiarachchi J. No effect of eletriptan administration during the aura phase of migraine. Eur J Neurol. 2004;11(10):671–7.
67. Nezvalová-Henriksen K, Spigset O, Nordeng H. Effects of codeine on pregnancy outcome: Results from a large population-based cohort study. Eur J Clin Pharmacol. 2011;67(12):1253–61.
68. Daniel S, Koren G, Lunenfeld E, Bilenko N, Ratzon R, Levy A. Fetal exposure to nonsteroidal anti-inflammatory drugs and spontaneous abortions. Cmaj. 2014;186(5):177–82.
69. Nezvalová-Henriksen K, Spigset O, Nordeng H. Triptan exposure during pregnancy and the risk of major congenital malformations and adverse pregnancy outcomes: Results from the Norwegian mother and child cohort study. Headache. 2010;50(4):563–75.
70. Worthington I, Pringsheim T, Gawel MJ, Gladstone J, Cooper P, Dilli E, et al. Canadian Headache Society Guideline: acute drug therapy for migraine headache. Can J Neurol Sci. 2013;40(5):S1–80.
71. Ward RM, Bates BA, Benitz WE, Burchfield DJ, Ring JC, Walls RP, et al. The transfer of drugs and other chemicals into human milk. Pediatrics. 2001;108(3):776–89.
72. Hendrickson RG, McKeown NJ. Is maternal opioid use hazardous to breast-fed infants? Clin Toxicol. 2012;50(1):1–14.