

NON- STEROİD ANTI-İNFLAMATUAR İLAÇ ZEHİRLENMELERİ

Yurdagül ÇETİN ŞEKER¹

Giriş

Non- steroid anti- inflamatuvar ilaçlar (NSAİİ'lar), ortak etki mekanizmasına sahip, ancak moleküler olarak farklı olan ilaç grubudur. Günümüz de analjezik, antipiretik ve antiinflamatuvar özellikleri için yaygın olarak kullanılmaktadırlar. Bu ilaç grubunun hem reçeteli hem de reçetesiz olarak satılabilmesi, tek başına farmasötik preparatlarda olabileceği gibi, öksürük ve soğuk algınlığı ilaçlarında da yer alabilmesi kullanım ve dolayısıyla toksisite yaygınlığını arttırmaktadır. (1, 2, 3)

Analjezikler yukarıda belirtilen kolay ulaşılabilirliği ve birçok ilaç kombinasyonunun da yer almaları nedeniyle aşırı dozda alımlar görülebilmektedir. Amerikan Zehir Kontrol Merkezleri Birliği Ulusal Zehir Veri Sistemi'nin (NPDS) 2009 yılı raporuna göre, analjeziklerin yetişkinlerde en yaygın, çocuklarda ise ikinci yaygınlıkta kullanımı gösterilmiştir. Amerika ve Birleşik Krallık verilerine göre ise analjezik olarak asetaminofen (parasetamol), NSAİİ'larda ise en sık gözlenen etken madde ibuprofen olarak raporlanmıştır. (4, 5, 6)

Genel Özellikler ve Etki Mekanizmaları

NSAİİ'ların yan etki ve toksisitelerini anlayabilmek için farmakolojik etki mekanizmalarını bilmek önemlidir. Bu ilaç grubunun terapötik ve toksik etkilerinin çoğu, siklooksijenaz (COX) grubundaki enzimlerin reversible inhibisyonundan kaynaklanır. (7,8) 1990'ların başlarında, iki siklooksijenaz izoenzimi

¹ Uzm. Dr. Yurdagül ÇETİN ŞEKER, Muş Devlet Hastanesi, Acil Tıp Bölümü
yrdglcetin@hotmail.com

KAYNAKLAR

1. Motola D, Vaccheri A, Silvani MC, et al. Pattern of NSAID use in the Italian general population: A questionnaire-based survey. *Eur J Clin Pharmacol.* 2004;60(10):731-738. doi:10.1007/s00228-004-0826-0.
2. Morita I. Distinct functions of COX-1 and COX-2. *Prostaglandins Other Lipid Mediat.* 2002;68-69:165-175. doi:10.1016/S0090-6980(02)00029-1.
3. Hunter LJ, Wood DM, Dargan PI. The patterns of toxicity and management of acute nonsteroidal anti-inflammatory drug (NSAID) overdose. *Open Access Emerg Med.* 2011;3:39-48. doi:10.2147/OAEM.S22795.
4. Bronstein AC, Spyker DA, Cantilena LR, Green JL, Rumack BH, Giffin SL. 2009 annual report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 27th annual report. In: *Clinical Toxicology.* Vol 48. Clin Toxicol (Phila); 2010:979-1178. doi:10.3109/15563650.2010.543906.
5. NPIS Annual Report 2009/2010 and Five Year Review. Available at: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1284474775986. Accessed April 25, 2011.
6. Rakovchik EE, Fein DM. Nonsteroidal anti-inflammatory drug and salicylate poisoning. *Pediatr Rev.* 2016;37(1):48-50. doi:10.1542/pir.2015-0052.
7. Vane JR. Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. *Nat New Biol.* 1971;231(25):232-235. doi:10.1038/newbio231232a0.
8. Vane JR, Botting RM. Mechanism of action of aspirin-like drugs. *Semin Arthritis Rheum.* 1997;26(6 SUPPL. 1):2-10. doi:10.1016/S0049-0172(97)80046-7.
9. Heim HK, Broich K. Selective COX-2 inhibitors and risk of thromboembolic events - regulatory aspects. *Thromb Haemost.* 2006 Oct;96(4):423-32.
10. Peck, T., & Hill, S. (2008). *Pharmacology for Anaesthesia and Intensive Care* (3rd ed.). Cambridge: Cambridge University Press. doi:10.1017/CBO9780511722172.
11. Ellenhorn, M. J., Schonwald, S., Ordog, G., & Wasserberger, I. (1997). *ELLENHORN's. Medical Toxicology: Diagnosis and Treatment of Human Poisoning.* 2nd ed. Baltimore, MD: Williams and Wilkins.
12. Burke, A., Smyth, E., & FitzGerald, G. A. (2006). Analgesic-antipyretic agents; pharmacotherapy of gout. *The pharmacological basis of therapeutics*, 1, 706.
13. Feldman M, McMahon AT. Do cyclooxygenase-2 inhibitors provide benefits similar to those of traditional nonsteroidal anti-inflammatory drugs, with less gastrointestinal toxicity? *Ann Intern Med.* 2000;132(2):134-143. doi:10.7326/0003-4819-132-2-200001180-00008.
14. Hillis WS. Areas of emerging interest in analgesia: cardiovascular complications. *Am J Ther.* 2002;9(3):259-269. doi:10.1097/00045391-200205000-00011.
15. Baron JA, Sandler RS, Bresalier RS, et al. Cardiovascular events associated with rofecoxib: final analysis of the APPROVe trial. *Lancet.* 2008;372(9651):1756-1764. doi:10.1016/S0140-6736(08)61490-7.
16. Flomenbaum, N. E., Goldfrank, L. R., Hoffman, R. S., Howland, M. A., Lewin, N. A., & Nelson, L. S. (2006). *Principles of managing the poisoned or overdosed patient. Toxicologic Emergency*, 8th Edition, McGraw-Hill, New York, 42-50.

17. Brooks PM. NSAIDs. In: Klippel JH, Dieppe PA (eds). Textbook of Rheumatology, 2th ed. Lon-don: Harcourt Publisher Ltd 2000; 3.5.1-6. No Title.
18. Vonkeman HE, van de Laar MAFJ. Nonsteroidal Anti-Inflammatory Drugs: Adverse Effects and Their Prevention Semin Arthritis Rheum. 2010;39(4):294-312. doi: 10.1016/j.semarthrit.2008.08.001.
19. Dollery C. (1999). Therapeutic Drugs. Second Edition. Edinburgh, Scotland: Churchill Livingstone.
20. Runkel R, Chaplin MD, Sevelius H, et al. Pharmacokinetics of naproxen overdoses. Clin Pharmacol Ther. 1976;20(3):269-277. doi:10.1002/cpt1976203269.
21. Balali-Mood M, Critchley JA, Proudfoot AT, et al. Mefenamic acid overdose. Lancet. 1981 Jun 20;1(8234):1354-6. doi: 10.1016/s0140-6736(81)92528-9.
22. Perry SJ, Streete PJ, Volans GN. Ibuprofen Overdose: The First Two Years of Over-the-Counter Sales. Hum Exp Toxicol. 1987;6(2):173-178. doi:10.1177/096032718700600211.
23. Cryer B, Kimmey MB. Gastrointestinal side effects of nonsteroidal anti-inflammatory drugs. Am J Med. 1998 Jul 27;105(1B):20S-30S. doi: 10.1016/s0002-9343(98)00071-0.
24. Gambaro G, Perazella MA. Adverse renal effects of anti-inflammatory agents: Evaluation of selective and nonselective cyclooxygenase inhibitors. J Intern Med. 2003;253(6):643-652. doi:10.1046/j.1365-2796.2003.01146.x.
25. Clive DM, Stoff JS. Renal Syndromes Associated with Nonsteroidal Antiinflammatory Drugs. N Engl J Med. 1984;310(9):563-572. doi:10.1056/nejm198403013100905.
26. Halpern SM, Fitzpatrick R, Volans GN. Ibuprofen toxicity. A review of adverse reactions and overdose. Adv Drug React and Toxicol Reviews. 1993;12(2):107-128.
27. Volans GN, Fitzpatrick R.(1999). Human Toxicity of ibuprofen. In: Rainsford KD, editor. Ibuprofen: A Critical Bibliographic Review (539-559). London, UK: Taylor and Francis.
28. McElwee NE, Veltri JC, Bradford DC, et al. A prospective, population-based study of acute ibuprofen overdose: Complications are rare and routine serum levels not warranted. Ann Emerg Med. 1990;19(6):657-662. doi:10.1016/S0196-0644(05)82471-0.
29. Sánchez-Hernandez MC, Delgado J, Navarro AM, et al. Seizures induced by NSAID. Allergy. 1999;54(1):90-91. doi:10.1034/j.1398-9995.1999.00931.x.
30. Smolinske SC, Hall AH, Vandenberg SA, et al. Toxic Effects of Nonsteroidal Anti-Inflammatory Drugs in Overdose: An Overview of Recent Evidence on Clinical Effects and Dose-Response Relationships. Drug Saf. 1990;5(4):252-274. doi:10.2165/00002018-199005040-00003.
31. Court H, Volans GN. Poisoning after overdose with non-steroidal anti-inflammatory drugs. Ad-verse Drug React Acute Poisoning Rev. 1984;3(1):1-21.
32. Walls, R., Hockberger, R., & Gausche-Hill, M. (2019). *Rosen's Emergency Medicine: Concepts and Clinical Practice -Rosen Acil Tıp: Kavramlar ve Klinik Uygulama.*(Doğaç Niyazi ÖZÜÇELİK,Çev.Ed.). İstanbul:Yeditepe Üniversitesi Yayınevi.
33. Kelly JP, Kaufinan DW, Shapiro S. Risks of agranulocytosis and aplastic anemia in

- relation to the use of cardiovascular drugs: The International Agranulocytosis and Aplastic Anemia Study. *Clin Pharmacol Ther.* 1991;49(3):330-341. doi:10.1038/clpt.1991.37
34. Wood DM, Monaghan J, Streete P, et al. Fatality after deliberate ingestion of sustained-release ibuprofen: A case report. *Crit Care.* 2006;10(2). doi:10.1186/cc4850.
 35. Jones R. Nonsteroidal anti-inflammatory drug prescribing: Past, present, and future. *Am J Med.* 2001 Jan 8;110(1A):4S-7S. doi: 10.1016/s0002-9343(00)00627-6.
 36. Holubek W, Stolbach A, Nurok S, et al. A report of two deaths from massive ibuprofen ingestion. *J Med Toxicol.* 2007;3(2):52-55. doi:10.1007/BF03160908.
 37. Jones A. Over-the-counter analgesics: a toxicology perspective. *Am J Ther.* 2002;9(3):245-257. doi:10.1097/00045391-200205000-00010.
 38. Adams, J. G. (2012). *Emergency medicine E-book: clinical essentials (expert consult--online)*. Elsevier Health Sciences.
 39. Chyka PA, Seger D, Krenzelok EP, et al. Position paper: Single-dose activated charcoal. *Clin Toxicol (Phila).* 2005;43(2):61-87. doi: 10.1081/clt-200051867.