

BÖLÜM 10

AMİNOGLİKOZİDLERİN ETKİ SPEKTRUMU VE KULLANIM ALANLARI

Pelin ADAR¹

Giriş

Aminoglikozid (AG) antibiyotikler, ekosistemde ve doğada yer alan *Actinomyctes* grubu gram pozitif bakterilerden elde edilen antimikrobiyal ajanlar olup bir *Streptomyces* türü tarafından üretilen ilk türev olan streptomisin 1940'lardan beri kullanılmaktadır. Sonu İngilizce dilinde -mycin ile bitenler doğrudan veya dolaylı olarak *Streptomyces* spp'den, sonu -micin ile bitenler *Micromonospora* spp'den türetilmiştir (1). Neomisin, kanamisin ve gentamisin, iki veya üç kimyasal bileşene sahip fermantasyon ürünleridir. Tüm AG'ler benzer fiziksel, kimyasal ve farmakolojik özellikleri taşımakta olup aminoglikozid ailesi Tablo 1'de özetlenmiştir.

Tablo1. Aminoglikozid Ailesi

KAYNAK			
Streptomyces spp.	YIL	Micromonospora spp.	YIL
Streptomisin	1944	Gentamisin	1963
Neomisin	1949	Sisomisin	1970
Kanamisin	1957	Netilmisin	1975
Paromomisin	1959	İsepamisin	1978
Spektinomisin	1961	Plazomisin	2018
Tobramisin	1967		
Dibekasin	1971		
Amikasin	1972		

¹ Uzm. Dr., Sağlık Bilimleri Üniversitesi, Tepecik Eğitim ve Araştırma Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği, pelinadar@gmail.com

Kaynaklar

1. Legget JE. Aminoglycosides. In: Bennett JE, Dolin R, Blase rMJ (eds) *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 9th ed. Philadelphia: Churchill Livingstone; 2020. p .417-436.
2. Houghton JL, Green KD, Chen W, et al. The future of aminoglycosides: the end or the renaissance? *Chembiochem*. 2010;11: 880–902. doi:10.1002/cbic.200900779.
3. Lynch SR, Puglisi JD. Structural origins of aminoglycoside specificity for prokaryotic ribosomes. *Journal of Molecular Biology*. 2001;306: 1037–1058. doi:10.1006/jmbi.2000.4420.
4. Mingeot-Leclercq MP, Glupczynski Y, Tulkens PM. Aminoglycosides: activity and resistance. *Antimicrobial Agents Chemotherapy*. 1999;43: 727. doi:10.1128/AAC.43.4.727.
5. Mistik R. Aminoglikozid antibiyotikler ve günde tek doz kullanımları. *Klinik Dergisi*. 2000;2(13): 43-45.
6. Fleischmann WA, Greenwood-Quaintance KE, Patel R. In vitro activity of plazomicin compared to amikacin, gentamicin, and tobramycin against multidrug-resistant aerobic gram-negative bacilli. *Antimicrobial Agents Chemotherapy*. 2020; 64. doi:10.1128/AAC.01711-19.
7. Karaiskos I, Lagou S, Pontikis K, et al. The “old” and the “new” antibiotics for MDR gram-negative pathogens: for whom, when, and how. *Frontiers in Public Health*. 2019;7: 151. doi:10.3389/fpubh.2019.00151.
8. Maurin M, Raoult D. Use of aminoglycosides in treatment of infections due to intracellular bacteria. *Antimicrobial Agents Chemotherapy*. 2001;45: 2977–2986. doi: 10.1128/AAC.45.11.2977-2986.2001.
9. Nahid P, Dorman SE, Alipanah N, et al. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases*. 2016; 63: 147. doi:10.1093/cid/ciw376.
10. McLean AJ, Ioannides Demos LL, Li SC, et al. Bactericidal effect of gentamicin peak concentration provides a rationale for administration of bolus doses. *Journal of Antimicrobial Chemotherapy*. 1993;32:301. doi:10.1093/jac/32.2.301.
11. Vogelman B, Craig WA. Kinetics of antimicrobial activity. *The Journal of Pediatrics*. 1986;108: 835–840. doi:10.1016/s0022-3476(86)80754-5.
12. Fantin B, Ebert S, Leggett J, et al. Factors affecting duration of in-vivo postantibiotic effect for aminoglycosides against gram-negative bacilli. *Journal of Antimicrobial Chemotherapy*. 1991;27: 829. doi:10.1093/jac/27.6.829.
13. Novelli A, Mazzei T, Fallani S, et al. In vitro postantibiotic effect and postantibiotic leukocyte enhancement of tobramycin. *Journal of Chemotherapy*. 1995;7: 355. doi:10.1179/joc.1995.7.4.355.
14. Craig WA, Gudmundsson S. Postantibiotic effect. In: Lorian V (ed) *Antibiotics in the Laboratory Medicine*. 4th ed. Baltimore: Williams & Wilkins; 1996. p. 296–329.
15. Allan JD, Moellering RC Jr. Management of infections caused by gram-negative bacilli: the role of antimicrobial combinations. *Reviews of Infectious Diseases*. 1985; Suppl 4(7): 559. doi: 10.1093/clinids/7.supplement_4.s559.
16. Eliopoulos GM, Moellering RC. Antimicrobial combinations. In: Lorian V (ed) *Antibiotics in Laboratory Medicine*. 4th ed. Baltimore: Williams & Wilkins; 1996. p. 330–383.
17. Gilbert DN, Lee BL, Dworkin RJ, et al. A randomized comparison of the safety and efficacy of once-daily gentamicin or thrice-daily gentamicin in combination with ticarcillin-clavulanate. *The American Journal of Medicine*. 1998;105: 182–191. doi: 10.1016/s0002-9343(98)00244-7.

18. Vanhaeverbeek M, Siska G, Douchamps J, et al. Comparison of the efficacy and safety of amikacin once or twice-a-day in the treatment of severe gram-negative infections in the elderly. *International Journal of Clinical Pharmacology and Therapeutics*. 1993;31: 153–156.
19. Zaske DE. Aminoglycosides. In: Ewans WE, Schentag JJ, Jusko WJ (eds) *Applied Pharmacokinetics. Principles of Therapeutic Drug Monitoring*. 3rd ed. Vancouver: Applied Therapeutics; 1992. p. 14-47.
20. Rougier F, Ducher M, Maurin M, et al. Aminoglycoside dosages and nephrotoxicity: quantitative relationships. *Clinical Pharmacology*. 2003;42: 493–500. doi:10.2165/00003088-200342050-00007.
21. Kim MJ, Bertino JS Jr, Erb TA, et al. Application of Bayes theorem to aminoglycoside-associated nephrotoxicity: comparison of extended-interval dosing, individualized pharmacokinetic monitoring, and multiple-daily dosing. *The Journal of Clinical Pharmacology*. 2004;44: 1072–1074. doi: 10.1177/00912700042466633.
22. Ipekci T, Seyman D, Berk H, et al. Clinical and bacteriological efficacy of amikacin in the treatment of lower urinary tract infection caused by extended-spectrum beta-lactamase-producing *Escherichia coli* or *Klebsiella pneumoniae*. *Journal of Infection and Chemotherapy*. 2014;20: 762. doi: 10.1016/j.jiac.2014.08.007.
23. Eliasson H, Broman T, Forsman M, et al. Tularemia: current epidemiology and disease management. *Infectious Disease Clinics of North America*. 2006;20: 289. doi:10.1016/j.idc.2006.03.002.
24. Nelson CA, Meaney-Delman D, Fleck-Derderian S, et al. Antimicrobial treatment and prophylaxis of plague: recommendations for naturally acquired infections and bioterrorism response. *MMWR Recommendations and Reports*. 2021; 70:1. doi:10.15585/mmwr.rr7003a1.
25. Workowski KA, Berman S. Centers for Disease Control and Prevention. Sexually transmitted diseases, treatment guidelines, *MMWR Recommendations and Reports*. 2010;59(RR-12): 1–110.
26. Houpt E, Hung CC.. Entamoeba histolytica (Amebiasis). In: Magill AJ, Ryan ET, Solomon T, Hill DR (eds) *Hunter's Tropical Medicine and Emerging Infectious Diseases*. 9th ed. Philadelphia: Saunders; 2012. p.659.
27. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *American Journal of Health-System Pharmacy*. 2013;70: 195. doi: 10.2146/ajhp120568.
28. Scudeller L, Righi E, Chiamenti M, et al. Systematic review and meta-analysis of in vitro efficacy of antibiotic combination therapy against carbapenem-resistant gram-negative bacilli. *International Journal of Antimicrobial Agents*. 2021;57(5): 106344. doi:10.1016/j.ijantimicag.2021.106344.
29. Niederman MS, Alder J, Bassetti M, et al. Inhaled amikacin adjunctive to intravenous standard-of-care antibiotics in mechanically ventilated patients with gram-negative pneumonia (INHALE): a double-blind, randomised, placebo-controlled, phase 3, superiority trial. *The Lancet Infectious Diseases*. 2020;20: 330–340. doi:10.1016/S1473-3099(19)30574-2.
30. Ghannam DE, Rodrigues GH, Raad II, et al. Inhaled aminoglycosides in cancer patients with ventilator-associated gram-negative bacterial pneumonia: safety and feasibility in the era of escalating drug resistance. *European Journal of Clinical Microbiology & Infectious Diseases*. 2009;28: 253–259. doi: 10.1007/s10096-008-0620-5.

31. Thwaites M, Hall D, Stoneburner A, et al. Activity of plazomicin in combination with other antibiotics against multidrug-resistant Enterobacteriaceae. *Diagnostic Microbiology and Infectious Disease*. 2018;92(4): 338–345. doi: 10.1016/j.diagmicrobio.2018.07.006.
32. Eljaaly, K., Alharbi, A., Alshehri, S. et al. Plazomicin: a novel aminoglycoside for the treatment of resistant gram-negative bacterial infections. *Drugs*. 2019;79: 243–269. doi: 10.1007/s40265-019-1054-3.
33. Cosgrove SE, Vigliani GA, Campion M, et al. Initial low-dose gentamicin for *Staphylococcus aureus* bacteremia and endocarditis is nephrotoxic. *Clinical Infectious Diseases*. 2009;48: 713–721. doi:10.1086/597031.
34. Buchholtz K, Larsen CT, Hassager C, et al. Severity of gentamicin's nephrotoxic effect on patients with infective endocarditis: a prospective observational cohort study of 373 patients. *Clinical Infectious Diseases*. 2009;48: 65–71. doi: 10.1086/594122.
35. Denamu S, Van Bambeke F, Mingeot-Leclercq MP, et al. Apoptosis induced by aminoglycosides in LCC-PK1 cells: comparative study of neomycin, gentamicin, amikacin, and isepamicin using electroporation. *Antimicrobial Agents Chemotherapy*. 2008;52: 2236–2238. doi:10.1128/AAC.01680-07.
36. Munckhof WJ, Grayson ML, Turnidge JD. A meta-analysis of studies on the safety and efficacy of aminoglycosides given either once daily or as divided doses. *Journal of Antimicrobial Chemotherapy*. 1996; 37:645. doi:10.1093/jac/37.4.645.
37. Huth ME, Ricci AJ, Cheng AG. Mechanisms of aminoglycoside ototoxicity and targets of hair cell protection. *International Journal of Otolaryngology*. 2011;2011: 937861. doi: 10.1155/2011/937861.
38. Akumida M, Anniko M, Shimizu A, et al. Neuroprotection of vestibular sensory cells from gentamicin ototoxicity obtained using nitric oxide synthase inhibitors, reactive oxygen species scavengers, brain-derived neurotrophic factors and calpain inhibitors. *Acta Oto-Laryngologica*. 2003;123: 8–13. doi: 10.1080/0036554021000028078.
39. Göpel W, Berkowski S, Preuss M, ,et al. Mitochondrial mutation m. 1555A> G as a risk factor for failed newborn hearing screening in a large cohort of preterm infants. *BMC Pediatrics*. 2014;14: 210. doi:10.1186/1471-2431-14-210.
40. Amiko M, Bagger-Sjöback D, Wersäll J, et al. Gentamicin binding to the isolated crista ampullaris of the guinea pig. *Research Communications in Chemical Pathology and Pharmacology*. 1982;37: 333–342.