

Bölüm 18

İLAÇLARA BAĞLI HİPERTANSİYON

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GİRİŞ

Genel olarak sistolik kan basıncının ≥ 140 mmHg ve / veya diyastolik kan basıncının ≥ 90 mmHg olarak tanımlanan hipertansiyon (1), dünya genelinde 1,2 milyardan fazla kişiyi etkileyen en önemli toplum sağlığı sorunlarından biridir (2). Hipertansiyon, primer ve sekonder hipertansiyon olarak sınıflandırılır (3). Primer hipertansiyon hipertansif hastaların büyük bir çoğunluğunu oluştururken açık bir etiyolojisi yoktur (4, 5). Hipertansif hastaların çok az bir kısmını oluşturan sekonder hipertansiyon ise, hem potansiyel olarak genellikle geri dönüşümlüdür hem de etiyolojisi açık olup farklı sebeplere bağlı olarak meydana gelir (6-8). Sekonder hipertansiyonun çeşitli sebepleri arasında renal parankimal hastalık, renal arter stenozu, obstrüktif uyku apne sendromu, primer hiperaldosteronizm, cushing sendromu, aort koarktasyonu, tiroid hastalıkları, akromegali, hiperparatiroidi, feokromositoma gibi hastalıklar ve birçok terapötik ajanın kullanımı/kötüye kullanımı sayılabilir (9).

İlaçlara bağlı hipertansiyon bir ilaçın istenmeyen etkilerinden ya da anjiyotensin dönüştürücü enzim inhibitörleri (ADEİ), anjiyotensin reseptör blokerleri (ARB), diüretikler, beta blokerler gibi yaygın antihipertansif ilaçlar üzerindeki antagonistik etkisinden kaynaklanan hipertansiyon olarak tanımlanır ve sekonder hipertansiyonun çok fazla bilinmeyen bir nedenidir (10).

Birçok ilaç veya kimyasal maddenin kullanımı/kötüye kullanımı çeşitli mekanizmalar ile hem kan basıncında kalıcı veya geçici bir artışa neden olarak hem de antihipertansif ilaçların etkisine müdahale ederek hipertansiyona sebep olur. Kan basıncındaki bu artışın temel mekanizmaları; doğrudan vazokonstriksiyon,

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herhangi bir etki meydana getirmezken başka bir bireyde ciddi bir artışa sebep olabilir (13). Bununla birlikte, epidemiyolojik veriler, kan basıncında küçük değişiklikler yaşaynlarda bile, kan basıncı yükselmeleri ile olumsuz kardiyovasküler sonuçlar arasında sürekli bir ilişki olduğunu göstermektedir. Bu nedenle ilaca bağlı hipertansiyon, morbidite ve mortalitede önemli bir etkiye sahip olabilir (69).

KAYNAKLAR

1. Siu AL. Screening for high blood pressure in adults: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2015; 163: 778-786.
2. Rahimi K, Emdin CA, MacMahon S. The epidemiology of blood pressure and its worldwide management. *Circulation research* 2015; 116: 925-936.
3. Grossman A, Messerli FH, Grossman E. Drug induced hypertension—An unappreciated cause of secondary hypertension. *European journal of pharmacology* 2015; 763: 15-22.
4. Charles L, Triscott J, Dobbs B. Secondary Hypertension: Discovering the Underlying Cause. *American family physician* 2017; 96.
5. Ker JA. Secondary hypertension. *South African Family Practice* 2011; 53.
6. Chobanian A. National heart, lung, and blood institute; national high blood pressure education program coordinating committee. seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension* 2003; 42: 1206-1252.
7. Omura M, Saito J, Yamaguchi K et al. Prospective study on the prevalence of secondary hypertension among hypertensive patients visiting a general outpatient clinic in Japan. *Hypertension Research* 2004; 27: 193-202.
8. Vongpatanasin W. Resistant hypertension: a review of diagnosis and management. *Jama* 2014; 311: 2216-2224.
9. Setters B, Holmes HM. Hypertension in the older adult. *Primary Care: Clinics in Office Practice* 2017; 44: 529-539.
10. Sager P, Heilbraun J, Turner JR et al. Assessment of drug-induced increases in blood pressure during drug development: report from the Cardiac Safety Research Consortium. *American heart journal* 2013; 165: 477-488.
11. Kassel LE, Odum LE. Our own worst enemy: pharmacologic mechanisms of hypertension. *Advances in chronic kidney disease* 2015; 22: 245-252.
12. Fournier JP, Sommet A, Bourrel R et al. Non-steroidal anti-inflammatory drugs (NSAIDs) and hypertension treatment intensification: a population-based cohort study. *European journal of clinical pharmacology* 2012; 68: 1533-1540.
13. Calhoun DA, Jones D, Textor S et al. Resistant hypertension: diagnosis, evaluation, and treatment: a scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. *Circulation* 2008; 117: e510-526.
14. Russo AL, Passaquin A, Cox C, Rüegg U. Cyclosporin A potentiates receptor-activated [Ca²⁺]c increase. *Journal of Receptors and Signal Transduction* 1997; 17: 149-161.
15. Rossi GP, Seccia TM, Maniero C, Pessina AC. Drug-related hypertension and resistance to antihypertensive treatment: a call for action. *J Hypertens* 2011; 29: 2295-2309.
16. White WB. Cardiovascular effects of the cyclooxygenase inhibitors. *Hypertension* 2007; 49: 408-418.
17. Johnson AG, Nguyen TV, Day RO. Do nonsteroidal anti-inflammatory drugs affect blood pressure? A meta-analysis. *Ann Intern Med* 1994; 121: 289-300.
18. Masi S, Uliana M, Gesi M et al. Drug-induced hypertension: Know the problem to know how to deal with it. *Vascular pharmacology* 2019; 115: 84-88.
19. Grossman E, Messerli FH. High blood pressure. A side effect of drugs, poisons, and food. *Arch-*

- hives of internal medicine 1995; 155: 450-460.
- 20. Hussain SF. Progestogen-only pills and high blood pressure: is there an association?: A literature review. Contraception 2004; 69: 89-97.
 - 21. Zalcman G, Mazieres J, Margery J et al. Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial. The Lancet 2016; 387: 1405-1414.
 - 22. Caletti S, Paini A, Coschignano MA et al. Management of VEGF-targeted therapy-induced hypertension. Current hypertension reports 2018; 20: 68.
 - 23. Salerno SM, Jackson JL, Berbano EP. Effect of oral pseudoephedrine on blood pressure and heart rate: a meta-analysis. Archives of internal medicine 2005; 165: 1686-1694.
 - 24. Beck KR, Thompson GR, 3rd, Odermatt A. Drug-induced endocrine blood pressure elevation. Pharmacological research 2019; 104311.
 - 25. Atkinson HC, Stanescu I, Anderson BJ. Increased phenylephrine plasma levels with administration of acetaminophen. The New England journal of medicine 2014; 370: 1171-1172.
 - 26. Samuels JA, Franco K, Wan F, Sorof JM. Effect of stimulants on 24-h ambulatory blood pressure in children with ADHD: a double-blind, randomized, cross-over trial. Pediatric Nephrology 2006; 21: 92-95.
 - 27. Hennissen L, Bakker MJ, Banaschewski T et al. Cardiovascular effects of stimulant and non-stimulant medication for children and adolescents with ADHD: a systematic review and meta-analysis of trials of methylphenidate, amphetamines and atomoxetine. CNS drugs 2017; 31: 199-215.
 - 28. Liang E, Lim S, Tam W et al. The effect of methylphenidate and atomoxetine on heart rate and systolic blood pressure in young people and adults with attention-deficit hyperactivity disorder (ADHD): systematic review, meta-analysis, and meta-regression. International journal of environmental research and public health 2018; 15: 1789.
 - 29. Roesch B, Corcoran M, Haffey M et al. Pharmacokinetics of coadministration of guanfacine extended release and methylphenidate extended release. Drugs in R&D 2013; 13: 53-61.
 - 30. Beck KR, Thompson III GR, Odermatt A. Drug-induced endocrine blood pressure elevation. Pharmacological research 2019; 104311.
 - 31. Heal DJ, Smith SL, Gosden J, Nutt DJ. Amphetamine, past and present—a pharmacological and clinical perspective. Journal of Psychopharmacology 2013; 27: 479-496.
 - 32. Steer C, Froelich J, Soutullo CA et al. Lisdexamfetamine dimesylate. CNS drugs 2012; 26: 691-705.
 - 33. Sharman J, Pennick M. Lisdexamfetamine prodrug activation by peptidase-mediated hydrolysis in the cytosol of red blood cells. Neuropsychiatric disease and treatment 2014; 10: 2275.
 - 34. Jasinski D, Krishnan S. Abuse liability and safety of oral lisdexamfetamine dimesylate in individuals with a history of stimulant abuse. Journal of Psychopharmacology 2009; 23: 419-427.
 - 35. Freudenmann RW, Freudenmann N, Zurowski B et al. Arterial Hyper-and Hypotension associated with psychiatric medications: a risk assessment based on the summaries of product characteristics (SmPCs). Deutsche medizinische Wochenschrift (1946) 2017; 142: e100-e107.
 - 36. Zimmerman JL. Cocaine intoxication. Critical care clinics 2012; 28: 517-526.
 - 37. Cohen DL, Townsend RR. Does consumption of high-caffeine energy drinks affect blood pressure? The Journal of Clinical Hypertension 2006; 8: 744-745.
 - 38. Mesas AE, Leon-Muñoz LM, Rodriguez-Artalejo F, Lopez-Garcia E. The effect of coffee on blood pressure and cardiovascular disease in hypertensive individuals: a systematic review and meta-analysis. The American journal of clinical nutrition 2011; 94: 1113-1126.
 - 39. Licht CM, De Geus EJ, Seldenrijk A et al. Depression is associated with decreased blood pressure, but antidepressant use increases the risk for hypertension. Hypertension 2009; 53: 631-638.
 - 40. Bymaster FP, Dreshfield-Ahmad LJ, Threlkeld PG et al. Comparative affinity of duloxetine and venlafaxine for serotonin and norepinephrine transporters in vitro and in vivo, human serotonin receptor subtypes, and other neuronal receptors. Neuropsychopharmacology 2001; 25: 871.
 - 41. Thase ME. Effects of venlafaxine on blood pressure: a meta-analysis of original data from 3744

- depressed patients. In. 1998.
42. Harvey AT, Rudolph RL, Preskorn SH. Evidence of the dual mechanisms of action of venlafaxine. *Archives of General Psychiatry* 2000; 57: 503-509.
 43. Shelton RC. Serotonin and norepinephrine reuptake inhibitors. 2018.
 44. Feighner JP. Mechanism of action of antidepressant medications. In *Assessing Antidepressant Efficacy: A Reexamination.*, Jan, 1998, Phoenix, AZ, US. Physicians Postgraduate Press 1999.
 45. Licht CM, Penninx BW, De Geus EJ. Effects of antidepressants, but not psychopathology, on cardiac sympathetic control: a longitudinal study. *Neuropsychopharmacology* 2012; 37: 2487.
 46. Fava M, Rush AJ, Thase ME et al. 15 years of clinical experience with bupropion HCl: from bupropion to bupropion SR to bupropion XL. Primary care companion to the Journal of clinical psychiatry 2005; 7: 106.
 47. Lovell AR, Ernst ME. Drug-induced hypertension: focus on mechanisms and management. *Current hypertension reports* 2017; 19: 39.
 48. Gillman PK. A reassessment of the safety profile of monoamine oxidase inhibitors: elucidating tired old tyramine myths. *Journal of Neural Transmission* 2018; 125: 1707-1717.
 49. Miyashita K, Tojo A, Kimura K et al. Blood pressure response to erythropoietin injection in hemodialysis and predialysis patients. *Hypertension Research* 2004; 27: 79-84.
 50. El-Gowelli HM, El-Mas MM. Central modulation of cyclosporine-induced hypertension. *Nanuny-Schmiedeberg's archives of pharmacology* 2015; 388: 351-361.
 51. El-Gowelli HM, Helmy MW, Ali RM, El-Mas MM. Celecoxib offsets the negative renal influences of cyclosporine via modulation of the TGF- β 1/IL-2/COX-2/endothelin ETB receptor cascade. *Toxicology and applied pharmacology* 2014; 275: 88-95.
 52. Issa N, Kukla A, Ibrahim HN. Calcineurin inhibitor nephrotoxicity: a review and perspective of the evidence. *American journal of nephrology* 2013; 37: 602-612.
 53. Nash EF, Stephenson A, Helm EJ et al. Impact of lung transplantation on serum lipids in adults with cystic fibrosis. *The Journal of Heart and Lung Transplantation* 2011; 30: 188-193.
 54. Yanagimachi M, Naruto T, Tanoshima R et al. Influence of CYP3A5 and ABCB1 gene polymorphisms on calcineurin inhibitor-related neurotoxicity after hematopoietic stem cell transplantation. *Clinical transplantation* 2010; 24: 855-861.
 55. Ingawale DK, Mandlik SK, Naik SR. Models of hepatotoxicity and the underlying cellular, biochemical and immunological mechanism (s): a critical discussion. *Environmental toxicology and pharmacology* 2014; 37: 118-133.
 56. Navegantes LCC, Mendes GEF, Lira EC et al. Effect of cyclosporine a on glucose interstitial concentration in renal cortex and medulla from rats. *American journal of nephrology* 2006; 26: 163-169.
 57. El-Mas MM, El-Gowelli HM, Abd-Elrahman KS et al. Pioglitazone abrogates cyclosporine-evoked hypertension via rectifying abnormalities in vascular endothelial function. *Biochemical pharmacology* 2011; 81: 526-533.
 58. Seibert F, Behrendt C, Schmidt S et al. Differential effects of cyclosporine and tacrolimus on arterial function. *Transplant International* 2011; 24: 708-715.
 59. El-Mas MM, Afify EA, Omar AG et al. Testosterone depletion contributes to cyclosporine-induced chronic impairment of acetylcholine renovascular relaxations. *European journal of pharmacology* 2003; 468: 217-224.
 60. El-Mas MM, El-Din MMM, El-gowilly SM, Sharabi FM. Regional and endothelial differences in cyclosporine attenuation of adenosine receptor-mediated vasorelaxations. *Journal of cardiovascular pharmacology* 2004; 43: 562-573.
 61. El-Mas MM, El-Din MMM, El-gowilly SM, Sharabi FM. Relative roles of endothelial relaxing factors in cyclosporine-induced impairment of cholinergic and β -adrenergic renal vasodilations. *European journal of pharmacology* 2004; 487: 149-158.
 62. Miller LW. Cardiovascular toxicities of immunosuppressive agents. *American Journal of Transplantation* 2002; 2: 807-818.
 63. El-Mas MM, El-Din MMM, Helmy MM, Omar AG. Redox imbalances incite the hypertensive,

- baroreflex, and autonomic effects of cyclosporine in rats. European journal of pharmacology 2012; 694: 82-88.
- 64. Hardy G, Stanke-Labesque F, Deveaux G et al. Cyclosporine A and cremophor EL induce contractions of human saphenous vein: involvement of thromboxane A2 receptor-dependent pathway. Journal of cardiovascular pharmacology 2000; 36: 693-698.
 - 65. Cauduro RL, Costa C, Lhulier F et al. Endothelin-1 plasma levels and hypertension in cyclosporine-treated renal transplant patients. Clinical transplantation 2005; 19: 470-474.
 - 66. Nishiyama A, Kobori H, Fukui T et al. Role of angiotensin II and reactive oxygen species in cyclosporine A-dependent hypertension. Hypertension 2003; 42: 754-760.
 - 67. Louhelainen M, Merasto S, Finckenberg P et al. Lipoic acid supplementation prevents cyclosporine-induced hypertension and nephrotoxicity in spontaneously hypertensive rats. Journal of hypertension 2006; 24: 947-956.
 - 68. Penninga L, Möller CH, Gustafsson F et al. Tacrolimus versus cyclosporine as primary immunosuppression after heart transplantation: systematic review with meta-analyses and trial sequential analyses of randomised trials. European journal of clinical pharmacology 2010; 66: 1177-1187.
 - 69. Lewington S, Clarke R, Qizilbash N et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet (London, England) 2002; 360: 1903-1913.