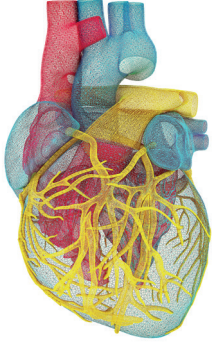


BÖLÜM 19



Antiaritmik Tedaviler

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| GİRİŞ

Günümüzde hızla ilerleyen teknolojiler sonucu ablasyon tekniklerinin gelişmesi ile ablasyon tedavisi ve cihaz kullanımı, antiaritmik ilaçların yetersizliği ve toksisiteyi nedeni ile aritmi tedavisinde önemli bir yer almıştır (1). Yeni ablasyon teknikleri sayesinde çoğu atriyal ve ventriküler aritmiler antiaritmik ilaç kullanımına gerek kalmadan tedavi edilebilmektedir (2). Buna rağmen yapısal kalp hastalığı bulunan hastalarda atriyal fibrilasyon ve ventriküler taşikardinin tedavisi güçtür ve tüm hastalar her zaman ablasyona uygun olamayabilmektedir (2). Aritmilerde profilaktik tedavinin değerlendirildiği CAST çalışmasında ve antiaritmik tedavi alan yaklaşık 100.000 akut miyokard enfarktüsü hastasının değerlendirildiği bir meta-analizde; profilaktik etki gücü, yan etkilerine ağır basan ilaçlarla tedavi planlanması gerektiği vurgulanmıştır (3, 4). Antiaritmik ilaçların dar terapötik penceresi bulunmaktadır ve ölümcül proaritmik etkileri olabilmektedir (5). Proaritmik etkiler, iyon kanalı üzerindeki etkilere bağlı olarak terapötik aralıkta iken de gelişebile-

ceği için yan etkilerden ayrı olarak değerlendirilmelidir (2). Bu sebeple antiaritmik ilaç seçiminde hastaların fayda ve zarar açısından değerlendirilmesi kritik önem taşır. Bu önemli ve güçlü ilaçları anlamak için, hücresel elektrofizyolojiyi bilmek önemlidir.

| KARDİYAK AKSİYON POTANSİYELİ

Ventriküler miyokard hücresinin aksiyon potansiyeli (AP) Şekil-1'de gösterilmiştir (2).

Depolarizasyon

İstirahat membran potansiyelinden her Na⁺ iyon geçişi, membranı pozitifleştirir ve depolarizasyon ile sonuçlanır: Faz 0 elektrokardiyogramda (EKG) QRS intervali olarak yansır. Denge durumundaki kardiyak miyosit -80 ve -95 mV arasında polarizedir (6). Faz 4'te iken dinlenme istirahat potansiyeli eşik değere geldiğinde, voltaj duyarlı sodyum iyon kanalı aracılığı ile hücre içerisine hızlı Na⁺ iyonları geçişi olur ve aksiyon potansiyelinin Faz 0 fazı gelişir.

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KAYNAKLAR

- Curtis AB, Narasimha D. Arrhythmias in women. *Clinical Cardiology*, 2012. **35**(3): p. 166-171. doi: 10.1002/clc.21975.
- Mankad P, Kalahasty G. Antiarrhythmic drugs: risks and benefits. *Medical Clinics*, 2019. **103**(5): p. 821-834. doi: 10.1016/j.mcna.2019.05.004.
- Cardiac Arrhythmia Suppression Trial (CAST) Investigators. Preliminary report: effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. *The New England Journal of Medicine*, 1989. **321**(6): p. 406-412. doi: 10.1056/NEJM198908103210629.
- Teo KK, Yusuf S, Furberg CD. Effects of prophylactic antiarrhythmic drug therapy in acute myocardial infarction: an overview of results from randomized controlled trials. *JAMA*, 1993. **270**(13): p. 1589-1595.
- Echt DS, Liebson PR, Mitchell LB, et al., Mortality and morbidity in patients receiving encainide, flecainide, or placebo: the Cardiac Arrhythmia Suppression Trial. *The New England Journal of Medicine*, 1991. **324**(12): p. 781-788. doi: 10.1056/NEJM199103213241201.
- Arnsdorf MF. The Cellular Basis of Cardiac Arrhythmias a: A Matrical Perspective. *Annals of the New York Academy of Sciences*, 1990. **601**(1): p. 263-280. doi:10.1111/j.1749-6632.1990.tb37306.x.
- Antzelevitch C, Burashnikov A. Overview of basic mechanisms of cardiac arrhythmia. *Cardiac Electrophysiology Clinics*, 2011. **3**(1): p. 23-45. doi: 10.1016/j.ccep.2010.10.012.
- Kowey PR, Marinchak RA, Rials SJ, et al., Pharmacologic and pharmacokinetic profile of class III antiarrhythmic drugs. *The American Journal of Cardiology*, 1997. **80**(8): p. 16G-23G. doi: 10.1016/s0002-9149(97)00710-8.
- The 'Sicilian Gambit'. A new approach to the classification of antiarrhythmic drugs based on their actions on arrhythmogenic mechanisms. The Task Force of the Working Group on Arrhythmias of the European Society of Cardiology. *European Heart Journal*, 1991. **12**(10): p. 1112-1131.
- Lei M, Wu L, Terrar DA, et al., Modernized classification of cardiac antiarrhythmic drugs. *Circulation*, 2018. **138**(17): p. 1879-1896. doi: 10.1161/CIRCULATIONAHA.118.035455.
- Campbell TJ, Vaughan Williams EM. Voltage- and time-dependent depression of maximum rate of depolarisation of guinea-pig ventricular action potentials by two new antiarrhythmic drugs, flecainide and lorcainide. *Cardiovascular Research*, 1983. **17**(5): p. 251-258. doi: 10.1093/cvr/17.5.251.
- Dukes ID, Vaughan Williams EM. Effects of selective alpha 1-, alpha 2-, beta 1- and beta 2-adrenoceptor stimulation on potentials and contractions in the rabbit heart. *The Journal of Physiology*, 1984. **355**(1): p. 523-546. doi: 10.1113/jphysiol.1984.sp015436.
- Vaughan Williams EM. Classification of antidysrhythmic drugs. *Pharmacology & Therapeutics*. Part B: General & systematic pharmacology, 1975. **1**(1): p. 115-138. doi: 10.1016/0306-039x(75)90019-7.
- Belhassen B, Glick A, Viskin S. Efficacy of quinidine in high-risk patients with Brugada syndrome. *Circulation*, 2004. **110**(13): p. 1731-1737. doi: 10.1161/01.CIR.0000143159.30585.90.
- McNamara RL, Tamariz LJ, Segal JB, et al. Management of atrial fibrillation: review of the evidence for the role of pharmacologic therapy, electrical cardioversion, and echocardiography. *Annals of Internal Medicine*, 2003. **139**(12): p. 1018-1033. doi: 10.7326/0003-4819-139-12-200312160-00012.
- Hwang HS, Hasdemir C, Laver D, et al., Inhibition of cardiac Ca²⁺ release channels (RyR2) determines efficacy of class I antiarrhythmic drugs in catecholaminergic polymorphic ventricular tachycardia. *Circulation: Arrhythmia and Electrophysiology*, 2011. **4**(2): p. 128-135. doi: 10.1161/CIRCEP.110.959916.
- Kochiadakis GE, Igoumenidis NE, Parthenakis FI, et al., Amiodarone versus propafenone for conversion of chronic atrial fibrillation: results of a randomized, controlled study. *Journal of the American College of Cardiology*, 1999. **33**(4): p. 966-971. doi: 10.1016/s0735-1097(98)00678-0.
- Khan IA. Oral loading single dose flecainide for pharmacological cardioversion of recent-onset atrial fibrillation. *International Journal of Cardiology*, 2003. **87**(2-3): p. 121-128. doi: 10.1016/s0167-5273(02)00467-9.
- Kuck KH, Cappato R, Siebels J, et al., Randomized comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest: the Cardiac Arrest Study Hamburg (CASH). *Circulation*, 2000. **102**(7): p. 748-754. doi: 10.1161/01.cir.102.7.748.
- Ellison KE, Hafley GE, Hickey K, et al., Multicenter UnSustained Tachycardia Trial Investigators: Effect of beta-blocking therapy on outcome in the Multicenter UnSustained Tachycardia Trial (MUSTT). *Circulation*, 2002. **106**(10): p. 2694-2699. doi: 10.1161/01.cir.0000038499.22687.39.
- Dargie HJ. Commentary:(Beta) blockers in heart failure. *The Lancet*, 2003. **362**(9377): p. 2-2. doi: 10.1016/S0140-6736(03)13842-1.
- Investigators, C.-I., The cardiac insufficiency bisoprolol study II (CIBIS-II): a randomised trial. *The Lancet*, 1999. **353**(9146): p. 9-13.
- Goldstein S, Fagerberg B, Hjalmarson A, et al., Metoprolol controlled release/extended release in patients with severe heart failure: analysis of the experience in the MERIT-HF study. *Journal of the American College of Cardiology*, 2001. **38**(4): p. 932-938. doi: 10.1016/s0735-1097(01)01516-9.
- Manz M, Jung W, Lüderitz B. Interactions between drugs and devices: experimental and clinical studies. *American Heart Journal*, 1994. **127**(4): p. 978-984. doi: 10.1016/0002-8703(94)90076-0.
- Pacifico A, Hohnloser SH, Williams JH, et al., Prevention of implantable-defibrillator shocks by treatment with sotalol. *New England Journal of Medicine*, 1999. **340**(24): p. 1855-1862. doi: 10.1056/NEJM199906173402402.
- Connolly SJ. Evidence-based analysis of amiodarone efficacy and safety. *Circulation*, 1999. **100**(19): p. 2025-2034. doi: 10.1161/01.cir.100.19.2025.
- Nattel, S. Pharmacodynamic studies of amiodarone and its active N-desethyl metabolite. *Journal of Cardiovascular Pharmacology*, 1986. **8**(4): p. 771-777.

28. Zimetbaum P, Amiodarone for atrial fibrillation. *New England Journal of Medicine*, 2007. **356**(9): p. 935-941. doi: 10.1056/NEJMct065916.
29. Vassallo, P. and R.G. Trohman, Prescribing amiodarone: an evidence-based review of clinical indications. *JAMA*, 2007. **298**(11): p. 1312-1322.
30. AFFIRM First Antiarrhythmic Drug Substudy Investigators. Maintenance of sinus rhythm in patients with atrial fibrillation: an AFFIRM substudy of the first antiarrhythmic drug. *Journal of the American College of Cardiology*, 2003. **42**(1): p. 20-29. doi: 10.1016/s0735-1097(03)00559-x.
31. Connolly SJ, Camm AJ, Halperin JL, et al., Dronedarone in high-risk permanent atrial fibrillation. *New England Journal of Medicine*, 2011. **365**(24): p. 2268-2276. doi: 10.1056/NEJMoa1109867.
32. Køber L, Torp-Pedersen C, McMurray JJ, et al., Increased mortality after dronedarone therapy for severe heart failure. *New England Journal of Medicine*, 2008. **358**(25): p. 2678-2687. doi: 10.1056/NEJMoa0800456.
33. Strickberger SA, Hummel JD, Bartlett TG, et al., Amiodarone versus implantable cardioverter-defibrillator: randomized trial in patients with nonischemic dilated cardiomyopathy and asymptomatic nonsustained ventricular tachycardia—AMIOVIRT. *Journal of the American College of Cardiology*, 2003. **41**(10): p. 1707-1712. doi: 10.1016/s0735-1097(03)00297-3.
34. Murray KT. Ibutilide. *Circulation*, 1998. **97**(5): p. 493-497. doi: 10.1161/01.cir.97.5.493.
35. Bernard EO, Schmid ER, Schmidlin D, et al., Ibutilide versus amiodarone in atrial fibrillation: a double-blinded, randomized study. *Critical Care Medicine*, 2003. **31**(4): p. 1031-1034. doi: 10.1097/01.CCM.0000053555.78624.0F.
36. Boriani G, Lubinski A, Capucci A, et al., A multicentre, double-blind randomized crossover comparative study on the efficacy and safety of dofetilide vs sotalol in patients with inducible sustained ventricular tachycardia and ischaemic heart disease. *European Heart Journal*, 2001. **22**(23): p. 2180-2191. doi: 10.1053/euhj.2001.2679.
37. Stambler BS, Wood MA, Ellenbogen KA, et al., Efficacy and safety of repeated intravenous doses of ibutilide for rapid conversion of atrial flutter or fibrillation. *Circulation*, 1996. **94**(7): p. 1613-1621. doi: 10.1161/01.cir.94.7.1613.
38. Belhassen B, Rotmensch HH, Laniado S. Response of recurrent sustained ventricular tachycardia to verapamil. *Heart*, 1981. **46**(6): p. 679-682. doi: 10.1136/hrt.46.6.679.
39. Chow T, Galvin J, McGovern B. Antiarrhythmic drug therapy in pregnancy and lactation. *The American Journal of Cardiology*, 1998. **82**(4): p. 58I-62I. doi: 10.1016/s0002-9149(98)00473-1.
40. DiMarco, J. Adenosine and digoxin. *Cardiac electrophysiology: From cell to bedside*. 3rd ed. Philadelphia, Pa: WB Saunders, 2000: p. 933-938.
41. Tokuda M, Matsuo S, Isogai R, et al., Adenosine testing during cryoballoon ablation and radiofrequency ablation of atrial fibrillation: A propensity score-matched analysis. *Heart Rhythm*, 2016. **13**(11): p. 2128-2134. doi: 10.1016/j.hrthm.2016.08.018.
42. Vickers NJ. Animal communication: when i'm calling you, will you answer too? *Current Biology*, 2017. **27**(14): p. R713-R715. doi: 10.1016/j.cub.2017.05.064.
43. Chadda KR, Jeevaratnam K, Lei M, et al., Sodium channel biophysics, late sodium current and genetic arrhythmic syndromes. *Pflügers Archiv-European Journal of Physiology*, 2017. **469**(5): p. 629-641. doi: 10.1007/s00424-017-1959-1.
44. Mathew ST, Po SS, Thadani U. Inappropriate sinus tachycardia—symptom and heart rate reduction with ivabradine: A pooled analysis of prospective studies. *Heart Rhythm*, 2018. **15**(2): p. 240-247. doi: 10.1016/j.hrthm.2017.10.004.
45. Zellerhoff, S., et al., Ivabradine in patients with inappropriate sinus tachycardia. *Naunyn-Schmiedeberg's archives of pharmacology*, 2010. **382**(5): p. 483-486.
46. Mulder P, Barbier S, Chagraoui A, et al., Long-term heart rate reduction induced by the selective I f current inhibitor ivabradine improves left ventricular function and intrinsic myocardial structure in congestive heart failure. *Circulation*, 2004. **109**(13): p. 1674-1679. doi: 10.1161/01.CIR.0000118464.48959.
47. Brugada J, Katritsis DG, Arbelo E, et al., 2019 ESC guidelines for the management of patients with supraventricular tachycardia the task force for the management of patients with supraventricular tachycardia of the European society of Cardiology (ESC) developed in collaboration with the association for European paediatric and congenital Cardiology (AEPC). *European Heart Journal*, 2020. **41**(5): p. 655-720. doi: 10.1093/eurheartj/ehz467.
48. Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al., 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Developed by the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC) Endorsed by the Association for European Paediatric and Congenital Cardiology (AEPC). *European Heart Journal*, 2022. **43**(40): p. 3997-4126. doi: 10.1093/eurheartj/ehac262.
49. Morady F, DiCarlo LA Jr, Baerman JM, et al. Effect of Propranolol on Ventricular Rate During Atrial Fibrillation in the Wolff-Parkinson-White Syndrome. *Pacing and Clinical Electrophysiology*, 1987. **10**(3): p. 492-497. doi: 10.1111/j.1540-8159.1987.tb04511.x.
50. Sellers TD Jr, Bashore TM, Gallagher JJ. Digitalis in the pre-excitation syndrome. Analysis during atrial fibrillation. *Circulation*, 1977. **56**(2): p. 260-267. doi: 10.1161/01.cir.56.2.260.
51. January CT, Wann LS, Alpert JS, et al., 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Journal of the American College of Cardiology*, 2014. **64**(21): p. e1-e76. doi: 10.1016/j.jacc.2014.03.022.
52. Waldo AL, Camm AJ, deRuyter H, et al., Effect of d-sotalol on mortality in patients with left ventricular dysfunction after recent and remote myocardial infarction. *The Lancet*, 1996. **348**(9019): p. 7-12. doi: 10.1016/s0140-6736(96)02149-6.