

The effect of pharmacological agents on left atrial appendage function in patients with atrial fibrillation

Atriyal fibrilasyonu olan hastalarda, farmakolojik ajanların sol atriyal apendiks fonksiyonları üzerine etkisi

Non-rheumatic atrial fibrillation (AF) is a common arrhythmia with a high prevalence in the elderly population. It is associated with increased risk of thromboembolism like ischemic stroke. For appropriate treatment of patients with AF, there are two main approaches: rhythm control and rate control. In both approaches, anticoagulation is recommended. Anti-arrhythmic drugs and atrioventricular nodal blocking agents are frequently used to control ventricular rate or restore the sinus rhythm (1).

Left atrial appendage (LAA) function assessed by transeophageal echocardiography identifies patients with AF at high risk for systemic embolism (2-4). There are limited studies about relationship between LAA function and agents used in the treatment of AF. Kamiyama et al. (5) have reported two cases of decreased LAA blood flow velocity caused by atenolol - beta-blocking agent, and pirmanol - class I anti-arrhythmic agent. Furthermore, they observed a new LAA thrombus after pirmanol administration (5). Bilge et al. also investigated effect of acute-phase beta-blocker therapy on LAA function in patients with chronic non-valvular AF. They found that in patients who have normal left ventricular systolic function and a poorly controlled ventricular rate despite the use of digoxin, acute-phase beta blockade may have a harmful effect on LAA function (6). Therefore, negative inotropic agents may result in a suppression of atrial contractility and decreased LAA flow velocities with AF. This hypothesis was also supported with the study of Kamalesh et al (7). They have investigated the effect of inotropic stimulation on LAA in patients with chronic AF. They observed that with dobutamin infusion, LAA emptying velocity increased and maximal LAA area decreased significantly.

In this issue of The Anatolian Journal of Cardiology, Karaca et al. (8) studied the acute effects of diltiazem and metoprolol on LAA function in patients with chronic nonvalvular AF. They measured LAA flow velocities with transesophageal echocardiography after applying 5 mg metoprolol to one group and 25 mg diltiazem to another group. They could not observe any significant change in LAA flow velocities with metoprolol. There was an insignificant decrease in LAA flow rate with diltiazem infusion and evident increase in spontaneous echo contrast density. The authors studied only acute effects of metoprolol and diltiazem infusions on LAA functions in a limited patient group.

Conversion of atrial fibrillation to sinus rhythm results in a transient mechanical dysfunction of left atrium and LAA regard-

less of the cardioversion method attempted, termed atrial stunning (9). In one study, irbesartan significantly attenuated left atrial stunning after electrical cardioversion of AF (10). In another study, following pharmacological cardioversion, of the degree of left atrial stunning was higher in patients treated with propafenone than in subjects receiving amiodarone (11). Also, verapamil, isoproterenol and dofetilide have been reported to protect from atrial stunning (12-14). While the effect of isoproterenol and dofetilide have positive inotropic action on LAA, attenuation of AF-induced contractile dysfunction by verapamil may be partially mediated by cellular calcium overload according to authors.

It has been demonstrated that >15% of strokes originate from the heart and from the LAA in particular and LAA flow velocities are important for determining the risk of thromboembolism (15). Further studies are needed on the effect of pharmacological agents used in the treatment of AF on left atrium and LAA functions. Summarizing results of studies on the subject, in future, some group of drugs like those with less negative inotropic action may be preferred in the treatment of AF.

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References

1. The AFFIRM investigators. Relationship between sinus rhythm, treatment and survival in the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. *Circulation* 2004;109:1509-13.
2. Corrado G, Klein AL, Santarone M. Echocardiography in atrial fibrillation. *J Cardiovasc Med* 2006;7:498-504.
3. Handke M, Harloff A, Hetzel A, Olschewski M, Bode C, Geibel A. Left atrial appendage flow velocity as a quantitative surrogate parameter for thromboembolic risk: determinants and relationship to spontaneous echocontrast and thrombus formation-a transesophageal echocardiographic study in 500 patients with cerebral ischemia. *J Am Soc Echocardiogr* 2005;18:1366-72.
4. Donal E, Yamada H, Leclercq C, Herpin D. The left atrial appendage, a small, blind-ended structure: a review of its echocardiographic evaluation and its clinical role. *Chest* 2005;128:1853-62.

5. Kamiyama N, Koyama Y, Suetsuna R, Saito Y, Kaji S Akasaka T, et al. Decreased left atrial appendage flow velocity with atrial fibrillation caused by negative inotropic agents. *Circ J* 2003; 67: 277-8.
6. Bilge M, Guler N, Eryoncu B, Erkoc R. Does acute-phase beta blockade reduce left atrial appendage function in patients with chronic nonvalvular atrial fibrillation? *J Am Soc Echocardiogr* 2001;14:194-9.
7. Kamalesh M, Copeland TB, Sawada S. Effect of inotropic stimulation on left atrial appendage function in atrial myopathy of chronic atrial fibrillation. *Echocardiography* 2000;17:313-8.
8. Karaca I, Coşkun N, Yavuzkır M, İlkay E, Dağlı N, Işık A, et al. Effect of diltiazem and metoprolol on left atrial appendix functions in patients with nonvalvular chronic atrial fibrillation. *Anadolu Kardiyol Derg* 2007; 7: 37-41.
9. Khan IA. Atrial stunning: basics and clinical considerations. *Int J Cardiol* 2003;92:113-28.
10. Dagnes N, Karatasakis G, Panou F, Athanassopoulos G, Maounis T, Tsougos E, et al. Pre-treatment with Irbesartan attenuates left atrial stunning after electrical cardioversion of atrial fibrillation. *Eur Heart J* 2006;27:2062-8.
11. Zapolski T, Wysokinski A. Stunning of the left atrium after pharmacological cardioversion of atrial fibrillation. *Kardiol Pol* 2005;63:254-64.
12. Daoud EG, Marcovitz P, Knight BP, Goyal R, Man KC, Strickberger SA, et al. Short-term effect of atrial fibrillation on atrial contractile function in humans. *Circulation* 1999;99:3024-7.
13. Date T, Takahashi A, Iesaka Y, Miyazaki H, Yamane T, Noma K, et al. Effect of low-dose isoproterenol infusion on left atrial appendage function soon after cardioversion of chronic atrial tachyarrhythmias. *Int J Cardiol* 2002;84:59-67.
14. Decara JM, Pollak A, Dubrey S, Falk RH. Positive atrial inotropic effect of dofetilide after cardioversion of atrial fibrillation or flutter. *Am J Cardiol* 2000;86:685-8.
15. Goldman ME, Pearce LA, Hart RG, Zabalgoitia M, Asinger RW, Safford R, et al. Pathophysiologic correlates of thromboembolism in nonvalvular atrial fibrillation: I. Reduced flow velocity in the left atrial appendage (The Stroke Prevention in Atrial Fibrillation [SPAF-III] study). *J Am Soc Echocardiogr* 1999;12:1080-7.