Decreased Left Atrial Appendage Flow Velocity With Atrial Fibrillation Caused by Negative Inotropic Agents

Report of 2 Cases

Norio Kamiyama, MD; Yuji Koyama, MD; Ryouji Suetsuna, MD; Yasuhiro Saito, MD; Shuichiro Kaji, MD; Takashi Akasaka, MD; Kiyoshi Yoshida, MD

Although pharmacological agents are frequently used to control ventricular rate or restore sinus rhythm of patients with atrial fibrillation (AF), there are no reports of the relationship between those agents and left atrial appendage (LAA) function. Two cases of a decrease in LAA blood flow velocity caused by negative inotropic agents are presented as an indication that negative inotropic agents are a risk factor for systemic thromboembolism with AF. (Circ J 2003; 67: 277–278)

Key Words: Atrial fibrillation; Left atrial appendage; Negative inotropic agents; Thromboembolism; Transesophageal echocardiography

Atrial fibrillation (AF) is the most common cardiac disorder causing stroke and systemic emboli. Transesophageal echocardiography (TEE) visualizes the potential sources of embolism in patients with AF, and left atrial appendage (LAA) function identifies patients with AF at high risk for systemic embolism.1–4 Although pharmacological agents are frequently used to control ventricular rate or restore sinus rhythm of patients with AF, there are no reports of the relationship between those agents and LAA function. We report 2 cases of decreased LAA blood flow velocity caused by negative inotropic agents.

Case Reports

Case 1
A 54-year-old man was admitted to hospital because of palpitations. He had no past history of cardiac illnesses, operations or hospitalizations. His pulse rate was 72 beats/min with an irregular rhythm, and his blood pressure was 130/90 mmHg. Breath sounds were unremarkable. The third sound was noted without audible murmurs.

An electrocardiogram (ECG) showed AF. The chest roentgenogram and transthoracic 2-dimensional echocardiography were within normal limits. Transesophageal echocardiographic examinations (TEE) were performed on the patient before and after administration of atenolol (daily dose; 25 mg po). TEE was performed using a commercially available system (Hewlet-Packard Sonus 1500) equipped with a 5 MHz transducer. LAA velocity profiles were obtained 1 cm below the orifice of the appendage by pulsed-wave Doppler. Gain settings were adjusted as required to distinguish spontaneous echo contrast (SEC); that is, dynamic smoke-like echoes within the atrial cavity, from echoes caused by excessive gain. Peak velocities were averaged off line for 5 cardiac cycles. Drugs, excluding atenolol, were not given during those examinations. The mean peak LAA emptying flow velocities were 43.3 cm/s without (Fig 1A), and 29.4 cm/s with atenolol (Fig 1B). Left atrial SEC was not present in either case.

Case 2
A 60-year-old man who had been treated for dilated cardiomyopathy was admitted because of electroconversion of AF. He had AF of 72 beats/min, and had blood pressure of 140/80 mmHg. A pansystolic murmur was heard at the apex with the third heart sound. There was no pretibial edema. An ECG confirmed AF with a nonspecific intraventricular conduction defect. The transthoracic echocardiogram was characteristic for dilated cardiomyopathy and showed mild mitral regurgitation. The left ventricular ejection fraction was 16% by the area–length method. Mean peak LAA emptying flow velocities and images were investigated in the same way as for case 1 before the patient was given a daily dose of pirmenol 200 mg orally, and than repeated after 10 days. The mean peak velocities were 21.8 cm/s without (Fig 1C) and 10.3 cm/s with pirmenol (Fig 1D). On left atrial images, after he was given pirmenol, the severity of SEC increased from mild to moderate, and a LAA thrombus was present (Fig 2). The drugs used, excluding pirmenol, were: enalapril 20 mg, furosemide 20 mg, metoprolol 20 mg, amiodarone 200 mg and warfarin 2.5 mg daily. The International Normalized Ratios (INR) of the prothrombin time were 2.61 with and 2.73 without pirmenol, respectively.

Discussion

The incidence of thromboembolic complications is high in patients with AF.5 The TEE phenomenon (ie, SEC) is considered to presage thrombus formation and its presence is associated with an increased thromboembolic risk.2,3 In high-risk patients with AF, subsequent rates of thromboembolism correlate with dense spontaneous echocardiogra-
Phasic contrast, thrombus of the atrial appendage, and aortic plaque. Pollick et al found that LAA thrombus formation in AF is associated with both poor LAA contraction and LAA dilation. In addition, some studies have indicated that LAA function:flow velocity may identify those patients with AF who are prone to systemic embolism. In both of the present cases, the LAA flow velocities decreased with the administration of atenolol or pirmenol. Furthermore, in case 2, a LAA thrombus appeared after pirmenol administration was begun. These findings suggest the possibility that the thromboembolic risk in both cases was increased by these drugs.

A negative inotropic effect on the myocardium is one of the well-known effects of &-adrenoceptor blockers, including atenolol. The antiarrhythmic class I agent, pirmenol, similarly has a negative inotropic effect. Experimental study has shown that LA pump function is augmented by volume overloading and decreased by propranolol, but unchanged by heart rate increments. Goldman et al showed that verapamil given during the increased inotropic state resulting from ouabain or dopamine administration, significant decreased LA pump function. We consider that negative inotropic agents, which includes nearly all antiarrhythmic drugs, result in a suppression of atrial contractility and decreased LAA flow velocity with AF.

Beta-blockers, calcium antagonists or antiarrhythmic drugs (either alone or in combination with digoxin) are used to control heart rate and/or to restore sinus rhythm, and all these drugs have negative inotropic effect.

This report shows there was a decrease in LAA blood flow velocity with AF after therapy with negative inotropic agents. Although there have been no previous studies of the relationship between these drugs and thromboembolism, it is possible that they are a risk factor for systemic thromboembolism with AF.

References