Ivabradine as an Alternative to AV Node Ablation in a Patient With Permanent Atrial Fibrillation

Ivabradina como alternativa a la ablación del nódulo AV para un paciente con fibrilación auricular permanente

To the Editor,

For patients with atrial fibrillation (AF) to respond adequately to cardiac resynchronization therapy, ventricular rate should be strictly controlled to ensure the biventricular pacing rate is as close to 100% as possible.[1] For this control, drugs are used that block atrioventricular (AV) conduction. When these fail, atrial node ablation is indicated, although this makes the patient pacemaker dependent. We present the case of a patient with AF with an implanted cardiac resynchronization device, in whom ivabradine was used as an alternative to AV node ablation for heart rate control.

The 60-year old male patient had received a prosthetic mitral valve replacement as treatment for rheumatic mitral stenosis. He was in permanent AF with left bundle branch block. During follow-up, he showed severe systolic left ventricular dysfunction and heart failure in the absence of coronary lesions. A cardiac resynchronization therapy defibrillator was required. During postimplantation follow-up, 74% biventricular pacing was observed despite bisoprolol escalation to the maximum tolerated dose (5 mg/12 h) and device programming in VVIR mode with a minimum rate of 70 bpm. Digoxin was not administered due to a history of digitalis toxicity and renal failure. Before considering AV node ablation, we decided to try ivabradine (5 mg/12 h). Eleven days later, the device showed a biventricular pacing rate of 95% (Figure). In subsequent follow-up 1 month after Ivabradine initiation, pacing was maintained at 96% and therefore ablation was not required.

Ivabradine is an inhibitor of If current, which is the main determinant of sinus node discharge rate. The beneficial effect as a drug that slows heart rate in patients with sinus rhythm has been clearly demonstrated, both in coronary artery disease and in heart failure.

However, the sodium channel that controls If current is not located exclusively in the sinus node but is also present in high concentrations both in the compact AV node and in the posterior nodal extension.[2] In addition to determining the automaticity of the subsidiary sinus node pacemaker, If current also seems to be directly related to the conduction properties of the AV node (impulse conductivity). In a clinical trial administering either an If current inhibitor (zatabradine) or placebo to patients without structural heart disease, active treatment induced a significant increase in the electrophysiological parameters of node conduction (AH interval, AV nodal effective refractory period, and Wenckebach cycle length).[3] More recently, ivabradine has also been found to exercise this depressor effect on node conduction. In an animal model published by Verrier et al.,[4] ivabradine administration during paced atrial rhythm led to a lengthening of the PR and AH intervals. This was more marked at rapid atrial pacing rates (use dependence) without affecting His-Purkinje system conduction or QT interval. When the drug was administered during AF, decreased ventricular response was observed without affecting the dominant atrial rates.

There is less extensive experience with ivabradine as a drug for controlling ventricular response during AF in humans. In a small case series, oral administration of ivabradine improved control of ventricular response and functional capacity in 4 of the 6 patients with rapid AF, despite treatment with beta blockers.[5] More recently, a clinical trial with 32 patients with AF showed that ivabradine significantly decreased average and maximum heart rates compared with placebo, with no relevant changes in minimum heart rate after 1 month of treatment.[6]

Very few drugs are available to control heart rate for patients with ventricular dysfunction and therefore AV node ablation is often indicated. The safety of ivabradine, demonstrated in large clinical trials in patients at risk (coronary artery disease and heart failure), in conjunction with the lack of vasodilatory effects or myocardial contractility depression, make it a promising option for control of ventricular response in patients with AF. The inclusion of

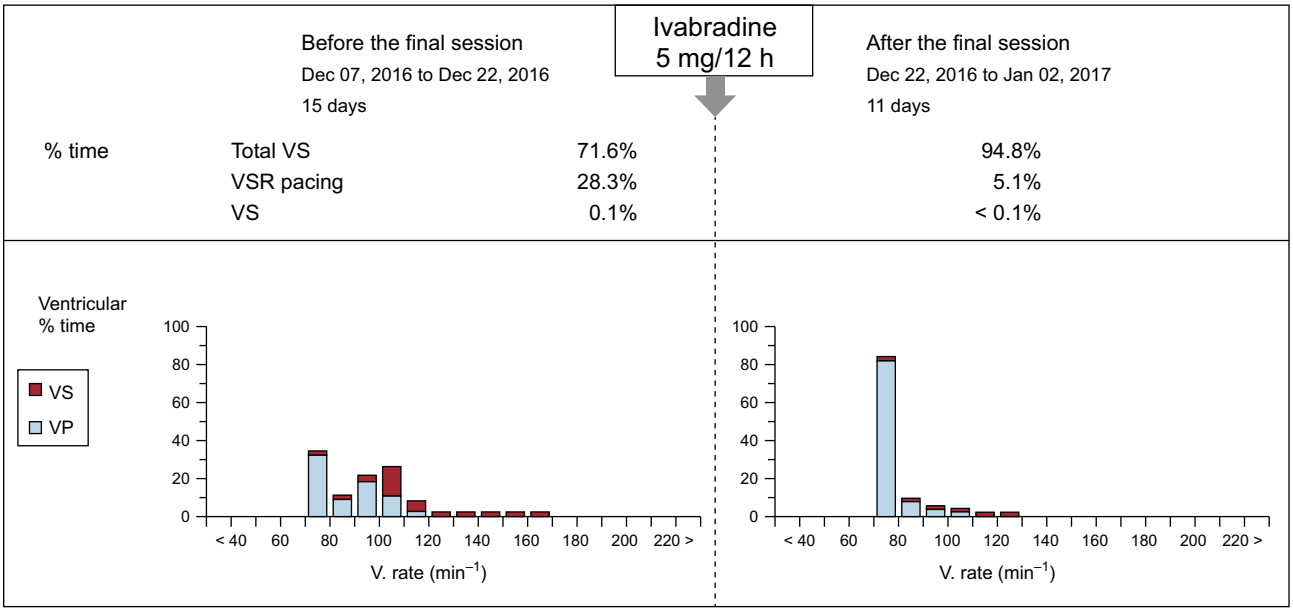

Figure. Cardiac resynchronization therapy device register in 2 consecutive follow-up visits (before and after initiation of oral ivabradine). The biventricular pacing rate increased from 71.6% to 94.8% after 11 days of ivabradine treatment. The rate of intrinsic ventricular rhythm (not resynchronized) is expressed as VS and VSR pacing, which corresponds to a pacing algorithm in response to the ventricular beats detected. VP pacing, ventricular pacing; VS, ventricular sensing; VSR, ventricular sensing response.

ivabradine in the therapeutic arsenal for inhibition of AV node conduction should be supported by *ad hoc* clinical trials.

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Implantation of a Long-term Left Ventricular Assist Device in a Patient With Obstructive Hypertrophic Cardiomyopathy

Implante de dispositivo de asistencia ventricular izquierda de larga duración en un paciente con miocardiopatía hipertrófica obstructiva

To the Editor,

Although the number of patients requiring a heart transplant has remained stable in our setting, the time on the transplant waiting list has lengthened. This has increased implantation of long-term left ventricular assist devices (LVADs) in patients with end-stage heart failure.[1] However, when the cause is hypertrophic cardiomyopathy (HCM) or restrictive cardiomyopathy, mechanical support is not a clear-cut option because the anatomical characteristics associated with these conditions are usually considered a contraindication for LVAD therapy.[2,3] The left ventricle is often too small or trabeculated, which implies a risk of collapse while on support, insufficient circulatory assistance with low output, suction of surrounding tissue, thrombosis, and stroke.[2,3] Optimizing flow without creating suction becomes even more complex when the patient begins to move and change position because of changes in the orientation of the inlet cannula. For these reasons, HCM patients seldom receive LVADs, and studies on the topic include small, single-center series that have even included both hypertrophic and restrictive cardiomyopathy patients.[2,3] We present the case of an HCM patient in our hospital who received an LVAD, the first indicated in Spain. The objectives were to confirm that selected patients can benefit from this therapy and to provide information on the anatomic, functional, and surgical parameters that may be useful for LVAD implantation in patients with HCM.

The patient reported is a 66-year-old man with obstructive HCM, who underwent defibrillator implantation in 2004 following resuscitation from an episode of sudden death due to ventricular fibrillation. In 2013 he was treated with septal ablation, which was unsuccessful. He was admitted for heart failure in 2015, and was referred for pretransplantation evaluation. Three months later, after optimization of the medical and resynchronization therapy, he was included on the elective waiting list. After 1 year on the list, he developed irreversible pulmonary artery hypertension, and we opted to evaluate LVAD therapy a bridge to decision. Right heart catheterization (September 2016) showed right atrial pressure (RAP) at 11 mmHg; mean pulmonary artery pressure, 45 mmHg; pulmonary capillary wedge pressure (PCWP), 22 mmHg; cardiac index, 1.5 L/min/m^2; and pulmonary vascular resistance, 9.2 UW. The RAP/PCWP ratio was 0.45 and the right ventricular (RV) stroke work index was 397 mmHg/mL/m^2. Transthoracic echocardiography was performed (Figure 1) to evaluate the RV and its dimensions, which seemed sufficient. The patient had grade III/IV mitral regurgitation due to anterior systolic movement and a dynamic outflow tract gradient of 50 mmHg, with no aortic regurgitation. The basal RV diameter was 48 mm, tissue Doppler S' was 9 cm/s, tricuspid annular plane systolic excursion (TAPSE) was 14 mm, radial function was preserved on subjective evaluation, and the fractional area change was 59%. Transesophageal echocardiography ruled out intraventricular thrombi and shunts. The relevant analytical results were creatinine clearance, 53 mL/min and N-terminal probrain natriuretic peptide, 4.866 pg/mL. The calculated HeartMate II score was 2.67.

In October 2016, a HeartWare HVAD system was implanted, with 113 min of on-pump circulation. The need for additional surgical procedures was ruled out. Septal myectomy was considered unnecessary, as it would make the surgery more complex and require aortic clamping with a risk of subsequent aortic regurgitation or residual shunts. Transesophageal echocardiography was used during the procedure to visually confirm that the apical trabeculae did not interfere with the inflow orifice of the system. Resecting the trabeculae is technically difficult as it is done through the small orifice made by coring the ventricular apex. By obviating this procedure, there would be no remnants from incomplete resection that could be suctioned by the LVAD. At the pump outlet, the RV was supported with milrinone and adrenaline, and nitric oxide was used to reduce the afterload. Nitric oxide discontinuation was rapidly achieved, with extubation at 9 hours.