Scientific letters

Preoperative Levosimendan for Right Ventricular Dysfunction Before Heart Valve Replacement Surgery

Tratamiento preoperatorio con levosimendán para paciente con disfunción ventricular derecha previa a cirugía de sustitución valvular

To the Editor,

The severity of preoperative right ventricular dysfunction contributes to early and long-term postoperative outcomes of heart valve surgery; therefore, patients with abnormal right ventricular contractility or morphology are considered to be at high perioperative risk.[1,2] EuroSCORE I and II underestimate the risk of these patients because right ventricular chamber parameters are not included in these risk scores. Several studies have demonstrated the benefit of preoperative levosimendan administration in patients with ventricular dysfunction.[3] Preoperative levosimendan administration[4] improved myocardial function in the early postoperative period and its early use produced significantly more benefits than late administration.[3,4] The preoperative use of levosimedan has been evaluated in patients with left ventricular dysfunction[4,5] undergoing cardiac or noncardiac surgery but not in patients with right ventricular dysfunction. We report a case series of patients with right ventricular dysfunction who were administered levosimendan before heart valve replacement surgery to prevent right ventricular failure as the primary target.

Preoperative levosimendan was prescribed to 9 patients with tricuspid valve disease and/or right ventricular dysfunction. Our aim was to determine whether levosimendan improved hemodynamic parameters, inotropic support, and renal function within the first 48 h of the postoperative period. The indication of preoperative levosimendan was based on tricuspid annular plane systolic excursion (TAPSE) <15 or the presence of moderate or severe right ventricular dilatation (moderate, 33-39 mm; severe >39 mm) on Doppler echocardiography. After the 9 patients had provided informed consent, levosimendan was administered before surgery to optimize cardiac function (all the patients were in functional class IV/IV) as continuous intravenous infusion, without previous bolus injection, at a rate of 0.15-0.10 µg/kg/min until a cumulative dose of 12.5 mg was reached. Standard routine monitoring was used (electrocardiogram, noninvasive blood pressure measurement, urine output and body temperature). None of the patients required cessation of infusion due to adverse effects. Central venous pressure was measured before the patient entered the operating room (12-16 mmHg). All the patients underwent heart valve replacement surgery (Table).

Forty-eight hours after levosimendan administration, Doppler echocardiography showed improvement of TAPSE in all patients except one.

In patients with a tricuspid valve prosthesis, both TAPSE and right ventricular ejection fraction improved.

Regarding the use of vasopressor and inotropic agents, 3 patients required low-dose norepinephrine, which was stopped in 2 of them after extubation (within 12 h after surgery). Another 3 patients required inotropic support with dobutamine or epinephrine during the first day after surgery (which was withdrawn before they underwent Doppler echocardiography); in 1 of these patients, treatment was continued during the second day after surgery. During the first 48 h, in 8 patients creatinine levels and urine output remained within normal values under furosemide at a mean dose of 30 mg/day; 1 of the patients developed kidney failure and needed renal replacement therapy.

We have reported the largest case series of patients who underwent levosimendan infusion to improve right ventricular function before heart valve replacement surgery.

In 8 of these nine patients, right ventricular contractility was impaired before surgery and improved after surgery with preserved renal function. Our patients belonged to a group commonly associated with longer stay in intensive care units and with greater mortality than other types of patients. Case series

Table
Preoperative, Operative, and Postoperative Data of the 9 Patients

Patient	Surgery	TAPSE, mm, before/after	RV volume	LVEF, %	PASP, mmHg	CBP time, min	Aortic cross-clamp time,min	Postoperative CV complications	ICU/ward stay, days
1	TVR	9/15*	Normal	50	47	309	0	Atrial fibrillation, rapid ventricular response	5/7
2	MVR+TA	10/15	Normal	70	62	115	82	Need for vasopressor support	5/8
3	TA	11/16	Severe	65	65	94	0	No	6/12
4	MVR+AVR+TA	14/15	Moderate	55	65	155	116	Need for vasopressor support	6/10
5	TA+MA	10/17	Moderate	60	60	94	75	Need for inotropic support	2/7
6	TVR	9/15*	Severe	70	27	34	0	Need for inotropic support	2/5
7	TVR	15/20*	Moderate	60	35	122	93	Need for inotropic and vasopressor support	13/15
8	MVR+TA	15/17	Moderate	60	73	147	125	No	3/8
9	TA	10/15	Normal	70	59	89	71	No	2/6

AVR, aortic valve replacement; CBP, cardiopulmonary bypass; CV, cardiovascular; ICU, intensive care unit; LVEF, left ventricular ejection fraction; MA, mitral valve annuloplasty; MVR, mitral valve replacement; PASP, pulmonary artery systolic pressure; RV, right ventricular; TA, tricuspid valve annuloplasty; TAPSE, tricuspid annular plane systolic excursion; TVR, tricuspid valve replacement.
* These patients also underwent evaluation of RV ejection fraction. Preoperative RV ejection fraction was 20%, 25% and 35%, and increased to >35% in the postoperative period in all patients.

have no control group or other treatment group and consequently, given our results, further studies are warranted. Finally, as there were no complications associated with preoperative levosimendan infusion, we may assume that this technique is safe and could benefit patients with high perioperative risk, such as those with right ventricular dysfunction undergoing heart valve replacement surgery.

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Evaluation of Cardiac ^{123}I-MIBG Imaging in Patients With Severe Left Ventricular Dysfunction and Indication for Implantable Cardioverter Defibrillator

Estudio de la inervación simpática cardiaca con ^{123}I-MIBG en pacientes con disfunción ventricular izquierda grave e indicación de desfibrilador

To the Editor,

Identification of noninvasive prognostic markers in patients with left ventricular dysfunction (LVD) is a challenge for the clinician. Although LVD is in itself an important predictor of adverse cardiac events, other markers are needed to refine risk stratification, as a poor correlation between the degree of LVD and adverse cardiac events is often observed in clinical practice.

The presence of myocardial fibrosis in cardiac magnetic resonance imaging (MRI) with late gadolinium enhancement[1,2] and the deterioration of sympathetic cardiac innervation quantified by ^{123}I-metaiodobenzylguanidine (^{123}I-MIBG) scintigraphy[3–6] have been introduced as new risk markers in recent years. We designed a prospective observational study with the aim of assessing whether the combination of information from these 2 techniques can improve risk stratification when an implantable cardioverter defibrillator is indicated for primary prevention.

We studied 47 consecutive patients with cardiac failure in New York Heart Association functional class II or III at baseline, left ventricular ejection fraction ≤35%, optimum pharmacological treatment, and class I indication for implantable cardioverter defibrillators, who had undergone prior cardiac MRI and ^{123}I-MIBG scintigraphy. Events were recorded during follow-up. The study was approved by the ethics committee of our hospital and patients provided their informed consent in writing. Here, we present the findings of cardiac innervation and its association with cardiac events during follow-up.

Scintigraphy of cardiac innervation was performed by intravenous injection of 10 mCi of ^{123}I-MIBG and subsequent image acquisition in the anterior region of the chest at 15 min and 4 h after injection of the tracer. Myocardial uptake of ^{123}I-MIBG was quantified by the early and late heart-to-mediastinum ratio (HMR) and the washout rate.

Categorical variables are expressed as percentages and quantitative ones as mean (SD). Variables were compared using the χ^2 test (categorical) or the Fisher and Student t test (quantitative). Predictors of events were established by univariate analysis and variables with $P<.1$ were included in the Cox multivariate analysis and expressed as hazar ratio (HR). The cumulative incidence of events was estimated by the Kaplan-Meier method, and compared using the log-rank test. The SPSS Statistics 17 program was used. Statistical significance was set at $P<.05$.

Baseline characteristics and findings of the cardiac innervation study are shown in the Table. There was a predominance of male patients, who were relatively young and had limited comorbidities. The etiology of LVD was ischemic, as is usually the case in primary prevention of sudden death. Eighteen events were recorded during a mean follow-up of 12.9 (8.6) months: 2 deaths (1 sudden death and 1 death due to heart failure), 7 hospitalizations due to heart failure, 7 appropriate implantable cardioverter defibrillator shocks, and 1 acute myocardial infarction.

The sample was divided into 2 groups according to the incidence of events. The groups had comparable pharmacological treatment, LVD etiology, presence of late gadolinium enhancement, and left ventricular ejection fraction quantified by cardiac MRI. However, the QRS interval was significantly greater in patients with events. With regard to the findings of cardiac innervation, markedly pathologic HMR values were observed (<1.20, 15 patients; 1.20-1.40, 13 patients; 1.40-1.60, 15 patients; >1.60, 4 patients) and only 1 patient had a normal (>1.80) value. The patients with events had a significantly lower late HMR (1.27 [0.13] vs 1.37 [0.23]; $P=.049$). The multivariate analysis included QRS interval, creatinine levels, treatment with angiotensin converting enzyme inhibitors/angiotensin II receptor antagonists, and early and late HMR<1.38 (median). An association was observed between late HMR≤1.38 (HR=5.19; 95% confidence interval [95%CI], 1.4-19.6; $P=.015$) and creatinine levels (HR=3.84; 95%CI, 1.8-8.4; $P=.001$) and an increased risk of experiencing an event. When only arrhythmic events were analyzed, no significant differences were observed in any of the variables. The Figure shows the survival curves for cardiac events and arrhythmic events, stratified using the median value of late HMR (log-rank test, $P=.001$ and $P=.128$, respectively).

The results of our study show a marked deterioration in cardiac innervation, as assessed by ^{123}I-MIGB scintigraphy, in patients with severe LVD and indication for implantable cardioverter defibrillator. Moreover, this deterioration was more marked than