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Vasodilator challenge with levosimendan as alternative to nitric oxide in advanced heart failure heart transplant candidates

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Introduction: Vasodilator challenge (VC) during right heart catheterization in heart transplant (HTx) candidates is warranted whenever pulmonary artery (PA) systolic pressure $\geq$50 mmHg and either transpulmonary gradient (TPG) $\geq$15 mmHg or pulmonary vascular resistance (PVR) $>$3 WU as long as systolic arterial blood pressure $>$85 mmHg. Nitric oxide (NO) remains the mainstay but in doubtful cases a 24–48h course of diuretics, inotropes and vasoactive agents may be required. Our aim is to report our centre's experience with levosimendan (LEVO) as alternative to NO in VC in HTx candidates due to advanced heart failure (HF).

Methods: VC records with either NO (20 ppm for 5–10 mins) or within 72h of LEVO infusion (12 mg/kg/min for 24–48h) carried out between 2009 and September 2018 were retrieved from the centre's database. Analysis was carried out with Fisher's exact test or Student's t-test for categorical and continuous variables, respectively, or the equivalent non-parametric test for non-normal distribution variables. Data are presented as counts and percentage, or mean ± standard deviation and median, percentile 25–75, for categorical and continuous variables, respectively.

Results: Baseline demographic and clinical characteristics from 26 patients (NO=13; LEVO=13) were similar between groups (12% female; 54±10 years of age; left ventricular ejection fraction 20±7%; BNP 1550±1090 pg/mL; 88% on NYHA III-IV). Although no differences were observed in baseline cardiac index (CI, 1.6±0.3 vs 1.4±0.4 L/min.m-2, in NO and LEVO, respectively), LEVO patients showed higher right ventricular systolic (70±10 vs 60±13 mmHg; p=0.036) and diastolic pressures (16±4 vs 11±5 mmHg; p=0.009) and lower PA compliance (0.9±0.2 vs 1.3±0.4 ml/mmHg; p=0.007) as well as a trend for increased PA wedge pressure (26±4 vs 21±4 mmHg; p=0.09), translating worse hemodynamics. Upon VC only LEVO decreased PA pressure and the increase in CI was higher compared with NO (2.5±0.8 vs 1.9±0.5 L/min.m-2, p=0.004) thus PVR reduction was comparable between groups (7.8±2.7 to 4.7±1.8 vs 6.3±2.3 to 3.6±2.1 WU, respectively). Also, only LEVO increased right (497, 387–837 to 791, 570–946 mmHg.mL.m-2; p=0.006) and left ventricular stroke work index (895, 807–1364 to 1257, 1107–2957 mmHg.mL.m-2; p=0.005) and cardiac power output (0.4±0.1 to 0.6±0.1 W; p$<$0.001). Increase in PA compliance was also higher in LEVO (89±98 vs 22±30 Δ%, p=0.04). On the other hand, NO increased wedge pressure whereas LEVO had no effect thus TPG reduction was higher with NO (42±24% vs 17±27% drops, respectively; p=0.022). After HTx (NO=4; LEVO=10) mortality was similar in both groups (25% vs 30%; p=1.00).

Conclusion: LEVO is a safe and effective alternative in PVR reduction for VC. Its positive inotropic effect and long-lasting hemodynamic improvement may improve clinical status before HTx and allow better scrutiny of suitable candidates.

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