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Valvular Heart Disease

EFFECTS OF PHOSPHODIESTERASE TYPE 5 INHIBITION ON SYSTEMIC AND PULMONARY HEMODYNAMICS AND VENTRICULAR FUNCTION IN PATIENTS WITH SEVERE AORTIC STENOSIS

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Background: Patients with aortic stenosis (AS) often present with advanced heart failure symptoms and abnormal hemodynamics characterized by pulmonary venous congestion, pulmonary hypertension, afterload mismatch, and low cardiac output. Phosphodiesterase type 5 (PDE5) inhibition may help reverse this decompensated clinical state, thereby potentially reducing operative risk and improving symptoms. However, the use of PDE5 inhibitors in patients with AS is controversial because of concerns about vasodilation and hypotension.

Methods: During cardiac catheterization, we evaluated the hemodynamic response of subjects with severe symptomatic AS (aortic valve area [AVA] <1.0 cm2) to a single oral dose of sildenafil (40mg or 80mg). Measurements were taken at baseline and 60 minutes after sildenafil (mean±SD).

Results: We enrolled 20 subjects with mean AVA 0.7±0.2 cm2 and ejection fraction 60±14%. After 60 minutes, sildenafil reduced systemic (from 27±8 to 22±6 Wood units, -19%, p<0.001) and pulmonary (3.5±2.8 to 2.2±1.1 Wood units, -37%, p=0.001) vascular resistance, mean pulmonary artery (37±11 to 27±9 mmHg, -27%, p<0.001) and wedge (24±7 to 19±8 mmHg, -21%, p<0.001) pressure. Likewise, sildenafil increased systemic (0.57±0.2 to 0.66±0.2 ml/mmHg, +16%, p<0.001) and pulmonary (2.1±1.1 to 2.8±1.2 ml/mmHg, +33%, p<0.001) vascular compliance and stroke volume index (29±6 to 31±6 ml/m2, +7%, p=0.04). The increase in stroke volume was strongly associated with a decrease in systemic and pulmonary vascular afterload after sildenafil. The changes in hemodynamic measurements were not dose dependent. Sildenafil modestly decreased mean systemic arterial pressure (108±15 to 94±16 mmHg, -13%, p<0.001), but was well-tolerated without symptomatic hypotension.

Conclusion: This study shows for the first time that a single dose of a PDE5 inhibitor is safe and well-tolerated in patients with severe AS and is associated with acute improvements in pulmonary and systemic hemodynamics resulting in biventricular unloading. These findings support the need for longer-term studies to evaluate the role of PDE5 inhibition as adjunctive medical therapy in patients with AS.