26.4.1 - Pharmacotherapy

Levosimendan, milrinone and dobutamine in acute experimental pulmonary embolism

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Background/Introduction: Acute pulmonary embolism (PE) is a frequent condition in acute cardiac care and is potentially fatal. Cause of death is right ventricular (RV) failure due to increased RV afterload from both pulmonary vascular obstruction and vasoconstriction. Inodilators are interesting drugs of choice as they may improve RV function and lower its afterload.

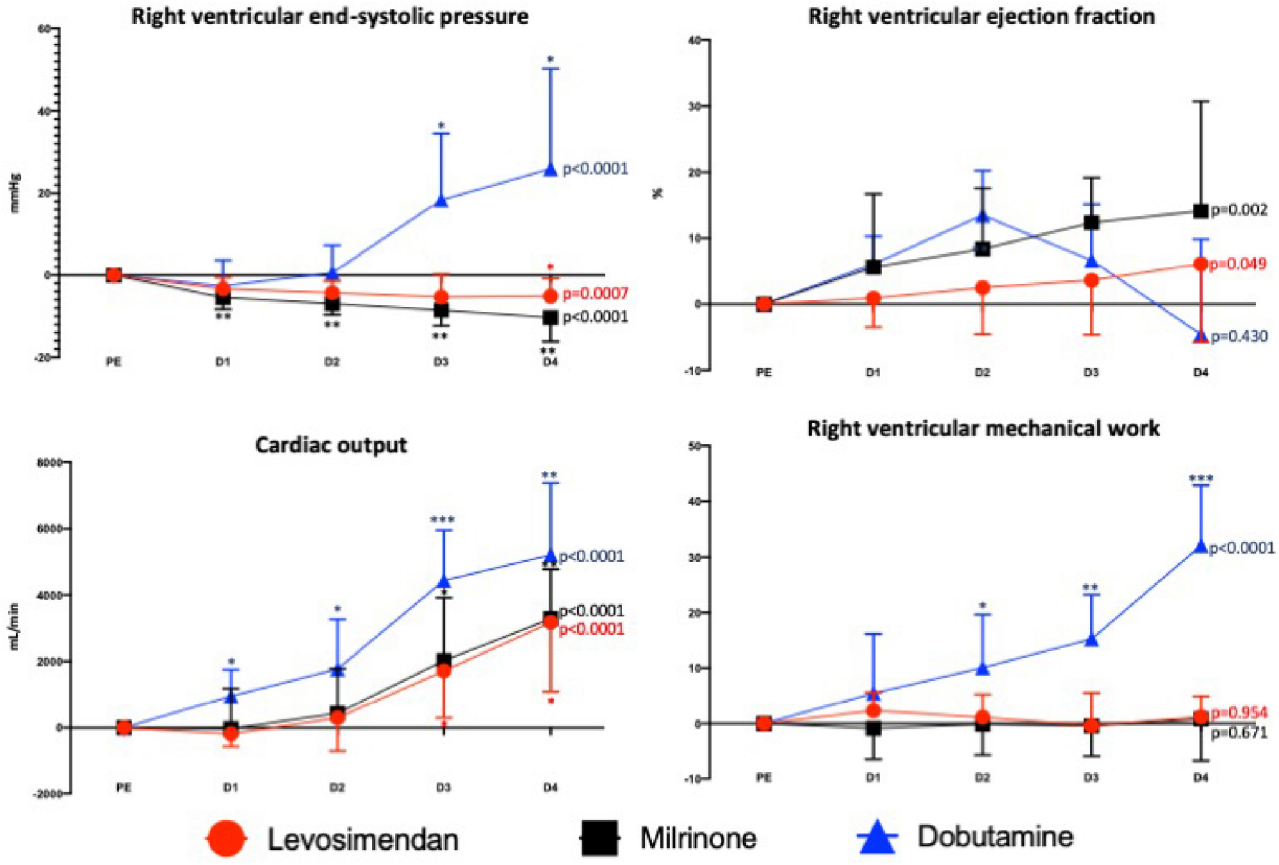
Purpose: We aimed to investigate the cardiovascular effects of three clinically relevant inodilators: levosimendan, milrinone and dobutamine in acute PE.

Methods: We conducted a randomized, blinded, animal study using 18 female pigs. Animals received large autologous PE until doubling of baseline mean pulmonary arterial pressure and were randomized to four logarithmically increasing doses of each inodilator. Effects were evaluated with bi-ventricular pressure-volume loop recordings, right heart catheterization and blood gas analyses.

Results: Induction of PE increased RV afterload and pulmonary pressure ($p < 0.05$) causing RV dysfunction. Levosimendan and milrinone showed beneficial hemodynamic profiles by lowering RV pressures and volume ($p < 0.001$) and improved RV function and cardiac output ($p < 0.05$) without increasing RV mechanical work. Dobutamine increased RV pressure and function ($p < 0.01$) but at a cost of increased mechanical work at the highest doses, showing an adverse hemodynamic profile. See Figure.

Conclusion(s): In a porcine model of acute PE, levosimendan and milrinone reduced RV afterload and improved RV function, whereas dobutamine at higher doses increased RV afterload and RV mechanical work. The study motivates clinical testing of inodilators in patients with acute PE and RV dysfunction.

Abstract Figure. Inodilators in acute pulmonary embolism



Absolute changes from pulmonary embolism (PE) measurement of each of the three inodilators. All were infused as four increasing doses D1-D4. P-values describe test-for-trend analyses. *p<0.01, **p<0.01. ***<0.001 vs PE. Data are mean±SD.