Pulmonary hypertension (PH) can lead to right-side heart failure (RHF) and death. There are no therapeutic recommendations for patients experiencing acute RHF in the course of PH. This study aimed to examine the safety and efficacy of inhaled iloprost in patients with precapillary PH and RHF. Between October 2007 and December 2008, 7 patients with precapillary PH and RHF were enrolled. Per protocol, iloprost was inhaled hourly for a minimum of 12 hours during a 24-hour period. The starting dose of 2.5 ?g was increased hourly by 2.5 ?g as long as the increases were tolerated. Safety and efficacy were determined by continuous invasive monitoring of systemic and pulmonary hemodynamic parameters. Systemic pressures remained stable during inhalation (66.1 ± 6.9 mm Hg at baseline and 69.1 ± 6.4 mm Hg immediately after inhalation therapy, P = 0.48). Cardiac index increased from 2.4 ± 0.7 L/min/m(2) to 2.9 ± 0.9 L/min/m(2) (P = .008). Pulmonary vascular resistance decreased from 634.6 ± 218.3 dyn-s-cm(-5) to 489.6 ± 173.8 dyn-s-cm(-5) (P = .044), and N-terminal B-type natriuretic peptide levels decreased from 13,591 ± 10,939 pg/mL to 9,944 ± 8,569 pg/mL (P = .051). Blood pressure-guided hourly inhalation of iloprost may offer a safe and effective strategy for the treatment of PH patients with RHF.