

VENTAVIS® (iloprost)

Use of VENTAVIS in Acute Vasoreactivity Testing

SUMMARY

- In the adult population, one study compared iloprost to intravenous (IV) adenosine for acute vasodilator testing in patients with severe pulmonary arterial hypertension (PAH) related to congenital heart defects.¹ Another study investigated iloprost as a diagnostic tool to find long-term responders to calcium channel blockers (CCBs).²
- Two studies were conducted in the pediatric population to evaluate the use of iloprost for vasodilator testing.^{3,4}
- Additional citations identified during a literature search are included in the REFERENCES section for your review.⁵⁻¹²

CLINICAL DATA

Adult population

Zhang et al¹ compared iloprost to IV adenosine for acute vasodilator testing in 75 patients with severe PAH related to congenital heart defects. The vasodilator effects of iloprost were more selective for pulmonary vasculature compared to adenosine. Patients in the adenosine group experienced a significant drop in mean systemic arterial pressure (baseline 91±10 mmHg to post-test 84±10 mmHg, $P<0.05$) while those in the iloprost group did not (baseline 88±10 mmHg to post-test 87±11 mmHg, $P>0.05$). Iloprost was better tolerated than adenosine with all patients in the iloprost group receiving the full dose (25 ng/kg/min if <40 kg; 1 mcg/min if ≥40 kg) during testing and only 1 patient experiencing transient cough versus seven patients in the adenosine group receiving a full dose (200 mcg/kg/min). The remaining 18 patients in the adenosine group received a lower dose (145±27 mcg/kg/min) after experiencing chest pain (n=3), dyspnea (n=4) and heart rate >100 beats per minute (bpm; n=11).

Jing et al² investigated the utility of iloprost in PAH diagnostic screening to identify long-term responders to CCBs. Seventy-four patients were screened for acute vasoreactivity to iloprost and IV adenosine. All patients who responded to adenosine also responded to iloprost. Nine acutely vasoreactive patients identified with iloprost were subsequently placed on CCB therapy for 12 months, of whom 5 experienced clinical benefits with CCB therapy. In the adenosine group, 35 patients (47.3%) experienced adverse events including hypotension (n=3), flushing (n=2), palpitations or shortness of breath (n=27), abdominal pain (n=2) and pharyngeal pain (n=1). Only 2 patients (2.7%) in the iloprost group experienced an adverse event, one each for increased cough and hypotension.

Pediatric population

Limsuwan et al³ examined the use of iloprost 0.5 mcg/kg over 10 minutes for vasodilator testing in 22 children (aged 7 months to 13 years). If patients did not respond to iloprost, they were tested using 100% oxygen for hyperoxia testing. Thirteen of 18 children with complete data available responded to iloprost and of the 5 who did not respond, 2 were responsive to hyperoxia testing. Adverse events related to the vasodilator test were not discussed in this publication.

Elkiran et al⁴ conducted a prospective cohort study that evaluated the use of iloprost 25 ng/kg/min diluted in 1.5 mL of isotonic saline nebulized with 100% oxygen in 16 children (15 with PAH associated with congenital heart disease and one with primary PH). At baseline, no significant difference in hemodynamic parameters was present between the responder and non-responder groups ($P>0.05$). Eleven of the 16 children were responders, meaning they experienced a drop in PVR and pulmonary-to-systemic vascular resistance ratio (Rp/Rs) >10% or PVR <6 Wood units/m² or Rp/Rs <0.3. No side effects were observed during the administration or in the 24 hours following inhalation.

LITERATURE SEARCH

A literature search of MEDLINE®, EMBASE®, BIOSIS Previews®, and DERWENT® (and/or other resources, including internal/external databases) was conducted on 17 May 2024.

REFERENCES

1. Zhang DZ, Zhu XY, Meng J, et al. Acute hemodynamic responses to adenosine and iloprost in patients with congenital heart defects and severe pulmonary arterial hypertension. *Int J Cardiol.* 2011;147(3):433-437.
2. Jing ZC, Jiang X, Han ZY, et al. Iloprost for pulmonary vasodilator testing in idiopathic pulmonary arterial hypertension. *Eur Respir J.* 2009;33(6):1354-1360.
3. Limsuwan A, Khosithseth A, Wanichkul S, Khowsathit P. Aerosolized iloprost for pulmonary vasoreactivity testing in children with long-standing pulmonary hypertension related to congenital heart disease. *Catheter Cardiovasc Interv.* 2009;73(1):98-104.
4. Elkiran O, Karakurt C, Kocak G. Combined effect of aerosolized iloprost and oxygen on assessment of pulmonary vasoreactivity in children with pulmonary hypertension. *Anadolu kardioloji dergisi : AKD = the Anatolian journal of cardiology.* 2014;14(4):383-388.
5. Tonelli AR, Alnuaimat H, Mubarak K. Pulmonary vasodilator testing and use of calcium channel blockers in pulmonary arterial hypertension. *Respir Med.* 2010;104(4):481-496.
6. Baker SE, Hockman RH. Inhaled iloprost in pulmonary arterial hypertension. *Ann Pharmacother.* 2005;39(7-8):1265-1274.
7. Ewert R, Schaper C, Halank M, Glaser S, Opitz CF. Inhalative iloprost - pharmacology and clinical application. *Expert Opin Pharmacother.* 2009;10(13):2195-2207.
8. Zhang HL, Liu ZH, Wang Y, et al. Acute responses to inhalation of Iloprost in patients with pulmonary hypertension. *Chinese medical journal.* 2012;125(16):2826-2831.
9. Goldsmith DR, Wagstaff AJ. Inhaled iloprost: in primary pulmonary hypertension. *Drugs.* 2004;64(7):763-773; discussion 774-765.
10. Sompradeekul S, Wattanasiriphakdee S. Hemodynamic effect of iloprost inhalation and oral sildenafil during acute vasoreactivity test in pulmonary arterial hypertension. *J Med Assoc Thai.* 2015;98(2):144-149.
11. Richter MJ, Ghofrani HA, Voswinckel R, et al. Acute hemodynamic effects of nebulized iloprost via the I-neb Adaptive Aerosol Delivery system in pulmonary hypertension. *Pulm Circ.* 2015;5(1):162-170.
12. Sun Y, Li Y, Meng X, Jiang R. Acute vasoreactivity testing predicts outcome of idiopathic pulmonary arterial hypertension patients with a negative acute response. *Ann Transl Med.* 2020;8.