The use of vasopressors in pulmonary hypertension on the intensive care unit

Pulmonary hypertension encompasses a range of disease processes affecting the pulmonary vasculature, defined as a mean pulmonary artery pressure >25 mmHg at rest or 30 mmHg on exercise. Pulmonary hypertension may be idiopathic, or associated with a variety of disorders including left-sided heart disease, lung disease, thromboembolic disease or other miscellaneous causes. Mortality remains significant despite increasing available therapeutic options, and it is likely that patients with pulmonary hypertension will be encountered more frequently.

In critical care, pulmonary hypertension most commonly occurs as a result of either elevated left atrial pressures leading to pulmonary venous hypertension, hypoxia, occlusion from pulmonary emboli or from vasoactive inflammatory mediators in acute lung injury. Treatment of the primary disease is central to management in these cases.

The principles of critical care management of pulmonary hypertension and ensuing right ventricular failure can be classified according to effects on right ventricular performance: optimization of preload with appropriate fluid resuscitation, maintenance of aortic root pressure therefore right ventricular coronary perfusion using vasopressors, reduction of afterload by optimizing gas exchange and using pulmonary vasodilators, and increasing right ventricular contractility with inotropes. The length of the history is important: a chronically hypertrophied right ventricle would able to withstand much a higher afterload than one following an acute pulmonary embolism.

Systemic hypotension in these patients has multiple causes including sepsis, overdiuresis, and progression of right ventricular failure itself, and management is complex. The right ventricle may be further compromised by common problems in critical care including hypoxia, acidosis, hypercapnia and the increase in pulmonary vascular resistance seen with invasive ventilation. Pulmonary vasodilators such as prostanoids and inhaled nitric oxide (NO) may be used to offset these acute problems.

Assuming 'right ventricular protective strategies' are in place, inotropes are now available that are more suited to the right ventricle. These include the phosphodiesterase III inhibitors (e.g. milrinone) with their more benign effects on the pulmonary circulation compared to catecholamines, and also levosimendan, the inotropic calcium sensitizer shown to have systemic vasodilating or 'inodilating' properties. These may also improve right ventricular performance through pulmonary vasodilatation (Missant et al, 2007), but systemic hypotension can occur.

Vasopressors therefore have an important role in maintaining systemic pressure. The ideal vasopressor would have greater systemic than pulmonary vasoconstrictive effects, even causing pulmonary vasodilatation, and exert minimal tachycardia.

The tachycardic effects of catecholamines via beta-agonism are disadvantageous with the right ventricular diastolic dysfunction associated with pulmonary hypertension. Furthermore, the catecholamines also all increase pulmonary vascular resistance. The non-catecholamine sympathomimetics include phenylephrine which, while not inducing tachycardia (as it exerts no beta effects), will increase pulmonary vascular resistance. Of the other drugs in this category, metaraminol also increases pulmonary vascular resistance, and ephedrine causes a tachycardia. In a dog model of acute pulmonary artery obstruction, the right ventricle appeared to recover better with dobutamine than norepinephrine, probably related to the additional inotropic effect of dobutamine on the right ventricle (Kerbaul et al, 2004).

Vasopressin, a directly acting vasopressor known for its potent systemic vasoconstrictive effect via endothelial vasopressinergic (V1) receptors, will increase systemic arterial pressure but may also have pulmonary vasodilating properties. A study in an isolated, perfused rat lung model, where the pulmonary arteries were pre-constricted, suggested that at low doses these effects are mediated by a NO-dependent mechanism (Russ and Walker, 1992).

There are no studies on the haemodynamic effects of vasopressin in patients with pulmonary hypertension, although there are several case reports of these patients benefiting from its use. Some of these, and also studies of the effects of vasopressin in patients with liver disease, have been reviewed by Smith et al (2006). One of these showed a reduction in systolic pulmonary artery pressure, estimated by echocardiography, following a bolus of terlipressin, a synthetic vasopressin analogue. As it appears that vasopressin acts on preconstricted pulmonary arteries, this may explain why patients with pulmonary hypertension may benefit from this agent.

Consideration of the multiple facets of management of systemic hypotension in these patients is important in the critical care setting, and more comparative data are needed on the use of vasoactive agents in these complex patients. **BJHM**

Dr LC Price *is Specialist Registrar in Respiratory and Intensive Care Medicine,* **Dr SJ Brett** *is Consultant in Intensive Care Medicine and* **Dr LS Howard** *is Consultant in Pulmonary Vascular Disease, Hammersmith Hospital, London W12 0HS*

Correspondence to: Dr LC Price

Kerbaul F, Rondaelet B, Motte S et al (2004) Effects of norepinephrine and dobutamine on pressure load-induced right ventricular failure. *Crit Care Med* **32**(4): 1035–40

Missant C, Rex S, Segers P et al (2007) Levosimendan improves right ventriculovascular coupling in a porcine model of right ventricular dysfunction. *Crit Care Med* **35**(3): 707–15

Russ RD, Walker BR (1992) Role of nitric oxide in vasopressinergic pulmonary vasodilatation. *Am J Physiol* **262:** 743–7

Smith AM, Elliot CM, Kiely DG et al (2006) The role of vasopressin in cardiorespiratory arrest and pulmonary hypertension. *QJM* **99**(3): 127–33

Anaesthetic and critical care dilemmas are coordinated by Dr Natasha Curran and Dr Ramani Moonesinghe, Research Fellows at the Centre for Anaesthesia, UCL, London

Ideas for future dilemmas can be sent to Rebecca Linssen bjhm@markallengroup.com