Applied Cardiopulmonary Pathophysiology 14: 182-184, 2010

Use of inhaled epoprostenol to improve arterial oxygenation post liver transplant in a ventilated patient with hepatopulmonary syndrome

S. J. Lustik, A. K. Chhibber

Department of Anesthesiology, University of Rochester Medical Center, Rochester, NY, USA

Abbreviations

HPS – Hepatopulmonary Syndrome

1. Introduction

Hepatopulmonary syndrome (HPS) occurs in approximately 4 to 29% of patients with liver disease [1]. Intrapulmonary vascular dilatation results in shunting and arterial hypoxemia. Although multiple treatments have been attempted with variable success, this is the first report of the acute use of inhaled epoprostenol to improve oxygenation in a ventilated patient with HPS who remained profoundly hypoxemic after liver transplantation.

2. Case Report

A 61 year old man presented to the emergency room while on vacation. He had been detained at a customs checkpoint with obvious dyspnea at rest and was found to be markedly hypoxemic. Exertional dyspnea had progressed over months, and he was subsequently diagnosed with end stage liver disease secondary to hepatitis C. Significant physical findings included clubbing of the fingers with nail bed cyanosis; he also had spider nevi on his hands. At the time of his evaluation for liver transplantation, his room air PaO2 was 37 mmHg and oxyhemoglobin saturation was 74%; supplementation with 4L oxygen by nasal cannula resulted in minimal improvement to PaO2 39 mmHg and oxyhemoglobin saturation 77%. His chest radiograph showed increased lower lobe interstitial markings, and pulmonary function tests revealed a mild restrictive defect and severely reduced diffusion capacity. On catheterization, the patient had a markedly elevated cardiac output with low filling pressures. A technetium lung perfusion scan confirmed a large right-to-left shunt, but there was no intracardiac defect on bubble contrasted transesophageal echocardiography. Shunt fraction was not formally measured. The patient did not have any other complications of cirrhosis. He was diagnosed with HPS, and he underwent uncomplicated orthotopic liver transplant.

Post-operatively, the patient remained on 100% inspired oxygen; he was easy to ventilate but refractory to PEEP. The intensivist started inhaled epoprostenol with a significant improvement in the A-a gradient and PaO2/FIO2 ratio (Table 1). The epoprostenol was titrated off over three days and the patient was extubated. A significant shunt remained, and refractory hypoxemia persisted on the surgical floor two weeks after transplantation. A computed tomography angiogram showed uniformly enlarged peripheral pulmonary arteries; branches of the right lower lobe pulmonary artery were particularly dilated. Inhaled epoprostenol was re-initiated, and pulmonary arterial branch emboliza-

Table 1: Changes in oxygen A-a (Alveolar-arterial) gradient and PaO2/FIO2 ratio after initiating inhaled epoprostenol at 01:00 on POD 1 (postoperative day 1) at 25 ng/kg/min.

Date/Time	Epoprostenol ng/kg/min	FIO2 (%)	PaO2 (mm Hg)	A-a gradient (mm Hg)	PaO2/FIO2 (mm Hg)
POD 0 23:23	0	100	50	621	50
POD 1 01:47	25	100	181	498	181
POD 1 04:07	25	60	90	300	150

tion was performed to attenuate the largest shunt. Over the remaining weeks of his hospitalization, inhaled epoprostenol was weaned. The patient was eventually discharged to home with a resting oxyhemoglobin saturation of 91% on 3 L/min oxygen. At a follow-up visit nine months post-transplantation, he had a resting oxyhemoglobin saturation of 88%; during a brief walk, he still had desaturation to 70% while using supplemental oxygen at 4 L/min.

3. Discussion

This patient with liver disease had HPS as demonstrated by hypoxemia, contrasted echocardiography, and intrapulmonary vascular dilatation. Post liver transplant, oxygenation remained inadequate despite 100% inspired oxygen. Inhaled epoprostenol resulted in a significant increase in oxygenation as demonstrated by a reduction in the alveolar-arterial gradient and an increase in the PaO2/FIO2 ratio. Although this is the first report of the acute use of epoprostenol in a ventilated patient to treat refractory hypoxemia in HPS, there is one previous report of nebulized iloprost successfully improving hypoxemia in a patient with hepatopulmonary syndrome prior to and post liver transplant [2]. In that report, the patient had a significant increase in exercise tolerance and decreased dyspnea as an outpatient.

Epoprostenol is a naturally occurring prostaglandin (PGI2) and potent vasodilator tonically produced in the pulmonary endothelium. The synthetic form is administered parenterally as a chronic outpatient therapy for pulmonary arterial hypertension [3,4]. When it is inhaled, adverse effects including systemic hypotension and VQ mismatch are attenuated. Inhaled epoprostenol has also been beneficial in reducing shunt and thus improving VQ matching and oxygenation in patients with ARDS [5]. The improvement in oxygenation in the HPS patient is likely due to the delivery method. Since inhaled epoprostenol will be best delivered to well-ventilated regions of the lung, it will cause selective vasodilation in well-oxygenated areas and draw perfusion away from poorly ventilated areas. In our patient, the largest of the dilated blood vessels was in the bases, and drawing blood flow away from there would improve oxygenation by reducing the degree of shunt.

Liver transplant frequently cures HPS, but this may take months to years [6,7]. The cause of vascular dilation may be the accumulation of vasoactive mediators, including nitric oxide, which are released in response to portal hypertension and poor bowel perfusion (1). An understanding of this hypothesis led to the use of intravenous methylene blue to block the vasodilating effects of nitric oxide [8, 9]; the strategy was successful in several patients acutely, but longer term use has not been reported. Garlic has been shown to

be successful in an outpatient setting, possibly by altering nitric oxide production. A randomized controlled trial with garlic demonstrated an improvement in oxygenation in 67% of patients taking garlic versus only one in twenty taking placebo [10].

This case illustrates the acute improvement in oxygenation with inhaled epoprostenol in a ventilated patient with hepatopulmonary syndrome. Inhaled epoprostenol may have decreased shunting by directing blood flow towards well ventilated areas. This strategy may improve the perioperative management of HPS patients with refractory hypoxemia.

References

1. Hoeper MM, Krowka MJ, Strassburg DP. Portopulmonary hypertension and hepatopulmonary syndrome. Lancet 2004; 363: 1461-1468
2. Krug S, Seyfartha H, Hagendorffb A et al. Inhaled iloprost for hepatopulmonary syndrome: improvement of hypoxemia. Eur J Gastroenterol Hepatol 2007; 19: 1140-1143
3. Humbert M, Sitbon O, Simonneau G. Treatment of pulmonary arterial hypertension. N Engl J Med 2004; 351: 1425-36
4. Kuo PC, Johnson LB, Plotkin JS et al. Continuous intravenous infusion of epoprostenol for the treatment of portopulmonary hypertension. Transplantation 1997; 4: 604-606
5. Siobal M. Aerosolized Prostacyclins. Respir Care 2004; 49: 640-652
6. Collisson EA, Nourmand H, Fraiman MH et al. Retrospective analysis of the results of liver transplantation for adults with severe hepatopulmonary syndrome. Liver Transpl 2002; 8: 925-931
7. Krowka MJ, Porayko MK, Plevak DJ et al. Hepatopulmonary syndrome with progressive hypoxemia as an indication for liver transplantation: case reports and literature review. Mayo Clin Proc 1997; 72: 44-53
8. Schenk P, Christian M, Rezaie-Majd S et al. Methylene Blue improves the hepatopulmonary syndrome. Ann Int Med 2000; 133: 701-706
9. Roma J, Balbi E, Pacheco-Moreira L et al. Methylene Blue Used as a Bridge to Liver Transplantation Postoperative Recovery: A Case Report. Transplant Proc 2010; 42: 601-604
10. De BK, Dutta D, Pal SK et al. The role of garlic in hepatopulmonary syndrome: a randomized controlled trial. Can J Gastroenterol 2010; 24 (3): 183-188

Correspondence address:
Stewart J. Lustik, M.D.
Department of Anesthesiology
University of Rochester Medical Center
601 Elmwood Avenue, Box 604
Rochester, NY 14642
USA
stewart_lustik@urmc.rochester.edu