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Patients with portopulmonary hypertension (POPH) pose significant diagnostic and therapeutic challenges from hemodynamic interpretations and choice of appropriate therapy. We are pleased to present this opinion from Dr Michael Krowka of the Mayo Clinic regarding a patient with liver disease and severe pulmonary hypertension. Dr Krowka is a pioneer in this complex field, leading the course of ongoing research.—MHP

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Question: *What are the treatment options for a 62-year-old patient with Child B cirrhosis (most likely due to alcohol abuse) presenting with severe shortness of breath with minimal exertion?*

Data: CT angiography shows dilated pulmonary arteries, right heart strain, and no intraparenchymal disease. V/Q scan negative for PE. Hepatitis and connective tissue disease serologies are negative. RHC showed the following: RAP 20 mm Hg, RV 130/22 mm Hg, PA 130/50 mm Hg, MPAP 76 mm Hg, PCWP 16 mm Hg, CO 4.9 L/min, CI 2.6 L/min/m^2, PVR 12 WU. Acute vasodilator trial demonstrated no response.

Response: POPH refers to the existence of pulmonary arterial hypertension that develops as a consequence of portal hypertension.[1] Portopulmonary hypertension is internationally recognized within Group 1 of the 2008 Dana Point classification of pulmonary hypertension.[2] Hemodynamically, POPH is defined by increased pulmonary vascular resistance (PVR) causing obstruction to arterial pulmonary flow as determined by right heart catheterization (RHC).

In genetically susceptible patients, portal hypertension is hypothesized to create a metabolic environment promoting the development of a pulmonary arterial vasculopathy, pathologically indistinct from idiopathic pulmonary arterial hypertension.[4] Such pathology includes endothelial/smooth muscle proliferation, in-situ thrombosis, and vasoconstriction.[1] The presence of any degree of POPH correlates poorly with the cause or severity of liver disease as measured by the Child-Turcotte-Pugh or Model for End-stage Liver Disease scoring systems. POPH appears to be more frequent in females and patients with autoimmune-related liver disease.[5] Portopulmonary hypertension portends a poor prognosis without medical treatment (5-year survival 14%).[3]

Portopulmonary Hypertension Diagnostic Criteria[3]

1. Existence of portal hypertension
2. RHC
   a. Mean pulmonary artery pressure (MPAP) >25 mm Hg
   b. PVR >240 dyns.s.cm^{-5}
   c. Transpulmonary gradient (TPG) >12 mm Hg[a]

   where TPG = MPAP – PCWP (pulmonary capillary wedge pressure)

   This replaces previous criteria of PCWP <15 mm Hg

Limited data suggest liver transplantation (LT) is considered high risk (35% post-transplant hospitalization mortality when untreated, pre-LT MPAP exceeds moderate levels; ie, >35 mm Hg).[1] Based on a 10-year prospective screening program from the Mayo Clinic, estimates are that 5% of all LT candidates have some degree of POPH.[6] Approximately 65% of all screened LT candidates with right ventricular systolic pressure >50 mm Hg by echo have POPH; 35% have high flow or excess volume states. Adverse prognosis of POPH is related to the severity of liver disease and reduced cardiac output.[7]

In my experience, this patient falls into the worst category of POPH because she no longer has the classic high cardiac output state as seen in most POPH patients. With the PVR of ~ 12 WU and dysfunctional RV, I would certainly favor an IV prostacyclin to start and titrate weekly and perhaps add an endothelin receptor antagonist such as ambrisentan if hemodynamics are not improved as desired. Try to avoid a beta blocker for variceal prophylaxis. Whether liver transplantation can ever be considered is problematic at this point.

Treatment options and experiences are evolving.[3,8-11] Endothelin receptor antagonists (bosentan and ambrisentan) and phosphodiesterase inhibitors (sildenafil) are the oral agents with published effectiveness in POPH. Infused prostacyclin remains the treatment of choice of many investigators for patients with severe POPH (MPAP >50 mm Hg).[1] Priority for LT in the setting of POPH remains problematic. Liver transplantation should not be attempted unless significant hemodynamic improvement, including improved right heart function, can be documented with medical therapy (current Mayo Clinic treatment targets: MPAP should be <35 mm Hg and PVR < 400 dynes s.cm^{-5}; or complete normalization of PVR [<240] in the setting of MPAP >35 mm Hg due to a high flow state). Total resolution of POPH and weaning from pulmonary vasodilator therapy after LT has been documented in more than 50% of POPH patients transplanted; others may need oral pulmonary vasomodulating therapy for control of post-LT pulmonary hypertension.[8-11]

Two multicenter studies will begin in 2010 for the exclusive treatment of POPH: one using oral ambrisentan in an open-label trial and one using open-label intravenous treprostinil as a bridge to LT.

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Components of Transitional Care for Consideration

Finally, **Table 2** lists the components of care that should be included in a transition program. Since there continues to be very limited outcomes data demonstrating the effectiveness of instituted transition models, the recommendations listed in the table have not all been validated in formal studies. Therefore, the pediatric and adult health care teams should work collaboratively to formalize a transition program that best meets the patients' needs.

Conclusion

Current practices to transition care of adolescent patients with a chronic disease demonstrate that health care providers must improve their practice to meet the needs of these patients. Understanding the factors that impact the development of adolescents with PAH and implementing the essential components of transitional care into practice may help to provide these patients with the knowledge and skills necessary to independently and safely manage their own care. The demands of PAH therapies, and the complex and serious nature of this disease warrant health care providers to prioritize the implementation of an effective transition program in order to truly provide comprehensive care that meets the medical and psychological needs of these adolescents.

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