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Non-Restrictive Ductal Patency in Management of Cardiac Failure in Congenital Diaphragmatic Hernia – Non-Invasive Biventricular Assist

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Abstract

The pulmonary vascular resistance (PVR) is elevated to some extent in all patients with congenital diaphragmatic hernia (CDH). In those with severely elevated PVR closure or restriction of a previously patent ductus arteriosus (PDA) can precipitate hemodynamic compromise secondary to acute heart failure. Maintaining ductal patency in this subset of patients is not a well-established therapeutic strategy. This report reviews the potential utility of maintaining ductal patency by discussing the pathophysiology and reviewing the published literature.

Keywords: Heart failure; Pulmonary hypertension; Congenital diaphragmatic hernia; Patent ductus arteriosus

Introduction

Closure of a patent ductus arteriosus (PDA) in patients with congenital diaphragmatic hernia (CDH) and severe elevation of pulmonary vascular resistance (PVR) can precipitate hemodynamic instability secondary to acute heart failure. The use of prostaglandin E1 (PGE1) to maintain a PDA to treat acute heart failure in patients with CDH is not well described in standard texts and is variably utilized based on institutional protocols either as standard or as rescue therapy [1-5].

In this report we will review the pathophysiology of acute heart failure precipitated by PDA closure or restriction and discuss the rationale to reopen the ductus arteriosus (DA) based on published literature.

Patient History

A 4.0 kg female infant with an antenatal diagnosis of left-sided CDH delivered spontaneously at term (Figure 1). Postnatal management included endotracheal intubation, sedation, neuromuscular blockade, intestinal decompression, high frequency ventilation, surfactant replacement and inotropic support. Initial pulmonary vasodilator therapy included 100% oxygen and inhaled nitric oxide (iNO). The pre-ductal saturation ranged from 80 to 93% and umbilical arterial blood gas parameters ranged from a pH of 7.14 – 7.40, $PaCO_2$ 38-71 torr and PaO_2 of 21 to 50 torr. Initial echocardiogram showed a structurally normal heart with bidirectional shunting at the level of the patent foramen ovale (PFO) and PDA. The estimated pulmonary artery pressure (PAP) was near systemic [tricuspid regurgitation (TR) 57 mm Hg, systemic blood pressure (SBP) = 65-75/44-49 mm Hg]. After the initial period of relative stability the patient developed acute progressive cardiorespiratory failure at 15 hours of age refractory to medical management including additional pulmonary vasodilator therapy with prostacyclin (PGI 2) (maximum dose limited by systemic hypotension), volume resuscitation and escalating inotropic support (epinephrine 1.8 mcg/kg/min, milrinone 0.5 mcg/kg/min, dopamine 15 mcg/kg/min). The patient had clinical evidence of poor systemic oxygen delivery evidenced by low mixed venous saturations, progressive lactic acidosis and acute kidney injury. Continuous renal replacement therapy was initiated to control volume overload. An echocardiogram was repeated and showed a restrictive PDA with right to left shunt, severe TR predicting supra-systemic PAP (TR 95 mm Hg, SBP 55/40 mm Hg), severe right ventricular (RV) dilation with septal bulge into the left ventricle (LV), and moderately reduced RV systolic function.

Extracorporeal membrane oxygenation (ECMO) was not available at our institution. Therefore we decided to initiate PGE1 (0.05 mcg/kg/min) to establish nonrestrictive ductal patency with the goal of decompressing the hypertensive pulmonary circuit, providing RV afterload reduction, and augmenting systemic cardiac output. There was rapid improvement (an hour) in systemic perfusion and oxygen delivery without significant worsening of systemic hypoxemia (secondary to larger right to left PDA shunt). Echocardiographic reassessment now showed a non-restrictive PDA with right to left shunting, improved RV systolic function, reduction in severity of TR, reduction in PAP from supra-systemic to systemic (TR 65 mm Hg, SBP 65/45 mm Hg), decreased septal shift (less LV compression). Over the next 24 hours inotropic support was weaned, there was resolution of metabolic acidosis and the patient underwent routine management for CDH. PGE1 infusion was discontinued 32 hours later when a pure left-to-right shunt was noted. Uncomplicated surgical repair was performed at 120 hours of age. Twenty-four hours following surgery, renal replacement therapy and iNO were discontinued, sildenafil was concomitantly started. She was discharged home at two weeks of age without oxygen and with sub-systemic PAP. Sildenafil was weaned off over the next 6 weeks. Her echocardiogram after discontinuing sidenafil shows a structurally and functionally normal heart with mild

TR, normal predicted PAP, normal RV size and function, and spontaneous closure of the PDA. At the most recent follow up at 7 years of age our patient is asymptomatic with normal growth.

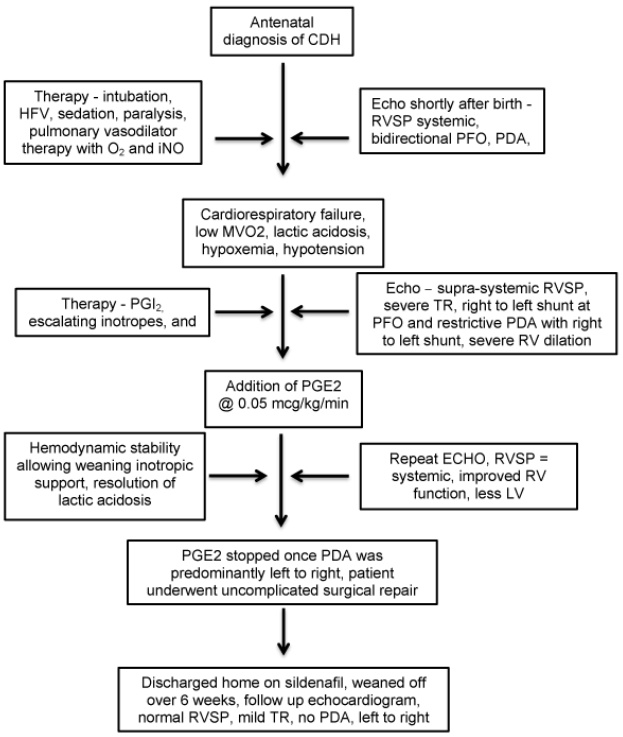

Figure 1: Hospital course of patient with antenatal diagnosis of congenital diaphragmatic hernia

Discussion

Severity of pulmonary hypertension (PH) determined by severity of pulmonary hypoplasia is the final determinant of prognosis of patients with CDH. A subgroup of patients with severely elevated PVR can present with acute heart failure after closure or restriction of a previously open DA. Our patient had severe PH but was initially stable with usual treatment protocols. Acute hemodynamic worsening prompted echocardiographic reassessment which showed evidence of acute right heart failure and severe PH. Reopening of the DA with PGE 1 resulted in reversal of the detrimental effects and allowing the right ventricle to support systemic circulation.

Closure or restriction of the PDA in patients with severe elevation of PVR can precipitate acute heart failure (Figure 2). Ductal closure or constriction results in further increase in already elevated RV afterload and causes RV dilation which in turn causes/worsens TR (annular dilation). The resulting right atrial dilation and pressure as well as the TR jet increase the magnitude of right to left shunting at the atrial level worsening systemic hypoxemia. RV dilation causes ventricular septal shift/bulge into the LV and limits LV filling and contributes to diastolic dysfunction, pulmonary venous hypertension which in turn worsening PAP (usually nonresponsive to NO) and limits systemic cardiac output. Systemic cardiac output is also reduced by loss of RV contribution to post ductal systemic flow. Systemic hypoxemia and decreased cardiac output result in failure of systemic oxygen delivery and consequently metabolic acidosis. All of these factors in turn increase PAP and PVR which then perpetuate a vicious cycle of acute heart failure worsening PAP and PVR.

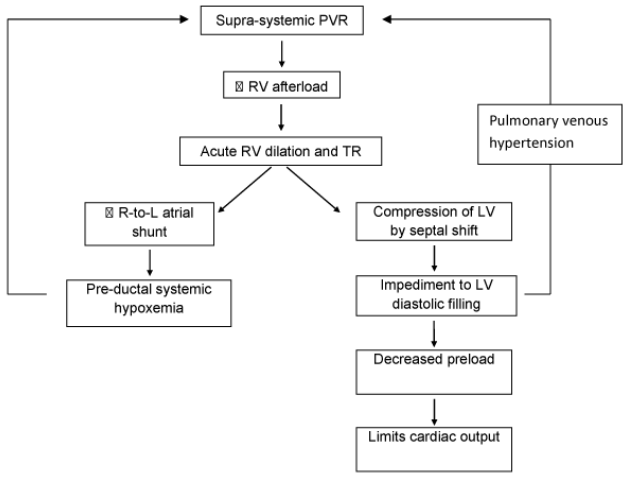

Figure 2: Ductal constriction/closure induces a vicious cycle in patients with CDH

Reopening of a previously closed or restrictive PDA can be beneficial in the setting of acute heart failure precipitated by ductal closure (Figure 3). A PDA sets a ceiling for the PVR to be no greater than the systemic vascular resistance (SVR). Reduction in RV afterload improves RV function and reduces RV dilation. These factors reduce TR and ventricular septal shift. As a result there is improved LV filling and diastolic function, reduced pulmonary venous hypertension and reduction in right to left shunt across the atrial septum improving systemic oxygenation. The PDA also augments postductal systemic output. Since ductal opening increases right to left shunt there is potential for worsening of systemic hypoxemia and this should be anticipated. Therefore PGE1 should never be used before maximizing pulmonary vasodilator therapy and oxygenation.

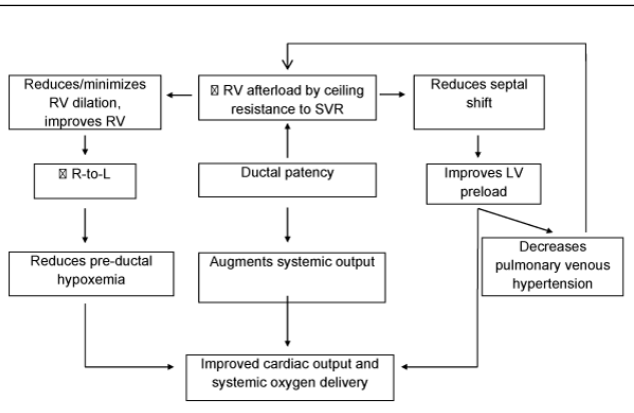

Figure 3: Rationale for maintaining ductal patency with PGE1

The utility of PGE1 to maintain a PDA is limited to published literature of case reports, retrospective case series, and expert opinion [1-5]. Buss et al. and Filan et al. have reported rescue of infants using

PGE1 to reestablish ductal patency [3,4]. These authors used PGE1 as rescue therapy based on clinical and echocardiographic evidence of acute heart failure with spontaneous ductal closure. Reopening of the PDA allowed interruption of the vicious cycle described above and successful treatment to discharge. Inamura et al. reported 19 patients, prostaglandin was used to maintain ductal patency if echocardiographic right to left shunt exceeded the left to right shunt with excellent outcomes 94.7% survival [2]. Echocardiograms were performed at birth and on day 2. The patients who received PGE1 were more likely to have smaller LV diastolic dimension, smaller pulmonary artery diameter indexed to body surface area (BSA), and a higher LV Tei index of combined myocardial systolic and diastolic performance even though the LV ejection fraction was not different between the groups. This supports the notion that LV diastolic dysfunction and pulmonary artery size together determine the severity of elevation in PVR and PH. Shiyanagi et al. on the other hand compared the outcome of 49 patients in two eras; in the earlier era all patients were treated with PGE1 and in the later era no PGE1 was used [1]. This series does not report details of the echocardiograms in the two groups. They showed no difference in the outcomes between the two groups (70% survival) and suggested that PGE1 was not beneficial and was associated with earlier surgery and shorter hospital stay.

Patient likely to benefit from PGE1 to maintain a PDA can be identified by clinical criteria including new onset worsening of pre-ductal saturation, loss of saturation difference between the upper and lower limbs, and acute right heart failure or by echocardiographic assessment in patients with new onset clinical deterioration after a relatively stable course [5,6]. Echocardiographic findings of supra-systemic PAP, worsening TR, RV septal shift compressing the LV, depressed RV systolic function, and finding of a closed DA or restriction at the ductal level (a right to left gradient across the PDA) all suggest patients that may benefit from ductal patency.

Echocardiography is now routinely used in the evaluation and management of cardiopulmonary interactions in patients with CDH. Assessment includes estimating the pulmonary artery pressure and intracardiac right to left shunting (PFO and PDA), the status of the PDA, surrogates for severity of CDH such as branch pulmonary artery size, left ventricular diastolic dimension, ventricular systolic performance (subjective and ejection fraction) [1,2,7]. Diastolic left ventricular dysfunction is increasingly recognized but difficult to quantify. There is growing literature utilizing objective measures of diastolic ventricular performance (routinely used adults) such as tissue Doppler imaging and the Tei index in children with CDH and normative data is being generated [2,8]. Utilization of these novel echocardiographic parameters in addition to current echocardiographic protocols may allow us to better understand and objectively define cardiovascular profile of this patient population and target and tailor the treatment approach.

We believe that similar to Inamura et al., selective use of PGE1 to maintain PDA in patients with echocardiographically confirmed evidence of acute heart failure and spontaneous ductal closure is beneficial to restore hemodynamic stability. Only further studies will be able to define if this selective strategy is beneficial or not, the optimal timing for initiation of PGE1, and the duration for which PGE1 should be continued.

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