Point:Counterpoint: Hypoxia is/is not the optimal means of reducing pulmonary blood flow in the preoperative single ventricle heart

POINT: HYPOXIA IS THE OPTIMAL MEANS OF REDUCING PULMONARY BLOOD FLOW IN THE PREOPERATIVE SINGLE VENTRICLE HEART

Patients with single ventricle are often quite ill and present complex management dilemmas. The distribution of blood flow to the systemic and pulmonary circulations, which in this patient population are in parallel rather than series, depends primarily on the relative resistances of the respective vascular beds. The entire cardiac output is managed by the single ventricle and must somehow divide itself between the systemic and pulmonary circuits. As pulmonary vascular resistance decreases after birth, many of these children will suffer from overcirculation into the pulmonary circuit. In patients with ductal-dependent systemic circulation, such as hypoplastic left heart syndrome, this can result in a paucity of systemic circulation with concomitant acidosis (Fig. 1A).

It was over 60 years ago that the idea of hypoxia-induced pulmonary vasoconstriction was first proposed, and this idea has been put to the test and validated many times in the past half century. In the normal heart, hypoxia to segments of lung, typically due to atelectasis or infiltrate, induces local pulmonary vasoconstriction, which minimizes ventilation-perfusion mismatching. For a patient with normal heart and lungs, this is a very effective way of limiting intrapulmonary right to left shunting of deoxygenated blood, thereby maintaining stable arterial oxygen saturations.

It is generally accepted that balancing the pulmonary (Qp) and systemic blood flows (Qs) is the best way of stabilizing the circulation in patients with single ventricle. These patients, however, often respond very differently to common interventions such as the administration of oxygen and mechanical ventilation. How will the pulmonary vascular bed of a single ventricle patient respond to not just isolated lung segment hypoxia but to global hypoxia?

Barnea et al. (1) developed a wonderful mathematical model of the univentricular circulation and tested it through various manipulations of cardiac output, systemic arterial and venous oxygen saturations, pulmonary venous oxygen saturations, and Qp:Qs. He demonstrated that maximal oxygen delivery to the tissues would be obtained by Qp:Qs slightly <1 and that for higher Qp:Qs ratios, oxygen delivery to the tissues would actually decrease. He also showed that with systemic arterial oxygen saturations greater than a certain value that was determined by cardiac output (typically in the 70–85% range), oxygen delivery falls off precipitously.

Various approaches aimed at normalizing Qp:Qs by either decreasing Qp or increasing Qs have been advocated by different authors (2, 5, 6, 7, 10). Controversy exists, however, as different centers with different approaches typically have equally good results with this patient population. Determining the optimal means of reducing Qp and thereby stabilizing circulation in the univentricular heart continues to be debated, although methods that mimic the stable fetal circulation seem to be most effective. In the womb, the fetus is hypoxic with oxygen saturations between 30 and 60% (3); pulmonary vascular resistance is high, and systemic vascular resistance is low, with systemic blood flow being supplied by the ductus arteriosus. Hypoxia allows one to duplicate this stable physiology in the newborn infant (Fig. 1B).

Using his mathematical model, Barnea calculated that ideal Qp:Qs balance would be obtained in patients with hypoplastic left heart syndrome by keeping arterial blood gases near the following parameters: pH ~7.4, arterial partial pressure of carbon dioxide (PaCO2) ~40 mmHg, with arterial partial pressure of oxygen (PaO2) ~40 mmHg, and arterial saturation ~75%. This, he suggests, could easily be managed by maintaining the patient in either room air, or by creating an hypoxic environment by adding additional nitrogen to lower the inspired concentration of oxygen.

Reddy developed a fetal animal model of single ventricle physiology in lambs and tested various therapies aimed at altering pulmonary vascular resistance and flow and measured arterial oxygen saturations to the tissues would be obtained by Qp:Qs...
several hemodynamic parameters (8). As one would expect, 100% oxygen proved to be a potent pulmonary vasodilator and resulted in a significant decrease in pulmonary vascular resistance with subsequent dramatic increase in Qp:Qs. Hypoxia produced a significant increase in pulmonary artery pressure of >20% that of baseline. Additionally, there was a significant decrease in systemic arterial pressure of >10% with subsequent decrease in Qp:Qs by over 32% to an average value of 1.19 (Fig. 1B). As shown by Barnea et al., Qp:Qs values near 1 are important for optimal tissue oxygen delivery in the univentricular patient.

An excellent study by Tabbutt et al. (9) looked at hypoxia and hypercarbia in patients with hypoplastic left heart syndrome before surgical palliation. They found that both hypoxia and hypercarbia decreased the Qp:Qs. Hypercarbia, however, was associated with a significant increase in the PaCO2 and hypercarbia decreased the Qp:Qs. Hypercarbia, however, was associated with a significant increase in the PaCO2 and decrease in pH. Hypoxia, on the other hand, is well tolerated in the newborn. The persistence of fetal hemoglobin in these infants allows for better tissue oxygen delivery at lower PaO2, similar to that of the fetus, when oxygen saturations between 30 and 60% are typical (3).

Day et al. (2) reported a series of patients with hypoplastic left heart syndrome and similar lesions treated effectively with hypoxia. They were able to increase the inspired nitrogen to maintain systemic oxygen saturations near 75% (2). For those being supported through mechanical ventilation, this was accomplished via the respiratory circuit. For those breathing spontaneously, additional nitrogen was supplied via nasal cannula. Eighty percent survived to either transplant or 1st stage palliation, whereas the 20% that died did so at 1–3 mo of age while awaiting transplant. Autopsy of these patients did not yield any hypoxia-induced pulmonary vascular changes. This study also commented that there were no instances of necrotizing enterocolitis (NEC) despite enteral feeding. NEC is a serious complication in premature infants and infants with ducal-dependent systemic circulation. It is felt that decreased oxygen delivery to the intestinal wall and diminished perfusion pressure related to the diastolic flow run off across the ductus arteriosus, combined with the increased metabolic demands associated with enteral feedings, play a role in the development of NEC (4). For this reason, many institutions delay enteral feedings in patients with ducal-dependant univentricular circulation until after surgical palliation. The authors of this paper suggest that this decreased incidence of NEC was due to improved bowel perfusion and tissue oxygen delivery related to increasing pulmonary vascular resistance, thereby decreasing diastolic flow reversal in the systemic circulation. This allowed for earlier enteral feedings and improved nutrition prior to surgical intervention.

In conclusion, hypoxia is the optimal means of reducing pulmonary blood flow in preoperative patients with single ventricle hearts. This can easily be facilitated by increasing nitrogen in the inspired gases without the need for mechanical ventilation in most patients. This allows for more normal newborn behaviors such as enteral feeding and being held by the parents prior to surgical palliation. The hypoxia itself is well tolerated in newborns with persistence of fetal hemoglobin, more readily mimicking the fetal state in which they were so stable.

COUNTERPOINT: HYPOXIA IS NOT THE OPTIMAL MEANS OF REDUCING PULMONARY BLOOD FLOW IN THE PREOPERATIVE SINGLE VENTRICLE HEART

Single ventricle physiology, as exemplified by hypoplastic left heart syndrome (HLHS), is characterized by complete intracardiac mixing of pulmonary and systemic venous return and a functional single great artery. As pulmonary vascular resistance (PVR) falls in the early postnatal period, blood flow is diverted to the lungs (Qp), often at the expense of the systemic (Qs) and coronary circulations (14). This Qp:Qs mismatch imposes three physiological perturbations: 1) excessive Qp leads to pulmonary edema and tachypnea and hence augments the global metabolic rate, 2) excessive Qp results in an added volume load to the single ventricle, with that chamber often seeing three to four times its intended volume, resulting in ventricular dysfunction and valvar regurgitation, and 3) Qs may fall, leading to diminished oxygen delivery (DO2), acidosis, necrotizing enterocolitis, renal and hepatic dysfunction, and other complications (14, 18). We contend that therapeutic hypoxia by administration of inhaled nitrogen (N2) can address some of these concerns; but is inadequate in severe cases where augmented oxygen delivery is needed most. Additionally, we assert there are therapies that are ultimately superior to hypoxia for some clinical scenarios.