Commentary: If a little is good, more must be better?

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In the current issue of the Journal, Liu and colleagues\(^1\) explore optimal perfusate oxygenation (PpO\(_2\)) in children who underwent cardiac surgery and evaluated the relationship among PpO\(_2\), systemic inflammatory response syndrome, and geographical altitude. They defined high altitude as greater than 500 m above sea level, which is lower than the usual definition of high altitude at approximately 2400 m above sea level. In this study, they showed a steeper association between PpO\(_2\) and the risk of severe systemic inflammatory response syndrome in patients from a low altitude than in patients from a high altitude. Their analysis suggested that patients from a low altitude might have the best outcomes with lower doses of PpO\(_2\), whereas patients from a high altitude might have the best outcomes with the optimal PpO\(_2\) of approximately 250 to 350 mm Hg.\(^1\)

It is not uncommon for one to approach a problem from the perspective that if a little is good, more must be better. However, Liu and colleagues\(^1\) and others\(^2,3\) have shown us that this is not necessarily true when it comes to cardiopulmonary bypass (CPB) in congenital heart disease. In a study by Caputo and colleagues,\(^4\) 67 cyanotic patients were randomized to receive controlled normoxic (50-80 mm Hg) or hyperoxic (150-180 mm Hg) CPB. Termination of CPB was 100 to 110 mm Hg for the normoxic group and the hyperoxic group with fraction of inspired oxygen (FiO\(_2\)) on CPB up to 100\% to maintain saturations greater than 95\%. Further, anesthesia was induced at an FiO\(_2\) of 0.21 in the normoxic group and 0.50 in the hyperoxic group. They showed that controlled reoxygenation on starting CPB was associated with reduced myocardial damage, oxidative stress, and cerebral and hepatic injury compared with hypoxic bypass. In their study, there was no discussion of actual peak PpO\(_2\). A study by Babu and colleagues\(^5\) randomized 31 cyanotic children to 1 of 2 groups: Group 1 had CPB initiation with FiO\(_2\) 0.21, and after 1 minute of full bypass, FiO\(_2\) was increased at increments of 0.1 per minute until reaching 0.6. Group 2 was initiated using FiO\(_2\) 0.6. After 5 minutes in both groups, arterial blood gas analysis was performed and PpO\(_2\) was maintained at 200 to 300 mm Hg. They found that a controlled oxygenation protocol was associated with significantly lower postoperative creatine phosphokinase myocardial band (CPK-MB) levels and decreased ventilation time. Again, they did not discuss peak PpO\(_2\) in their study.\(^5\)

There are numerous factors that appear to influence systemic inflammation reactions after CPB, and these include contact of blood with the CPB circuit, surgical operation, blood loss, and blood/blood product administration. Ultimately, a team approach toward congenital heart surgery to confront these issues should be applied. The problem with CPB is there is no accepted definition of optimal perfusion, and there is a continuum of quality ranging from adequate, sufficient, or minimally acceptable that progresses through superior, optimal, or maximal.\(^6\) Minimizing

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CENTRAL MESSAGE
Multiple variables including hyperoxygenation affect systemic inflammatory response syndrome with CPB. Electronic perfusion records and perfusion registries might provide a way to compare perfusion strategies and define best practices.
systemic inflammatory response is the goal for every CPB case. Ultimately, the approach is a “prescriptive perfusion” individualized to each patient. Circuit miniaturization, including biocompatible oxygenator (integrated filter), and tubing (arterial, venous, sucker, and sumps) can lessen the overall surface area of the bypass circuit, minimizing blood exposure and reducing the quantity administered while maximizing the desired target hematocrit on CPB. Ultrafiltration, especially when blood products are used in the prime, should be considered and the prime composition normalized to mimic patient arterial blood gas and electrolyte analysis and maintained for initiation of CPB. Bypass should be initiated with a PpO2 as close to the patient’s partial pressure of oxygen and maintained within a relatively normoxic target, as long as adequate oxygen delivery is achieved. Best efforts should be given toward reduction in blood transfusions through meticulous hemostasis, circuit miniaturization, blood sampling (volume and quantity), and establishment of and adherence to guidelines for blood and platelet transfusions.

The one issue in the study by Liu and colleagues is that it was based on the highest PpO2 during aortic occlusion, and that one time point after aortic occlusion may be too late for cause and effect.

One concern with the work looking at normoxic and hyperoxic CPB research is the variation in the definition of each. Further, because many aspects of the perfusion technique can contribute to the overall inflammatory response, there should be greater detail provided in the perfusion technique, especially to prime volume, circuitry used, and blood products used, in addition to the PpO2 and how that component was managed. With the advent of electronic perfusion records, and the use of inline blood gas analyzers, the ability to capture actual PpO2 at 10 seconds or less time intervals, and at precise time points, is now available. The significance of being able to do clinical research and report average PpO2 before crossclamp, average during crossclamp, average or actual at crossclamp removal, and at termination of CPB should lend a more significant evaluation of techniques and help define best practice in the future. The development of a pediatric/congenital perfusion registry to submit perfusion-related parameters is necessary to begin to define best practices so that we may eventually be able to compare practices and better define optimal perfusion.

Meanwhile, until we are able to overcome these challenges and variations in CPB research to produce tangible evidence of best perfusion practice, the studies by Liu and colleagues and others suggest that instead of “if a little is good, more must be better,” we should consider that possibly “less is more.”

References