LETTERS TO THE EDITOR

Inhaled nitric oxide after Glenn and Fontan procedures

To the Editor:

I read with interest the article by Gamillscheg and associates¹ concerning the use of inhaled nitric oxide in patients with high systemic venous pressures after a bidirectional Glenn shunt or modified Fontan procedure. When inhaled, nitric oxide is a selective pulmonary vasodilator in many patients with increased pulmonary vascular resistance. Thus nitric oxide may potentially assist patients with right heart failure after surgical palliation or repair. The authors correctly state that "even a small reactive increase of PVR [pulmonary vascular resistance] may cause deleterious systemic venous hypertension associated with resistant low cardiac output syndrome" in this subset of patients. However, their study does not provide any evidence that inhaled nitric oxide improved the immediate or long-term outcome of their patients.

Patients were treated with inhaled nitric oxide if the pulmonary pressure exceeded 20 mm Hg or the transpulmonary pressure gradient exceeded 10 mm Hg. There were no controls to determine whether these elevated pressures may have spontaneously improved without inhaled nitric oxide therapy. Further, the authors did not determine whether patients had significant pulmonary endothelial dysfunction at the onset of therapy. After 12 to 18 hours, therapy was abruptly withdrawn for 5 minutes and hemodynamic and oxygenation measurements were repeated. The authors used these data to calculate significant "improvements" in pulmonary pressure, transpulmonary pressure gradient, and oxygenation. Unfortunately, the acute changes after nitric oxide withdrawal may have simply resulted from the suppression of endogenous nitric oxide production by inhalation therapy.²

Goldman and associates³ have also reported a favorable hemodynamic effect of inhaled nitric oxide in patients after the fenestrated Fontan procedure. Unfortunately, they also had no controls and 50% of their patients with an oxygen saturation less than 85% subsequently died. Nonetheless, they recommend that nitric oxide be used after a fenestrated Fontan procedure if the oxygen saturation is less than 85% and/or the transpulmonary gradient exceeds 12 mm Hg. Perhaps appropriate patient selection may be a more effective alternative than inhaled nitric oxide in the palliation of functional single ventricle.

In my opinion, the beneficial effects of inhaled nitric oxide in patients with postoperative pulmonary hypertension have been overstated and not adequately documented by even small controlled studies. The reports of Gamillscheg,¹ Goldman,³ and their associates underscore the need for carefully designed studies

in determining the safety and efficacy of inhaled nitric oxide.

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REFERENCES

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Reply to the Editor:

We would like to thank Dr. Day for his comments relating to our article.¹ On the basis of our study design, we cannot rule out whether the elevated central venous pressures and the transpulmonary pressure gradients may not have spontaneously improved without inhaled nitric oxide treatment in our study patients. However, diagnoses, preoperative selection criteria (in particular pulmonary vascular resistance), surgical technique, and perioperative and postoperative management of the study patients did not differ from those of other patients undergoing the Fontan procedure during the study period; these patients did not meet our selection criteria for nitric oxide treatment: central venous pressure greater than 20 mm Hg or transpulmonary pressure gradient greater than 10 mm Hg. As stated in our article, treatment with inhaled nitric oxide was started after conventional therapy had failed to improve the hemodynamic state. Previously, Kirklin and associates² demonstrated a continuous relation between elevated right atrial pressures early after the Fontan operation and the probability of death or take-down within 30 days after the operation. They reported a probability of death or Fontan takedown of 38% and 52% when the right atrial pressure 3 hours after operation exceeded 20 and 22 mm Hg, respectively. Only one of our 13 patients died in the early postoperative period. This patient died of cerebral hemorrhage 5 days after being weaned from nitric oxide therapy, in stable hemodynamic condition. Among the remaining 12 patients, there was only one late death, which occurred 14 months after the