LWMHs cannot be monitored in the operating room and they are poorly neutralized by protamine, resulting in excessive postbypass bleeding.

Third, did the prophylactic cocktail provide protection or was it unnecessary? As Dr Bray states, this remains unknown in the absence of further immunologic investigation of the patient's previous adverse response to heparin. Measurement of plasma histamine concentrations would have aided this distinction: normal levels would suggest prior allergy to the preservative or to porcine heparin, whereas substantially increased concentrations would occur with an allergic response blocked with histamine antagonists. Steroid inhibition of histamine release provides an exception to this logic.

Fourth, should cimetidine play a role in protection from anaphylactoid reactions? Theoretically, it may exacerbate an anaphylactic response by blocking H_2 feedback receptors on mast cells. Its use for this purpose remains controversial. Finally, do the potential deleterious effects of epinephrine infusion (tachycardia and hypertension in this woman with coronary artery disease) outweigh any protective effect on anaphylaxis? Most likely so, because the treatment of anaphylaxis requires very large doses of epinephrine compared to the dose administered, 5 μg/min. However, that dose does substantially increase heart rate.

Dr Bray describes the successful management of a suspected lethal intervention. Many of the measures undertaken will prove useful to others placed in a similar situation.

Jan Charles Horrow, MD
Department of Anesthesiology
Hahnemann University
Philadelphia, PA

Use of Inhaled Nitric Oxide to Reduce Pulmonary Hypertension After Heart Transplantation

To the Editor:

Right ventricular dysfunction is a relatively frequent complication of heart transplantation, often due to preexisting pulmonary hypertension in the recipient. It has been noted that a transpulmonary gradient (TPG = mean pulmonary artery pressure minus pulmonary capillary wedge pressure) greater than 15 mmHg and/or a pulmonary vascular resistance (PVR) greater than 400 dynes · sec · cm^{-5} is associated with right ventricular dysfunction and a significant increase in perioperative mortality.[1-3] Isoprenaline and sometimes prostacyclin have been used to overcome this problem. Neither of these drugs, however, is a selective pulmonary vasodilator and may induce or worsen an already existing systemic hypotension. Recent reports, however, suggest that inhaled nitric oxide (NO) is a selective pulmonary vasodilator,[4-6] devoid of significant effects

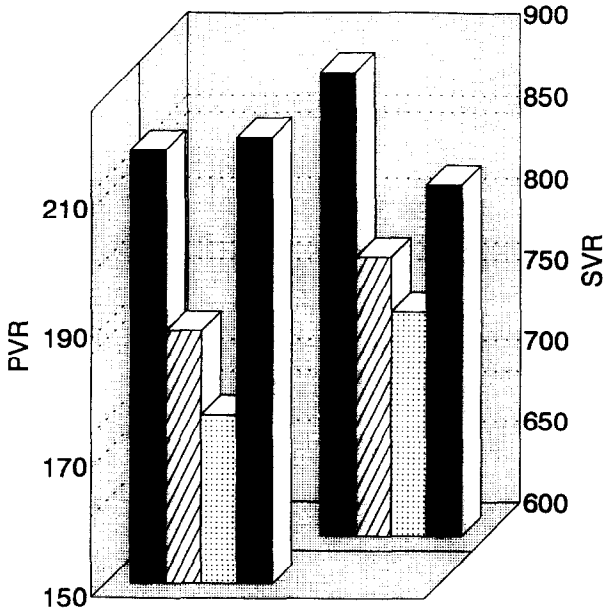

Fig 1. ■, baseline; ▨, 10 minutes NO; □, 20 minutes NO.

on the systemic circulation. We report the use of 40 ppm NO by inhalation via a ventilator in a patient after heart transplantation, known to have a preoperative TPG of 12 mmHg, who received the heart from a relatively small donor.

At the end of cardiopulmonary bypass (CPB) inodilator therapy consisting of dopamine, 7 μg/kg/min, and isoprenaline, 10 ng/kg/min was started. Weaning from CPB was uneventful. In the intensive care unit, baseline hemodynamic measurements were performed and the infusions of dopamine and isoprenaline were continued. Baseline systemic vascular resistance (SVR) was 885 dynes · sec · cm^{-5}, PVR was 217 dynes · sec · cm^{-5} and TPG 12 mmHg. During inhalation of 40 ppm, NO measurements were made at 10 and 20 minutes (Fig 1), SVR decreased from 885 (baseline) to 772 and 738 dynes · sec · cm^{-5} (10 and 20 minutes NO). PVR fell from 217 (baseline) to 189 and 176 dynes · sec · cm^{-5} (10 and 20 minutes NO). TPG decreased from 12 (baseline) to 11 and 10 mmHg (10 and 20 minutes NO). Ten minutes after the last NO was given, SVR increased to 817 dynes · sec · cm^{-5}, PVR to 219 dynes · sec · cm^{-5}, and TPG increased to 12 mmHg (Fig 1). The response to NO in previous studies on PVR[4,5] were reproducible in this patient, although the time course was longer (20 minutes compared to 5 or 6 minutes).

One can only speculate whether changes in the alveolar epithelium following CPB or histologic changes in the pulmonary vessels due to longstanding pulmonary hypertension in our patient may account for a slower diffusion of NO and/or slower response of the vascular smooth muscle cells. Of greater interest in patients after heart transplantation however is the ability of a drug to reduce TPG because of the implications for perioperative mortality. Inhaled NO may have a useful role both as an alternative to and in conjunction with isoprenaline during weaning from CPB in pulmonary hypertension. In contrast to previous work[4,5] we believe that NO may induce some systemic vasodilatation. Whether NO is also bound to proteins other than oxyhemoglobin, which may then release NO or NO-containing compounds further downstream in the systemic circulation, has yet to be elucidated. In one study,[6] a statistically significant decrease in SVR was noted, whereas other studies[4,5] only showed a tendency towards a decrease in SVR that is not reported to be statistically significant. Methemoglobin levels increased during NO administration to a maximum of 1% and decreased again after NO inhalation was stopped. It is interesting to note that no methemoglobin could be measured after 10 minutes NO inhalation. It only appeared after 20 minutes, which could reflect a slow diffusion of NO from the alveoli to the vessels.

Our data suggest that the inhalation of NO may be a useful new therapeutic technique to decrease PVR and TPG, and hence reduce the risk of right ventricular dysfunction during weaning from CPB following heart transplantation. In addition, data from this case indicate that it takes longer to act in this situation than previously reported. Also, its action is not entirely confined to the pulmonary vasculature but some systemic vasodilatation seems to occur.

Luc Foubert, MD
Ray Latimer, FFARCS
Amo Oduro, FFARCS
Stephen Gray FRCAnaes
David Snow, FRCAnaes
John Wallwork, FRCS
Stephen Large, FRCS
Department of Anaethesia
The Transplant Unit
Papworth Hospital
Cambridge, UK

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