Use of Inhaled Nitric Oxide (iNO) in the Preoperative Evaluation and Management of Heart Transplant Recipients with Pulmonary Hypertension

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Introduction: Inhaled nitric oxide has been successfully used as a selective pulmonary vasodilator to treat pulmonary hypertension in various disease states. Elevated pulmonary artery pressures (PAP) and irreversibility of elevation of the pulmonary vascular resistance (PVR) are known to be significant risk factors determining postoperative morbidity and outcome in heart transplant recipients. Therefore, severe pulmonary hypertension with fixed PVR generally precludes patients from being candidates for isolated heart transplant. This study aimed to: 1) Assess the efficacy of 100% O_2 and iNO in further decreasing PAP and demonstrating reversibility of PVR, after initial therapy with intravenous vasodilators; 2) Study the dose- response effect of two different doses of iNO on hemodynamic parameters.

Methods: After IRB approval and patient consent, 26 adults with dilated or ischemic cardiomyopathy and pulmonary hypertension were included in the study. These patients were admitted to ICU for the management of heart failure and a heart transplant evaluation. Medical therapy with intravenous vasodilators (NTG, NTP) and inotropes (Dopamine, Dobutamine, Milrinone) was instituted to optimize hemodynamics, as per a standard unloading protocol. At baseline, seven subjects received supplemental oxygen (1-2 L/min). Baseline hemodynamic parameters were recorded after maximal medical optimization. All patients were administered 100% O_2, iNO at 20ppm and 40ppm in sequential order, each for a duration of 15 minutes via a tight face mask. Hemodynamic parameters were measured at the end of each treatment period.

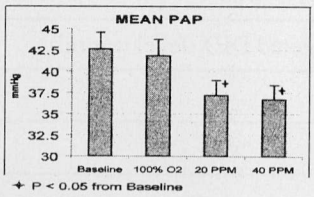
Results: 1) No statistical change was noted in any of the hemodynamic parameters between baseline and 100% O_2 groups (P>.05). (See Tables 1 and 2.) 2) At baseline, Mean Pulmonary Arterial Pressure (MPAP), Pulmonary Vascular Resistance Index (PVRI), Transpulmonary Gradient (TPG), Right Ventricular Stroke Work Index (RVSWI) were 42.6, 785, 21.2, and 13.7. After administration of 20 ppm iNO, these parameters decreased by 15%, 25%, 25%, 27%, respectively, (P<.05). No further change was noted upon increasing the dose to 40ppm. (See Figures 1 and 2.) 3) HR, MAP, SVRI, CI remained unchanged (P>.05) after administration of 100% O_2, 20ppm iNO and 40ppm iNO. (See Tables 1 and 2.)

Conclusions: As reported previously, iNO is an effective selective pulmonary vasodilator. The results of this study suggest that administration of iNO provides additional lowering of MPAP and PVR, even after presumed optimization with intravenous vasodilators. Positive response to iNO in the preoperative period can identify the heart transplant recipients, who may benefit from this RV afterload reducing therapy in the immediate postoperative period. Administration of 100% O_2 did not improve any of the hemodynamic parameters. Moreover, there is minimal additional benefit in the clinical response upon increasing the dose of iNO from 20ppm to 40ppm, while cost and the potential for adverse effects may be increased.

Table 1: Data Summary

	MAP	MPAP	CI	SVRI	PVRI	TPG	RVSWI
Baseline	64.42∀1.45	42.6∀1.9	2.19∀.03	1979∀66	785∀62.	21.2∀1.6	13.7∀1.2
100% O_2	65.15∀1.18	41.8∀1.9	2.17∀.03	2025∀58	754∀61	20.3∀1.6	13.0∀1.1
20 PPM	64.62∀1.43	37.2∀1.8	2.19∀.03	1992∀59	581∀61	15.7∀1.5	10.0∀1.0
40 PPM	65.46∀1.55	36.7∀1.7	2.18∀.03	2016∀69	563∀60	15.2∀1.5	9.8∀1.0

Figure 1:

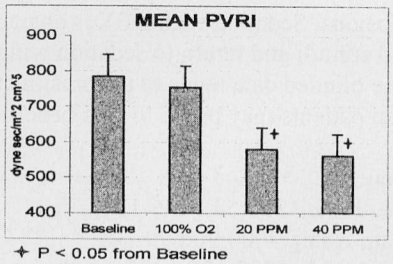


Mean ∀ S.E. MAP = Mean Arterial Pressure (mmHg); MPAP = Mean Pulmonary Arterial Pressure (mmHg); C.I. = Cardiac Index (L/min/m^2); SVRI = Systemic Vascular Resistance Index (dyne•s•cm^{-5}); PVRI = Pulmonary Vascular Resistance Index (dyne•s•cm^{-5}/m^2); TPG = Transpulmonary Gradient (mmHg); RVSWI = Right Ventricular Stroke Work Index (g/m/beat/m^2).

Table 2: Probability Table

	MAP	MPAP	CI	SVRI	PVRI	TPG	RVSWI
Baseline vs O_2	NS	NS	NS	P<0.001	NS	NS	NS
Baseline vs. 20 ppm	NS	P<0.001	NS	P<0.001	P<0.001	P<0.001	P<0.001
O_2 vs. 20 ppm	NS	P<0.001	NS	NS	P<0.001	P<0.001	P<0.001
Baseline vs. 40 ppm	NS	P<0.001	NS	P<0.001	P<0.001	P<0.001	P<0.001
20 ppm vs. 40 ppm	NS	NS	NS	NS	NS	NS	NS

Figure 2:



NS = P > 0.05. For other abbreviations, please see Table 1.