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Simplified Pulmonary Vasodilatory Testing in the Cardiac Catheterization Laboratory with Nasal Cannula Nitric Oxide

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Abstract. In patients with pulmonary hypertension, pulmonary vasodilator testing with inhaled nitric oxide (NO) during cardiac catheterization provides valuable data for defining future care plans. Previously, the use of delivery systems for spontaneously breathing individuals required a tight-fitting seal by face mask and an approved delivery and dilution device. We hypothesized that a simplified delivery system using nasal cannula could be utilized to effectively deliver NO during cardiac catheterization. We developed a simple delivery system to deliver through a nasal cannula a concentration of NO at 50 ppm at the nares along with supplemental oxygen (O_2) via face tent. We prospectively employed this system for 10-minute intervals on 11 patients (age range, 7 months to 41 years) with pulmonary hypertension undergoing scheduled cardiac catheterization. Mean pulmonary artery pressure (PA_p) decreased from 62 mmHg (range, 38–99) at room air testing to 45 mmHg (range, 36–91) with the addition of NO plus O_2 ($p = 0.014$). Pulmonary vascular resistance (PVR) decreased from 11.6 U · m^2 (range, 4.5–43.4) to 6.3 U · m^2 (range, 2.0–34.2) ($p = 0.001$). A response of 20% or more reduction in PVR was seen in all 11 patients. The initial ratio of pulmonary to systemic vascular resistance (R_p:R_s) was 0.49 (range, 0.25–3.5) and decreased to 0.35 (range 0.1–2.6) ($p = 0.002$). No adverse side effects were noted. We found this NO delivery system to be a simple and effective method of pulmonary vasodilatory testing that may have wide applicability in the cardiac catheterization laboratory.

Keywords: Nitric oxide — Pulmonary hypertension — Cardiac catheterization

Elevated pulmonary vascular resistance (PVR) complicates the diagnosis, clinical course, and outcomes of patients with congenital heart disease and end-stage pulmonary disease. In these patients, acute pulmonary vasodilatory testing with the combination of nitric oxide (NO) and oxygen (O_2) is a valuable tool in determining plans regarding the suitability for corrective surgery or transplantation [1–3]. Additionally, preoperative responsiveness has been shown to be predictive of postoperative survival [4].

The use of NO delivery systems for spontaneously breathing patients using a tight-fitting seal by face mask and an approved delivery and dilution device to therapeutic doses of 20-80 ppm has been described and proven effective [6]. Additionally, the use of an inhalation-triggered pulsed nasal cannula delivery technique in eight children has been described. With this system, nasopharyngeal concentrations of NO were found to be 1–5 ppm, and methemoglobin levels and nitrogen dioxide (NO_2) levels remained in subtoxic ranges. Using this delivery method, a decrease in the pulmonary-to-systemic resistance ratio from a baseline of 0.41 to 0.22 was also demonstrated [5].

We hypothesized that a simpler NO delivery system could be devised for pulmonary vasodilatory testing in the catheterization laboratory for spontaneously breathing patients. This system would be similar in safety and efficacy as previously employed techniques, would use commercially available components, and would not require the assistance of additional respiratory therapy personnel.

Materials and Methods

We employed the use of a 100 ppm NO source tank (Inotherapeutics, Clinton, NJ, USA), a readily available 100% O_2 tank, and a commercially available dual-source port nasal cannula (Salter Labs, Arvin, CA, USA). When NO was administered through one port of the nasal cannula at an equal flow rate to 100% oxygen via the other port, a gas mixture of 50 ppm NO and 50% FiO_2 was delivered to the patient at the nares. A face tent supplied additional supplemental 100% oxygen.

To determine the safety of this system, a model using this exact delivery system on a CPR mannequin was constructed. The

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Table 1. Patient demographics

Patient No.	Age (years)	Sex	Weight (kg)	BSA (m^2)	Diagnosis
1	41	Male	75	1.96	Unrepaired malalignment VSD
2	10	Male	36.8	1.17	Primary pulmonary hypertension
3	3	Female	10.5	0.51	Unrepaired membranous VSD
4	9	Male	21.5	0.85	Unrepaired membranous VSD
5	8.5	Female	23.2	0.91	TGA post-arterial switch
6	3.5	Male	13.6	0.59	Dilated cardiomyopathy
7	0.6	Male	8.5	0.35	Unrepaired secundum ASD
8	4.8	Female	16.7	0.71	Unrepaired CAVC
9	2	Female	9.5	0.47	Unrepaired VSD
10	17	Male	65.1	1.82	Portal pulmonary syndrome
11	18.5	Female	79.8	1.76	Repaired membranous VSD

ASD, atrial septal defect; BSA, body surface area; CAVC, complete atrioventricular canal; TGA; transposition of the great arteries; VSD, ventricular septal defect.

Table 2. Results

	Baseline	NO + O_2	p
PA_p	62 (38–99)	45 (36–91)	0.014
R_p	11.6 (4.5–43.4)	6.3 (2.0–34.2)	0.001
R_s	17.3 (12.3–36.9)	22.3 (12.9–37.2)	0.46
R_p:R_s	0.49 (0.25–3.5)	0.35 (0.1–2.6)	0.002
Q_p:Q_s	1.0 (0.26–2.5)	1.0 (0.37–6.5)	0.22

monitoring port from the Inovent (Inotherapeutics) was taped to the side of the face within the oxygen tent and constantly reported NO_2, oxygen, and NO concentrations over a 60-minute time period during constant infusion of NO and O_2. Steady-state concentrations of all gases were achieved within 10 minutes. NO_2 plateaued at 0.7 ppm in all trials. FiO_2 remained stable at 80% and NO levels remained at approximately 23 ppm within the face tent.

We prospectively employed this system on 11 spontaneously breathing patients with pulmonary hypertension (defined as PVR >3 U · m^2) undergoing scheduled cardiac catheterization. Patient's ages ranged from 7 months to 41 years and underlying diagnoses were varied (Table 1). A standard hemodynamic cardiac catheterization was performed, including measurements of atrial pressures, systemic blood pressure, pulmonary arterial pressure, pulmonary vascular resistance, systemic vascular resistance, the ratio of pulmonary to systemic vascular resistance (R_p:R_s), and the ratio of pulmonary to systemic blood flow (Q_p:Q_s) on room air and 10 minutes after the combination of NO and O_2 therapy. Levels of NO, NO_2, and FiO_2 at the nares were not directly measured. Median values of measurements at each condition were compared using the Wilcoxon signed rank test for nonparametric data.

Results

Mean pulmonary artery pressure (PA_p) decreased from 62 mmHg (range, 38–99) in room air to 45 mmHg (range, 36–91) with NO plus O_2. Additionally, PVR decreased from 11.6 U · m^2 (range, 4.5–43.4) to 6.3 U · m^2 (range, 2.0–34.2) ($p = 0.001$) (Table 2). A response of 20% (range, 21–73) or more reduction in PVR was seen in all 11 patients.

The R_p:R_s ratio decreased from 0.49 (range, 0.25–3.5) to 0.35 (range, 0.1–2.6) ($p = 0.002$). R_s did not significantly change, 17.3 U · m^2 range 12.3–36.9) to 22.3 U · m^2 (range, 12.9–37.2) ($p = 0.46$). Additionally, Q_p:Q_s did not significantly change. There were no significant changes in right or left atrial pressures.

Discussion

This system of NO delivery to spontaneously breathing patients is simple to use and effective. All components of the apparatus are commercially available and relatively inexpensive in comparison to standard delivery techniques.

However, there are some important limitations with this approach. Although the concentration of NO at the nares via this system is 50 ppm, concentrations of O_2 and NO at the alveolar level are uncertain. Additionally, we have no direct measurement of methemoglobin or NO_2 in our study patients. Historical controls and our own model testing have shown that they are likely well within acceptable ranges. Additionally, we have no head-to-head comparison of PVR responsiveness to standard NO delivery systems with the face mask. Lastly, this

system has not been tested for potential long-term use.

In conclusion, we believe this to be a simple delivery system with wide applicability. We have shown that it has similar efficacy as that of previously reported series using NO and O_2. Its safety profile appears to be comparable to that of standard, more complicated, delivery systems.

References

1. Adatia I, Perry S, Landzberg M, et al. (1995) Inhaled nitric oxide and hemodynamic evaluation of patients with pulmonary hypertension before transplantation. *J Am Coll Cardiol 25*:1656–1664
2. Atz AM, Adatia I, Lock JE, Wessel DL (1999) Combined effects of nitric oxide and oxygen during acute pulmonary vasodilator testing. *J Am Coll Cardiol 33*:813–819
3. Azeka E, Costa Auler JO, Kajita L, et al. (2002) Effects of low doses of inhaled nitric oxide combined with oxygen for the evaluation of pulmonary vascular reactivity in patients with pulmonary hypertension. *Pediatr Cardiol 23*:20–26
4. Balzer DT, Kort HW, Day RW, et al. (2002) Inhaled nitric oxide as a preoperative test (INOP Test I): the INOP Test Study Group. *Circulation 106*:I76–Ip81
5. Ivy DD, Griebel JL, Kinsella JP, Abman SH (1998) Acute hemodynamic effects of pulsed delivery of low flow nasal nitric oxide in children with pulmonary hypertension. *J Pediatr 133*:453–456
6. Wessel DL, Adatia I, Thompson JE, Hickey PR (1994) Delivery and monitoring of inhaled nitric oxide in patients with pulmonary hypertension. *Crit Care Med 22*:930–938