Oxygen Therapy Improves Cardiac Index and Pulmonary Vascular Resistance in Patients With Pulmonary Hypertension*

David H. Roberts, MD; John J. Lepore, MD; Anjli Maroo, MD; Marc J. Semigran, MD; and Leo C. Ginns, MD, FCCP

**Study objectives:** We tested the hypothesis that breathing 100% oxygen could result in selective pulmonary vasodilatation in patients with pulmonary hypertension, including those patients who would not meet current Health Care Finance Administration guidelines for long-term oxygen therapy.

**Design, setting, and patients:** From 1996 to 1999, 23 adult patients (mean ± SEM age, 51 ± 4 years) with pulmonary arterial hypertension without left-heart failure underwent cardiac catheterization in a university teaching hospital while breathing air and then 100% oxygen.

**Measurements and results:** Treatment with 100% oxygen increased arterial oxygen saturation (91 ± 1% to 99 ± 0.1%, p < 0.05) and $P_{aO_2}$ (64 ± 3 to 309 ± 28 mm Hg, p < 0.05). Treatment with 100% oxygen also decreased mean pulmonary artery pressure (56 ± 3 to 53 ± 2 mm Hg, p < 0.05) and increased cardiac index (2.1 ± 0.1 to 2.5 ± 0.2 L/min/m², p < 0.05). Calculated mean pulmonary vascular resistance (PVR) decreased from 14.1 ± 1.4 to 10.6 ± 1.0 Wood units (p < 0.05). Vasodilatation with 100% oxygen occurred preferentially in the pulmonary circulation (PVR/systemic vascular resistance, 0.53 ± 0.04 to 0.48 ± 0.03; p < 0.05). The magnitude of the PVR response to oxygen therapy was correlated only with decreasing patient age (r = 0.45, p < 0.05).

**Conclusions:** Treatment with 100% oxygen is a selective pulmonary vasodilator in patients with pulmonary hypertension, regardless of primary diagnosis, baseline oxygenation, or right ventricular function. Development of disease-specific oxygen prescription guidelines warrants consideration. *(CHEST 2001; 120:1547–1555)*

**Key words:** oxygen therapy; pulmonary hypertension; pulmonary vasodilatation

**Abbreviations:** BSA = body surface area; HR = heart rate; LV = left ventricular; MAP = mean arterial pressure; $MVO_2$ = mixed venous oxygen saturation; NS = not significant; $P(A-a)O_2$ = alveolar-arterial oxygen pressure difference; PAOP = pulmonary artery occlusion pressure; PAP = pulmonary artery pressure; PPH = primary pulmonary hypertension; PVR = pulmonary vascular resistance; RAP = right atrial pressure; RV = right ventricular; $Sao_2$ = arterial oxygen saturation; SVI = stroke volume index; SVR = systemic vascular resistance; $Vo_2$ = oxygen consumption

Pulmonary hypertension (mean pulmonary artery pressure [PAP] ≥ 25 mm Hg) may result from either primary disorders of the pulmonary vascula-

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main limited and many patients are eventually considered for lung transplantation.

Supplemental oxygen therapy may improve pulmonary hypertension as a pulmonary vasodilator, but as yet it has not been fully evaluated in patients with pulmonary hypertension without hypoxemia. In hypoxemic patients with smoking-related lung disease, long-term oxygen therapy has been shown to improve pulmonary hypertension and increase survival, as well as decrease exertional dyspnea and improve sleep.1–8

The data and the inclusion criteria from the Nocturnal Oxygen Treatment Trial and Medical Research Council trials are applied without change to patients with other pulmonary diseases, such as cystic fibrosis, interstitial lung disease, idiopathic pulmonary fibrosis, and pulmonary hypertension.9–10 The applicability of these narrow criteria, particularly the minimum oxygen saturation or arterial oxygen tension restrictions, to pulmonary disorders other than smoking-related obstructive lung disease is unknown.

The hemodynamic results of short-term oxygen administration to patients with pulmonary hypertension without smoking-related lung disease have been variable. In a patient with primary pulmonary hypertension (PPH) treated with 2 L of supplemental oxygen, the PAP and pulmonary vascular resistance (PVR) decreased by 50%.11 In a small study of hypoxemic patients with either PPH or systemic sclerosis-associated pulmonary hypertension, treatment with 60% oxygen decreased PVR and increased cardiac output only in the patients with systemic sclerosis. Similar nonsignificant trends in PVR and cardiac output were noted in the patients with PPH.12

In contrast, in a series of 14 normoxic patients with PPH and pulmonary hypertension due to connective tissue diseases, treatment with 50% oxygen did not change PVR, increased systemic vascular resistance (SVR), and decreased the thermodilution cardiac output.13 However, changes in the degree of tricuspid regurgitation were not accounted for during thermodilution cardiac output measurements. Most recently, 100% oxygen therapy resulted in marked selective pulmonary vasodilatation in a series of normoxic pediatric patients with pulmonary hypertension and various congenital cardiac diseases.14

We hypothesized that maximum supplemental oxygen therapy could have beneficial effects as a preferential pulmonary vasodilator in patients with pulmonary hypertension, including patients who would not meet the current Health Care Finance Administration guidelines for the prescription of long-term oxygen therapy. To assess for a beneficial effect of maximum supplemental oxygen therapy in adult patients with pulmonary hypertension and a range of resting arterial oxygen tensions, right-heart catheterizations were performed and oximetry and hemodynamics were measured with patients breathing air and 100% oxygen.

**Materials and Methods**

**Patient Selection**

From 1996 to 1999, adult patients (>18 years old) with mean PAP of ≥25 mm Hg without left-heart failure (pulmonary artery occlusion pressure [PAOP] ≤15 mm Hg) were recruited from primary-care physicians and from referrals for lung transplant evaluation. Patients with known or suspected coronary artery disease, mitral or aortic valvular disease, bleeding diathesis, or recent clinical bleeding, pregnancy, or hemodynamic instability (systolic arterial pressure of <85 mm Hg), were excluded. The Massachusetts General Hospital Subcommittee on Human Studies approved this study, and written informed consent was obtained prior to beginning the study.

**Study Population Characteristics**

In the 23 patients comprising the study group, the etiology of the pulmonary hypertension was PPH (n = 13), portopulmonary hypertension associated with cirrhosis (n = 4), and other varied conditions [COPD (n = 2), congenital heart disease (n = 2), CREST variant of systemic sclerosis (n = 1), and HIV (n = 1)]. Mean ± SEM age of the study patients was 51 ± 4 years, and there were 15 female and 8 male patients.

All patients underwent spirometry as part of their evaluation, except for three patients presumed by their referring physicians not to have pulmonary disease. Spirometry (n = 20) showed a FEV1 of 2.1 ± 0.2 L (76 ± 4% predicted). The carbon monoxide diffusing capacity was low at 12 ± 2 mL/min/mm Hg (50 ± 6% predicted; n = 16). Twelve of the 23 patients were documented former cigarette smokers with an average of 28 ± 5 pack-years (1 pack-year = 1 pack of cigarettes daily for 1 year) of smoking.

Echocardiographic LV systolic function (n = 20) was normal (LV ejection fraction, 65 ± 3%). Right ventricular (RV) dilatation (RV dimensions greater than normal range15) was noted in all 20 patients, RV hypertrophy (RV free wall >2 SD above the normal range15) was noted in 7 of 20 patients (35%), and diffuse RV hypokinesis was seen in 11 of 20 patients (55%).

**Study Protocol**

All vasoactive drugs and caffeine were held for 24 h prior to right-heart catheterization. Resting oxygen consumption (VO2) was measured with a metabolic monitor (Deltatrac Metabolic Monitor; SensorMedics; Yorba Linda, CA). After local anesthesia, all patients underwent radial and pulmonary arterial catheterization. After a stabilization period of 10 min, baseline pulmonary and systemic hemodynamic evaluations were completed with the patient breathing air. Measurements included heart rate (HR), arterial BP (mean arterial pressure [MAP] and phasic), right atrial pressure (RAP), RV pressures, PAPs (mean PAP and phasic), PAOP, radial PAO2, and simultaneous arterial oxygen saturation (SaO2) and mixed venous oxygen saturation (MVO2). One hundred percent oxygen was administered by tight facemask for at least 5 min, and hemodynamics and oximetry measurements were repeated.

**Data Analysis and Calculations**

In order to compensate for variability in PAPs in patients with pulmonary hypertension,16 values from hemodynamic and oxime-
Results

Baseline Oximetry and Hemodynamics

All patients underwent radial and pulmonary arterial catheterization without complications. The baseline oximetry data for all patients are shown in Table 1. Comparisons of baseline oximetry and hemodynamics in the three identified etiologic subgroups showed only that the patients with PPH had significantly lower MvO2 (58 ± 2%, p < 0.05) and lower cardiac index (1.9 ± 0.2 L/min/m², p < 0.05). No differences were found in baseline SaO2, Pao2, HR, MAP, RAP, PAOP, PAP, or PVR (data not shown). Given these baseline similarities, the 23 patients were analyzed as a single group in terms of response to treatment with supplemental oxygen.

At rest breathing air, the Pao2 was low at 64 ± 3 mm Hg and the SaO2 was low at 91 ± 1%. The MvO2 was normal at 62 ± 2%, and P(A-a)O2 was elevated at 27 ± 3 mm Hg. Normal values were found for resting MAP (100 ± 3 mm Hg) and HR (82 ± 3 beats/min). The cardiac index was low at 2.1 ± 0.1 L/min/m², and the SVI was low at 25 ± 2 mL/beat/m². Mean PAP (56 ± 3 mm Hg) and PVR (14.1 ± 1.4 Wood units) levels were elevated. Resting RAP (8 ± 1 mm Hg) and PAOP (8 ± 1 mm Hg) levels were within normal limits.

Effects of 100% Oxygen Administration

The results of breathing 100% oxygen for all patients are shown graphically for individual oximetry and hemodynamic measurements. The mean

| Table 1—Baseline Demographic, Oximetry, and Hemodynamic Data*

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All, mean ± SEM

51 ± 4
62 ± 2
81 ± 1
64 ± 3
81 ± 3
8 ± 1
8 ± 1
56 ± 3
21 ± 0.1
114 ± 6
1 ± 0.5
22 ± 0.53 ± 0.04

*ASD = atrial septal defect; VSD = ventricular septal defect; CREST = calcinosis, Raynaud’s phenomenon, esophageal dysmotility, scleroderma, and telangiectasia; PCW = pulmonary capillary wedge pressure; CI = cardiac index; NA = not available; F = female; M = male; Dx = diagnosis; %Sat = saturation.
values on 100% oxygen are shown in Table 2 in comparison to baseline mean values.

In terms of oximetry, breathing 100% oxygen acutely increased \( \text{PaO}_2 \) by 391 ± 43% (Fig 1), suggesting that supraphysiologic levels of oxygenation were achieved with the tight facemask. Additionally, breathing 100% oxygen increased radial \( \text{SaO}_2 \) by 9 ± 2% and pulmonary artery \( \text{MvO}_2 \) by 22 ± 2%.

In terms of hemodynamics, breathing 100% oxygen decreased mean PAP by 6 ± 1% (Fig 2), while mean RAP and PAOP were not different before and after oxygen therapy. Breathing 100% oxygen also increased the calculated cardiac index by 21 ± 4% (Fig 3). This was associated with both a decrease in HR of 7 ± 2% and an increase in SVI of 29 ± 5%.

Breathing 100% oxygen decreased PVR by 24 ± 3% (Fig 4) and SVR by 16 ± 3%. This vasodilator effect was greater in the pulmonary vasculature (PVR/SVR 0.53 ± 0.04 to 0.48 ± 0.03, \( p < 0.05 \)). Although SVR fell, mean arterial BP was unchanged while breathing 100% oxygen.

Regression Analysis

Univariate regression analysis of change in PVR was performed using demographics (age, gender, smoking history, primary diagnosis), echocardiographic RV and LV function, baseline oximetry \([\text{PaO}_2, \text{SaO}_2, \text{MvO}_2, \text{P(A-a)O}_2]\) and baseline hemodynamics \((\text{HR, MAP, RAP, PAP, PAOP, PVR, CI, SVI})\). Decreasing patient age was the only predictor of the magnitude of the pulmonary vasodilator response to breathing 100% oxygen \((r = 0.45, \ p < 0.05; \text{Fig 5})\). Additionally, decreasing patient age also predicted the magnitude of the increase in cardiac index in response to treatment with supplemental oxygen \((r = 0.60, \ p < 0.05)\). Notably, baseline oximetry, hemodynamics, and echocardiographic RV hypertrophy did not predict the magnitude of the vasodilator response to oxygen therapy.

Subgroup Analyses

PVR Response to Oxygen Therapy: The study population was analyzed by response to oxygen in terms of fall in PVR: “responders” had a fall in PVR of ≥ 20% and “nonresponders” had a fall in PVR of < 20%. Fifteen patients (68%) were responders with a mean PVR decrement of 31 ± 1%. In contrast, seven patients (32%) were nonresponders with a mean PVR decrement of 9 ± 3%. In one patient, cardiac output measurements while receiving supplemental oxygen are not available for technical reasons.

No significant differences in baseline oximetry, hemodynamics, or demographics were seen, al-
though there was a trend toward lower age in the responders (46 ± 5 years vs 60 ± 4 years, p = 0.07). The responders and nonresponders had similar percentage decrements in mean PAP with 100% oxygen therapy, but the responders had a significantly greater increase in cardiac output with oxygen therapy (30 ± 3% vs 2 ± 3%, p < 0.05). This effect was due to an increase in stroke volume (40 ± 6% vs 10 ± 4%, p < 0.05) as opposed to a decrease in HR (7 ± 2% vs 6 ± 2%, p = not significant [NS]).

Baseline Demographics

Etiology of Pulmonary Hypertension: Patients with PPH, portopulmonary hypertension, and all other disorders had similar responses to breathing 100% oxygen in terms of changes in oximetry and hemodynamics. No difference was found for the magnitude of decrease in PVR or the increase in cardiac index and SVI. The only notable finding was that patients with PPH had a smaller decrement in mean PAP as compared with all other patients (5 ± 1% vs 10 ± 2%, respectively; p < 0.05).

Smoking History: Subgroup analysis by history of cigarette smoking revealed only that those patients who had been smokers were older than lifetime nonsmokers (57 ± 4 years vs 42 ± 3 years, p < 0.05). All other demographic, hemodynamic, oximetry, and echocardiographic parameters were not different for the former smokers, including percentage change of cardiac index and PVR after supplemental oxygen therapy.

Gender: Female patients had a higher P(A-a)O2 at rest (32 ± 3 mm Hg vs 18 ± 4 mm Hg, p < 0.05) as compared with the male patients. No other demographic, hemodynamic, oximetry, and echocardiographic parameters varied with gender, including percentage change of cardiac index and PVR after supplemental oxygen therapy.

Baseline Oxygenation

Subgroup analysis by oxygenation (hypoxemic: resting PaO2 < 60 mm Hg; normoxic: resting PaO2 ≥ 60 mm Hg) documented that hypoxic patients were older (64 ± 5 years vs 42 ± 4 years, respectively; p < 0.05). Similarly, even when the PaO2 calculated was adjusted for age, hypoxic patients had a wider P(A-a)O2 (37 ± 3 mm Hg vs 19 ± 3 mm Hg, p < 0.05). The magnitude of increase in MvO2 was greater in hypoxic patients (27 ± 2% vs 18 ± 2%, p < 0.05), as was the increase in the SaO2 (14 ± 3% vs 6 ± 1%, p < 0.05). All other demographic, hemodynamic, oximetry, and echocardiographic parameters were not different based on oxygenation, including percentage change of cardiac index and PVR after supplemental oxygen therapy.
Echocardiographic RV Function

RV Hypertrophy: The subgroup of patients with echocardiographic RV hypertrophy had a higher baseline oxygen tension (P\textsubscript{aO\textsubscript{2}, 77 ± 4 mm Hg vs 58 ± 4 mm Hg; p < 0.05}) and narrower P(\textsubscript{A-a})O\textsubscript{2} (16 ± 5 mm Hg vs 32 ± 3 mm Hg, p < 0.05). All other demographic, hemodynamic, oximetry, and echocardiographic parameters were not different in the presence of RV hypertrophy, including percentage change of cardiac index and PVR after supplemental oxygen therapy.

Diffuse RV Hypokinesis: The presence of echocardiographic RV hypokinesis was associated with a greater response to breathing supplemental oxygen only in terms of M\textsubscript{V}\textsubscript{0\textsubscript{2}} (25 ± 2% vs 16 ± 2%, p < 0.05) and cardiac index (31 ± 6% vs 14 ± 5%, p < 0.05). All other demographic, hemodynamic, oximetry, and echocardiographic parameters were not different in the presence of RV hypokinesis, including percentage change of PVR after supplemental oxygen therapy.

DISCUSSION

In adult patients with pulmonary hypertension, the data show that breathing 100% supplemental oxygen decreases mean PAP, increases cardiac index, and decreases PVR. The beneficial effect on PVR was independent of the etiology of pulmonary hypertension, smoking history, gender, baseline oximetry (both arterial oxygen tension and percentage saturation of the pulmonary and systemic arterial circulation), baseline hemodynamics (including mean PAP and PVR), and echocardiographic RV and LV function.

Decreasing patient age was the only predictor of the magnitude of the pulmonary vasodilatation, particularly notable because the older patients (a greater proportion of whom had a history of smoking) had a larger P(\textsubscript{A-a})O\textsubscript{2}. While older age may be a marker of more chronic pulmonary hypertension, we are unable to assess the effects of disease chronicity given the inability to determine the disease duration prior to clinical diagnosis. Additionally, decreased PVR and increased cardiac index were not correlated with two of the current Health Care Finance Administration criteria for the prescription of supplemental oxygen therapy (baseline oxygenation and clinically evident RV hypertrophy).

The supraphysiologic arterial oxygen tensions achieved by tight-fitting masks with 100% supplemental oxygen resulted in a mean decrement in PVR of 24 ± 3% and a mean increase in cardiac index of 21 ± 4%. Prior studies\textsuperscript{11–13} with small numbers of patients with pulmonary hypertension not due to smoking-related lung disease have shown variable and somewhat contradictory effects of supplemental oxygen therapy. While others\textsuperscript{12,14} have found similar decrements in PVR with supplemental oxygen therapy, only Morgan et al\textsuperscript{12} found similar, albeit more variable, increases in cardiac output. Unlike the study of oxygen in obliterative pulmonary vascular disease by Packer et al,\textsuperscript{13} neither this study nor the work of Atz et al\textsuperscript{14} found increased SVR with oxygen therapy. Prior studies using thermodilution to measure cardiac output may have inadequately accounted for tricuspid regurgitation. Our cardiac output measurements using the Fick method rely on the assumption that \text{Vo}_2 did not change with 100% oxygen administration. This assumption has been validated by numerous studies that are reviewed elsewhere.\textsuperscript{15}

Mechanistically, the beneficial effects of maximum supplemental oxygen therapy on PVR seen in this study are partially explained by release of hypoxic pulmonary vasoconstriction and overcoming ventilation/perfusion imbalances. Although the oxygen content of arterial blood and oxygen delivery to tissues are generally not reduced unless the P\textsubscript{aO\textsubscript{2}} falls to < 60 mm Hg,\textsuperscript{19} some hypoxic pulmonary vasoconstriction may still be occurring at higher arterial oxygen tensions.

The correlation of decreasing patient age and magnitude of pulmonary vasodilatation could be explained by the physiology of age-related differences on hypoxic pulmonary vasoconstriction. Animal experimentation\textsuperscript{20} has documented that the alveolar oxygen tension threshold required for hypoxic pulmonary vasoconstriction varies with age. Hypoxic pulmonary vasoconstriction can be documented in newborn lambs at an alveolar oxygen tension of 360 ± 3 mm Hg. The threshold falls with age; in adult sheep, similar hypoxic pulmonary vasoconstriction does not occur until the alveolar oxygen tension falls to < 100 mm Hg. While the theoretical importance of this elevated threshold in newborns is obvious (to maintain flow through the ductus arteriosus in the fetal state), the exact mechanism of the increased sensitivity or its decline over time is less well understood. The anatomic difference in the location and degree of smooth muscle associated with the pulmonary vasculature in the newborn vs adult lung has been proposed\textsuperscript{20,21} as one potential mechanism.

Although maximum supplemental oxygen therapy did significantly increase M\textsubscript{V}\textsubscript{0\textsubscript{2}}, it is unlikely that the benefits of oxygen therapy seen in this study were mediated through changes in the pulmonary arterial oxygen tension. While both the sensors and mecha-
nisms of hypoxic pulmonary vasoconstriction are not known, alveolar hypoxia is a significantly greater stimulus for hypoxic pulmonary vasoconstriction than pulmonary arterial hypoxemia. The increased cardiac index after supplemental oxygen therapy seen in this study can be partially explained by the patients’ baseline cardiac function. All patients in this study were found to have normal LV function by echocardiography. In the setting of pulmonary vasodilatation, there likely was a transient increase in the LV end-diastolic volume. Given these patients’ adequate preload reserve, increased delivered volume to the LV resulted in significant improvement in cardiac index. While RAP and PAOP did not change with supplemental oxygen, this likely reflects the rapid nature of the reestablishment of a steady state and, again, adequate preload reserve.

The presence or absence of echocardiographic RV hypertrophy did not correlate significantly with response to supplemental oxygen therapy. While all patients had dilated RVs by echocardiography, only 55% had RV hypokinesis. In contrast to RV hypertrophy, echocardiographic diffuse RV hypokinesis was associated with a less vigorous response to breathing 100% oxygen in terms of cardiac index and SVI. While no difference was noted in the magnitude of decrement in PVR, the varied response in terms of cardiac function may reflect less RV/LV interaction and/or septal shift. This finding has prompted further investigation into the nature of the RV response to supplemental oxygen therapy.

**Limitations and Implications**

This pilot study was designed to measure the acute effects of maximal supplemental oxygen in patients with pulmonary hypertension not solely due to chronic hypoxemia. While a control group was not studied, the hemodynamic effects of acute hyperoxia in normal volunteers are known. Barratt-Boyes and Wood found that breathing 100% oxygen resulted in a small (6%) decrement in HR, a small increase in SVI, and no significant alterations in mean cardiac index. The radial artery systolic pressure increased by an average value of 6 mm Hg and the mean PAP fell by an average of 1 mm Hg. Daly and Bondurant found similar decrements in HR and elevations in mean systemic pressures, but no significant changes in SVI. Cardiac index decreased in proportion to the decrement in HR, and the effects were abolished by pretreatment with atropine.

In light of these data and other data, we could not justifiably draw a control population from our cardiac catheterization laboratory due to increased risk from prolonged procedures. In comparison to the limited pulmonary vasodilatation and systemic vasoconstriction seen in normal volunteers, our data suggest in patients with pulmonary hypertension with a spectrum of resting oxygen tensions that supplemental oxygen therapy may relieve hypoxic pulmonary vasoconstriction and improve cardiac index.

Future studies will include control groups, including nonhypoxic patients without pulmonary hypertension, as well as pulmonary hypertension patients with and without hypoxemia. Additionally, further studies with long-term ambulatory oxygen therapy could include sham oxygen delivery as a control. While patients may have interpreted an oxygen mask and supplemental oxygen as a potentially beneficial therapy, a volitional decrement in PVR seems unlikely.

In this study, a minimum equilibration time of 5 min was used before measurements of the effects of 100% oxygen were obtained. It has been our clinical experience in prior catheterization trials for pulmonary hypertension that equilibration occurs shortly after the initiation of 100% oxygen therapy. Additional data must be obtained in order to determine if these short-term effects of 100% oxygen are maintained over the course of long-term therapy. Similarly, at this time we are unable to advocate for the use of 100% oxygen in this population, given that potential adverse effects of long-term administration of high levels of inhaled oxygen are not known.

While the data suggest that the hemodynamic response to maximal supplemental oxygen was independent of the etiology of pulmonary hypertension, this study relies on data from a relatively small number of patients. Future confirmatory studies will require sufficient numbers of patients with forms of secondary pulmonary hypertension, such as HIV, structural heart disease, and COPD patients without hypoxemia, to determine if an etiology-specific response to oxygen exists.

Nearly 70% of the study patients could be classified as responders in terms of a ≥20% decrement in PVR. In other studies of pulmonary vasodilators, PVR response has been associated with greater survival. Currently, we believe that any statements regarding outcome would be premature, but we continue to monitor these patients for an outcome analysis in the future. In the near-term, additional studies using supplemental oxygen in concert with and in comparison to other pulmonary vasodilators, such as nitric oxide and prostacyclin, may provide guidance on how to interpret the PVR response to oxygen therapy in this population.

Given that the magnitude of pulmonary vasodilatation or improvement in cardiac index was not predicted by baseline PaO₂, we speculate that oxygen therapy may exert its beneficial effects by more than...
just releasing hypoxic pulmonary vasoconstriction. Although less likely to occur in the short-term, oxygen therapy may improve pulmonary hypertension via mechanisms similar to other pulmonary vasodilators, such as limiting endothelial dysfunction, improving imbalances in the endogenous vasoconstrictor-vasodilator system, or overcoming dysfunctional oxygen-sensing potassium channels. Finally, oxygen therapy could theoretically upregulate expression of prostacyclin synthase, which is decreased in patients with pulmonary hypertension, and which in an overexpression animal model is protective of hypoxic pulmonary vasoconstriction.32

CONCLUSION

This study demonstrates that maximizing supplemental oxygen therapy has a short-term beneficial effect as a selective pulmonary vasodilator in adult patients with pulmonary hypertension. Notably, this benefit was independent of baseline oximetry, hemodynamics, and echocardiographic RV function. Improvement in PVR in response to maximum supplemental oxygen therapy may also serve as a marker of pulmonary vasoreactivity in adult patients with pulmonary hypertension, as in the pediatric congenital heart disease population.

Our data suggest that supplementing arterial oxygen tension beyond the minimum goal of 60 mm Hg may improve PVR and cardiac index. These short-term effects are likely due at least partially to releasing hypoxic pulmonary vasoconstriction, but may also be due to additional mechanisms as yet unidentified. Further studies are indicated to document whether a dose-response relationship exists for oxygen therapy, whether the short-term beneficial effects of oxygen are maintained over the course of long-term therapy, and perhaps to help define more appropriate disease-specific guidelines for the prescription of supplemental oxygen therapy.

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