CASE REPORT

Successful treatment for collagen vascular disease-related respiratory failure with inhaled nitric oxide as a bridging therapy : A case report

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Abstract : Background : Inhaled nitric oxide (iNO) is approved in Japan for perioperative pulmonary hypertension and persistent pulmonary hypertension in newborns ; however, its role in non-cardiac respiratory failure is unclear. Case Presentation : A 47-year-old woman with Sjögren's syndrome developed severe acute type I respiratory failure due to collagen vascular disease. Despite high-F_IO_2 ventilation, her PaO_2/F_IO_2 ratio remained <80, and extracorporeal membrane oxygenation (ECMO) was considered. Administration of iNO at 10 ppm improved oxygenation, with a rapid increase in PaO_2/F_IO_2 ratio. This response allowed time for steroid pulse therapy, rituximab, plasma exchange, and pleural drainage, which stabilized the patient's condition without ECMO. Notably, the temporal association between iNO initiation and rapid oxygenation improvement suggests that pulmonary vascular dysfunction was a major contributor to hypoxemia. Subsequent stabilization with immunosuppressive therapy highlights the role of iNO as a bridging therapy rather than a definitive treatment. Conclusion : In this case, iNO may have served as a bridging therapy, improving oxygenation until immunosuppressive treatment was effective. iNO may serve as a useful interim measure for avoiding ECMO in collagen vascular disease-associated respiratory failure, particularly when pulmonary hypertension is suspected. J. Med. Invest. 73 : 270-273, February, 2026

Keywords **:** *inhaled nitric oxide, collagen vascular disease, respiratory failure, case report*

INTRODUCTION

Inhaled nitric oxide (iNO) is a selective pulmonary vasodilator that exerts its effects by activating soluble guanylate cyclase in vascular smooth muscle, thereby increasing cyclic guanosine monophosphate (cGMP) levels and promoting vasodilation (1). Its action is limited to the pulmonary circulation, as it is rapidly inactivated by hemoglobin, which minimizes systemic hypotension. In Japan, iNO is approved for the perioperative management of pulmonary hypertension in cardiac surgery and for persistent pulmonary hypertension in newborns. However, its use in non-cardiac acute respiratory failure remains off-label (2).

Previous studies have suggested that iNO can transiently improve oxygenation by decreasing pulmonary vascular resistance and optimizing ventilation–perfusion matching (3). Nonetheless, randomized controlled trials have not shown a survival benefit, underscoring its role as a supportive measure rather than a curative therapy (4). In clinical practice, iNO is often considered a bridging therapy that stabilizes oxygenation while definitive treatments are administered.

Collagen vascular diseases, including systemic lupus erythematosus, systemic sclerosis, and Sjögren's syndrome, may cause pulmonary vascular involvement owing to autoimmune inflammation, endothelial injury, and microthrombosis (5-8). These mechanisms predispose patients to pulmonary hypertension and refractory hypoxemia. In such cases, extracorporeal membrane oxygenation (ECMO) is often considered ; however, its invasive nature, resource requirements, and risks of bleeding, thrombosis, and infection, limit its applicability. Therefore, ECMO should be avoided whenever possible.

We present a case of severe acute type I respiratory failure associated with collagen vascular disease in which iNO was successfully used as a bridging therapy. The intervention allowed immunosuppressive therapy and pleural drainage to be performed, ultimately stabilizing the patient without ECMO.

CASE PRESENTATION

A 47-year-old woman with Sjögren's syndrome, immune thrombocytopenic purpura, and osteoporosis was admitted with progressive chest and abdominal pain. Her medications included low-dose prednisolone (3 mg/day), lansoprazole, and weekly alendronate. She was a non-smoker and occasionally consumed alcohol.

Over the three months preceding ICU admission, she developed worsening dyspnea. She was admitted to our hospital on ICU day -3 (i.e., three days before ICU admission) for further evaluation. Laboratory results showed elevated levels of inflammatory markers (C-reactive protein, 9.0 mg/dL ; white blood cell count, 12,000/μL). Autoantibody screening confirmed collagen vascular disease activity, with anti-SSA antibody positivity. Chest radiography revealed bilateral pleural effusions, predominantly on the right side (Figure 1a). Computed tomography corroborated these findings, demonstrating a large right-sided pleural effusion with relatively mild parenchymal infiltration (Figure 2). Transthoracic echocardiography revealed a tricuspid

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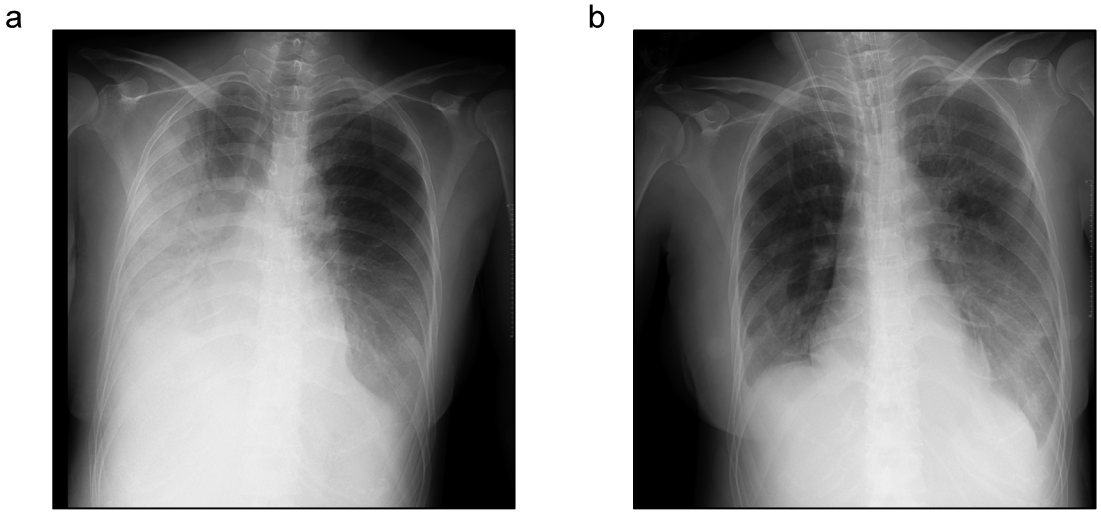

Figure 1. Chest radiographs. (a) ICU admission: bilateral pleural effusion, right predominant, with reduced aeration. (b) ICU day 1, the day after iNO initiation and pleural drainage : improved aeration and decreased effusion were observed.

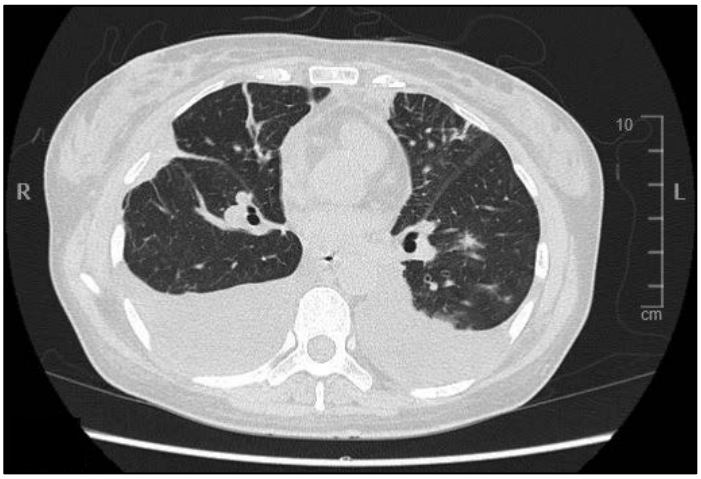

Figure 2. Chest computed tomography on ICU day -3. Bilateral pleural effusions, right predominant, with mild parenchymal involvement.

regurgitation pressure gradient of 35 mmHg, suggesting pulmonary hypertension (Figure 3). No NT-proBNP/BNP or additional echocardiographic parameters (e.g., tricuspid annular plane systolic excursion and inferior vena cava diameter) were obtained, and therefore performing an invasive hemodynamic assessment was not feasible.

Intravenous methylprednisolone (1,000 mg/day for 3 days) was initiated as steroid pulse therapy. However, on the day of ICU admission, the patient's respiratory condition deteriorated, necessitating endotracheal intubation and mechanical ventilation. On ICU arrival, an arterial blood gas analysis demonstrated severe hypoxemia with PaO_2/F_IO_2 76 ; SpO_2 of 83% under F_IO_2 1.0. Despite pressure-controlled ventilation (driving pressure, 18 cmH_2O ; PEEP, 8 cmH_2O ; F_IO_2, 1.0), oxygenation remained inadequate. These ventilator settings were kept unchanged during iNO initiation, and SpO_2 increased from 83% to 100% within 10 min.

ECMO was considered for refractory hypoxemia. To avoid invasive intervention, inhaled nitric oxide (iNO) was administered at 10 ppm. The off-label use of iNO was approved by the Safety Management Department of our institution. Immediately after iNO initiation, SpO_2 increased from 83% to 100% at F_IO_2 1.0. Shortly thereafter, therapeutic pleural drainage was performed, yielding 850 mL of serous fluid, and the SpO_2 remained at 100% under F_IO_2 1.0. A subsequent arterial blood gas showed PaO_2/F_IO_2 of 242.

In the subsequent ICU course, a second course of steroid pulse therapy was administered, followed by rituximab on ICU days 1 and 8, and plasma exchange on ICU days 2-6. C-reactive protein levels decreased progressively in parallel with stabilization of oxygenation, with PaO_2/F_IO_2 ratios maintained between 200 and 250. iNO was gradually tapered and discontinued by ICU day 6 without recurrence of hypoxemia. The patient was successfully extubated on ICU day 4 and transferred to a high-flow nasal cannula, followed by low-flow oxygen. She was discharged from the ICU in a stable condition.

Following ICU discharge, the patient maintained oxygenation on room air by hospital day 24 (4 days after ICU discharge), achieved assisted ambulation with a walker on room air by hospital day 50, and finally was transferred to a rehabilitation facility on hospital day 56.

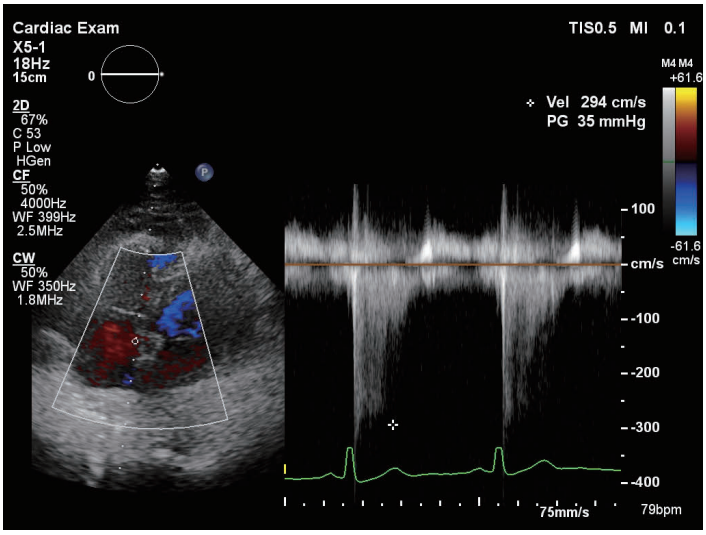

Figure 3. Transthoracic echocardiography on ICU day -3. Continuous-wave Doppler shows a tricuspid regurgitation pressure gradient of 35 mmHg, suggesting pulmonary hypertension.

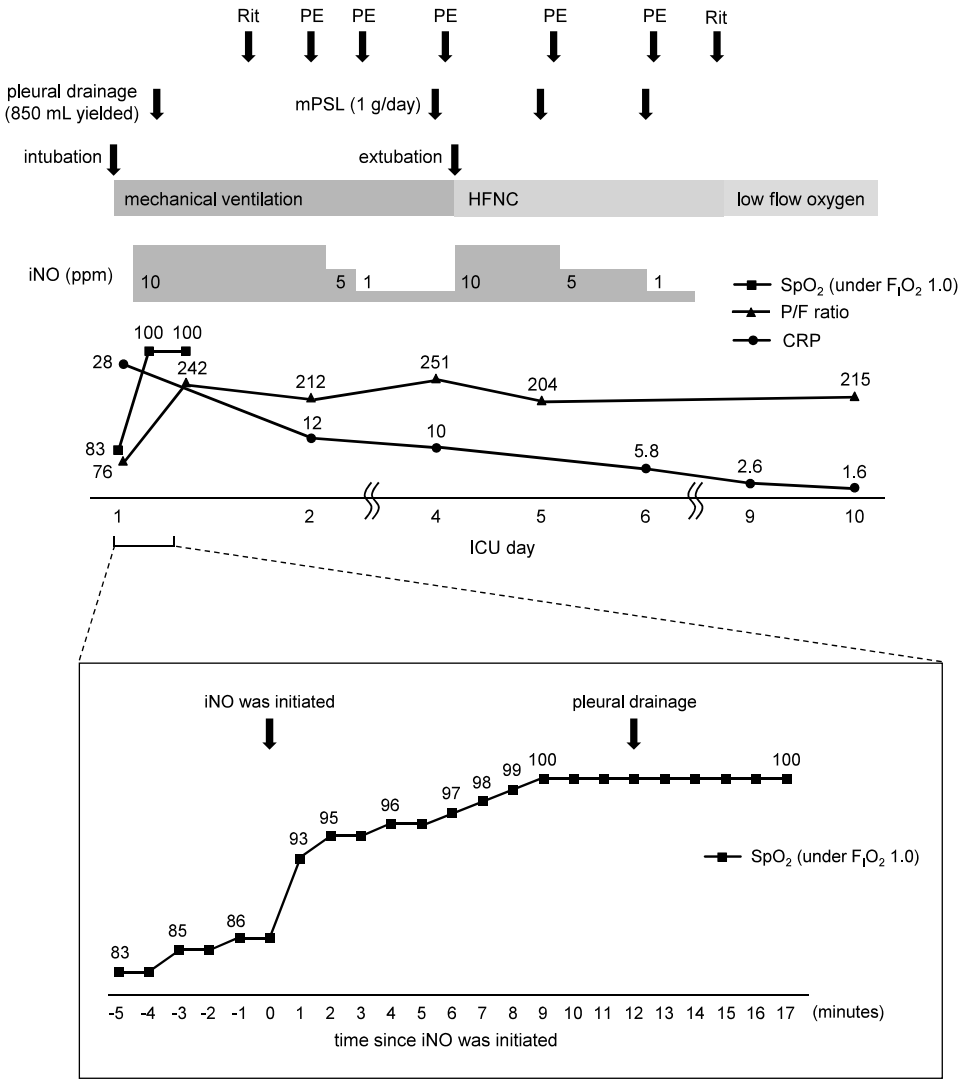

Figure 4. Clinical course in ICU. Rit, rituximab ; PE, plasma exchange ; mPSL, methylprednisolone ; HFNC, high-flow nasal cannula oxygen therapy. SpO_2 under F_IO_2 1.0 and PaO_2/F_IO_2 improved rapidly after iNO initiation, allowing pleural drainage, steroid pulse therapy, rituximab, and plasma exchange. CRP values and interventions are shown along the timeline.

DISCUSSION

This case highlights the potential role of iNO as a bridging therapy for collagen vascular disease-associated respiratory failure with pulmonary hypertension. Our patient presented with severe hypoxemia that was refractory to optimal mechanical ventilation, prompting consideration of ECMO. However, iNO rapidly improves oxygenation, providing a crucial window for pleural drainage and immunosuppressive therapy.

iNO reduces pulmonary vascular resistance and improves ventilation - perfusion matching, which is particularly relevant in patients with pulmonary hypertension secondary to autoimmune vascular disease. The immediate improvement observed following iNO initiation suggests that pulmonary vascular dysfunction contributed significantly to the hypoxemia in this case.

Although randomized trials have shown that iNO does not improve survival, its role as an interim measure remains valuable (9). Previous studies have reported improved short-term oxygenation but no mortality benefit in severe hypoxemia (10-12). Nonetheless, in contexts such as autoimmune disease-related respiratory failure, iNO may facilitate definitive therapy by averting ECMO. Avoiding ECMO is clinically meaningful given the risks of bleeding, thromboembolism, and infection, and its resource-intensive nature.

This case report had several limitations. First, pulmonary hypertension was inferred using echocardiography, without invasive confirmation. No NT-proBNP/BNP or additional echocardiographic parameters (e.g., tricuspid annular plane systolic excursion, inferior vena cava diameter) were obtained, and performing an invasive hemodynamic assessment was not feasible. Measuring the BNP or NT-proBNP levels could have provided supportive evidence of either right ventricular strain or volume overload, thereby strengthening the interpretation of pulmonary hypertension in this case. Second, pleural drainage was performed after the initiation of iNO administration. However, the SpO_2 increased from 83% to 100% within 10 min of iNO initiation, before pleural drainage was performed. Therefore, pleural drainage likely contributed to the patient's sustained oxygenation, but the immediate improvement was temporally associated with iNO. Third, as a single case report, generalizability is limited. Nevertheless, the clear temporal association between iNO initiation and improved gas exchange underscores the potential utility of iNO.

Future studies should collate similar cases to identify predictors of iNO responsiveness, such as echocardiographic signs of pulmonary hypertension/right ventricular strain, biomarkers (e.g., NT-proBNP), and early oxygenation kinetics after iNO initiation.

CONCLUSION

Inhaled nitric oxide provided rapid, transient improvement in oxygenation in a patient with collagen vascular disease-associated respiratory failure, enabling the initiation of immunosuppressive therapy and pleural drainage, and avoiding ECMO. Although not curative, iNO may serve as an important bridging therapy in selected cases, particularly when pulmonary hypertension contributes to severe hypoxemia.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest in association with the present study.

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PATIENT CONSENT

Informed consent was obtained from the patient for publication of this case report.

REFERENCES

1. Ichinose F, Roberts JD Jr, Zapol WM : Inhaled nitric oxide : a selective pulmonary vasodilator. Current uses and therapeutic potential. Circulation 109 : 3106-3111, 2004
2. Kaplish D, Vagha JD, Meshram RJ, Lohiya S : A comprehensive review of inhaled nitric oxide therapy : current trends, challenges, and future directions. Cureus 16 : e53558, 2024
3. Matthay MA, Zemans RL, Zimmerman GA, Arabi YM, Beitler JR, Mercat A, Herridge M, Randolph AG, Calfee CS : Acute respiratory distress syndrome. Nat Rev Dis Primers 5 : 18, 2019
4. Wu X, Zheng R, Zhao Z : Inhaled nitric oxide rescued a hypoxemia patient caused by dermatomyositis complicated with interstitial pneumonia : a case report. Front Med (Lausanne) 11 : 1371183, 2024
5. Bhansing KJ, Vonk-Noordegraaf A, Oosterveer FP, van Riel PL, Vonk MC : Pulmonary arterial hypertension, a novelty in idiopathic inflammatory myopathies : insights and first experiences with vasoactive therapy. RMD Open 3 : e000331, 2017
6. Kobak S, Kalkan S, Kirilmaz B, Orman M, Ercan E : Pulmonary arterial hypertension in patients with primary Sjögren's syndrome. Autoimmune Dis 2014 : 710401, 2014
7. Hwang JA, Yang TH, Lee JY, Koo DW, Choi IS, Cho SY, Kim MS : Severe pulmonary hypertension in primary Sjögren's syndrome. Korean Circ J 43 : 504-507, 2013
8. Kim EJ, Collard HR, King TE Jr : Rheumatoid arthritis-associated interstitial lung disease : the relevance of histopathologic and radiographic pattern. Chest 136 : 1397-1405, 2009
9. Afshari A, Brok J, Møller AM, Wetterslev J : Inhaled nitric oxide for acute respiratory distress syndrome (ARDS) and acute lung injury in children and adults. Cochrane Database Syst Rev 2016 : CD002787, 2016
10. Adhikari NK, Burns KE, Friedrich JO, Granton JT, Cook DJ, Meade MO : Effect of nitric oxide on oxygenation and mortality in acute lung injury : systematic review and meta-analysis. BMJ 334 : 779, 2007
11. Lotz C, Muellenbach RM, Meybohm P, Mutlak H, Lepper PM, Rolfes CB, Peivandi A, Stumpner J, Kredel M, Kranke P, Torje I, Reyher C : Effects of inhaled nitric oxide in COVID-19-induced ARDS - is it worthwhile? Acta Anaesthesiol Scand 65 : 629-632, 2021
12. Nathan SD, Flaherty KR, Glassberg MK, Raghu G, Swigris J, Alvarez R, Ettinger N, Loyd J, Fernandes P, Gillies H, Kim B, Shah P, Lancaster L : A randomized, double-blind, placebo-controlled study of pulsed, inhaled nitric oxide in subjects at risk of pulmonary hypertension associated with pulmonary fibrosis. Chest 158 : 637-645, 2020