Received: 26 September 2023 | Accepted: 12 April 2024

DOI: 10.1002/ams2.957

ACUTE MEDICINE & SURGERY WILEY

CASE REPORT

Veno-venous extracorporeal membrane oxygenation for acute respiratory distress syndrome caused by nitrogen dioxide inhalation: A case report

Tomoya Nishimura | **Makoto Aoki** | **Hiroyuki Suzuki** | **Hiroya Hagiwara** | **Akira Kawauchi** | **Kenji Fujizuka** | **Mitsunobu Nakamura**

Advanced Medical Emergency Department and Critical Care Center, Japanese Red Cross Maebashi Hospital, Maebashi, Japan

Correspondence
Tomoya Nishimura, Advanced Medical Emergency Department and Critical Care Center, Japanese Red Cross Maebashi Hospital, 389-1, Asakura-machi, Maebashi, Gunma 371-0811, Japan.
Email: t.nishi.maebashi@gmail.com

Abstract

Background: Nitrogen dioxide (NO_2) is known to cause lung injury, but there is no established treatment for acute respiratory distress syndrome (ARDS) caused by NO_2 inhalation.

Case Presentation: A 35-year-old man was accidentally exposed to NO_2 fumes and presented to the emergency department. On admission, his oxygen saturation was 87% on ambient air and he was diagnosed with ARDS caused by NO_2 inhalation and immediately intubated; however, hypoxemia and hypercapnia were not ameliorated. Hence, veno-venous extracorporeal membrane oxygenation (V-V ECMO) was introduced and the ventilator settings were set for lung-protective ventilation. Methylprednisolone was also administered. After the initiation of these treatments, oxygenation gradually improved. Therefore, ECMO was weaned off on day 11 and he was extubated on day 12.

Conclusion: Lung injury caused by NO_2 inhalation can cause ARDS, and lung-protective ventilation with V-V ECMO induction, as well as glucocorticoid administration, may be effective for this condition.

KEYWORDS
extracorporeal membrane oxygenation, glucocorticoids, inhalation exposure, nitrogen dioxide, respiratory distress syndrome

INTRODUCTION

The accidental inhalation of nitrogen dioxide (NO_2) often occurs in metal plating workers, cleaning operations, or factory work involving the handling of nitric acid.[1–3] Although acute poisoning with NO_2 is known to cause pulmonary edema and lung injury over several hours after exposure,[4] there is no established treatment for acute respiratory distress syndrome (ARDS) caused by NO_2 inhalation and its prognosis is unknown. In this report, we describe a case of ARDS caused by NO_2 inhalation, who was successfully treated with veno-venous extracorporeal membrane oxygenation (V-V ECMO) support and glucocorticoids.

CASE REPORT

A 35-year-old man with a childhood history of asthma was accidentally exposed to NO_2 fumes while cleaning a boiler. He was obese, with a height of 160 cm and a weight of 87 kg. Cough and dyspnea occurred approximately 3 h after exposure. He presented to the emergency department in the previous hospital the next morning, 17 h after exposure.

On admission, he was conscious, but his respiratory rate was 32 breaths/min and oxygen saturation was 87% on ambient air. He was breathing effortfully and coarse crackles were heard in both lungs. Oxygen administration was started immediately, and oxygen saturation increased to 98% at 10 L/

min of oxygen. Arterial blood gases showed a pH of 7.39, $PaCO_2$ 38.6 mmHg, PaO_2 151.4 mmHg, HCO_3^- 23.0 mmol/L, and BE −1.5 mmol/L. Chest computed tomography (CT) was performed immediately thereafter, and the CT image showed bilateral ground-glass opacities (Figure 1A). Echocardiography showed normal cardiac function. These findings indicated lung injury and ARDS caused by NO_2 inhalation. He was intubated and mechanically ventilated due to difficulty in breathing 1 h after arrival at the hospital. The ventilator settings were FIO_2 1.0, PEEP 18 cmH_2O, inspiratory pressure 42 cmH_2O, and respiratory rate 35 breaths/min. The arterial blood gases showed pH 7.20, $PaCO_2$ 78.9 mmHg, PaO_2 68.4 mmHg, HCO_3^- 30.1 mmol/L, and BE −0.7 mmol/L. The post-intubation chest X-ray showed diffuse infiltration throughout all lung fields (Figure 1B). Because hypoxemia and hypercapnia were not ameliorated despite ventilator management, the decision was made to introduce V-V ECMO. Our hospital was contacted and an ECMO team was dispatched. V-V ECMO was introduced 6.5 h after the patient's arrival using a MERA centrifugal blood pump system (Senko Medical Instrument Mfg. Co., Ltd, Tokyo, Japan). A 25 Fr, 38 cm drainage cannula and a 19 Fr, 15 cm return cannula were percutaneously inserted into the right internal carotid vein and left femoral vein, respectively. The initial ECMO flow was 4.5 L/min with an oxygen flow of 6.0 L/min.

He was transferred to our hospital and admitted to the intensive care unit (ICU), and a neuromuscular blocking agent (NMBA) was continuously administered. The ventilator settings were set to FIO_2 0.4, PEEP 10 cmH_2O, inspiratory pressure 10 cmH_2O, and respiratory rate 10 breaths/min for lung-protective ventilation. Methylprednisolone (mPSL) 1.0 mg/kg/day was also administered. The NMBA was discontinued on days 3 and 4 but was resumed due to high respiratory effort. This was likely a result of inadequate improvement in chest X-ray and dynamic lung compliance. As a response, NMBA was reintroduced, and lung-protective ventilation and mPSL administration were sustained, with the NMBA ultimately discontinued on day 6. The dose of mPSL was reduced to 0.5 mg/kg/day on day 8. The chest X-ray and dynamic lung compliance gradually improved; however, there was an elevated inflammatory response and antibiotics were started for ventilator-associated pneumonia (VAP) on day 8. The treatment for VAP was successful, leading to further improvement in lung function. Therefore, an ECMO weaning trial was performed on day 10, and the ECMO was weaned off on day 11 without any ECMO-related complications. He was extubated on day 12 and discharged from the ICU on day 15. After rehabilitation, he was discharged home on day 20. Two months have passed without any sequelae. The course of treatment and the laboratory results of the patient at each time point were shown in Figure 2 and Table S1.

DISCUSSION

In this case, the cleaning agent for the boiler was mixed with an antiseptic, and the hydrogen chloride and sodium nitrite in each component reacted as shown in the following chemical equation, producing NO_2.

$$2HCl + 2NaNO_2 \rightarrow N_2O_3 + 2NaCl + H_2O.$$

$$N_2O_3 \rightarrow NO + NO_2.$$

Lung injury caused by the inhalation of nitrogen oxides can be mild, requiring only oxygen administration or it can be severe enough to require intubation.[5] Previous literature reporting the prognosis for severe cases is limited. Yu et al.[3] showed that ECMO was effective in the treatment of ARDS caused by the inhalation of toxic gases, including nitrogen oxides. Shin et al.[1] reported that the induction of ECMO was associated with a favorable outcome in cases of fatal pulmonary edema caused by nitric and hydrofluoric acid fumes.

Table 1 lists previously reported cases of ARDS caused by nitrogen oxides inhalation with a PaO_2 /FIO_2 ratio less than 100, and 4 out of 5 patients were discharged alive after the induction of ECMO.[1–7] These reports suggest that ECMO management may be effective in severe cases. Therefore, if ARDS caused by NO_2 inhalation develops, the clinician should consider transferring the patient to a hospital with an ECMO center before or after ECMO establishment. In this case, we deemed it safer to transfer the patients to our center after ECMO establishment. We are active participants in the Japan-ECMO network and possess sufficient experience and training to perform ECMO establishment at the previous hospital.[8]

In addition, glucocorticoid have been administered in some cases. Kido et al.[9] also reported that glucocorticoid

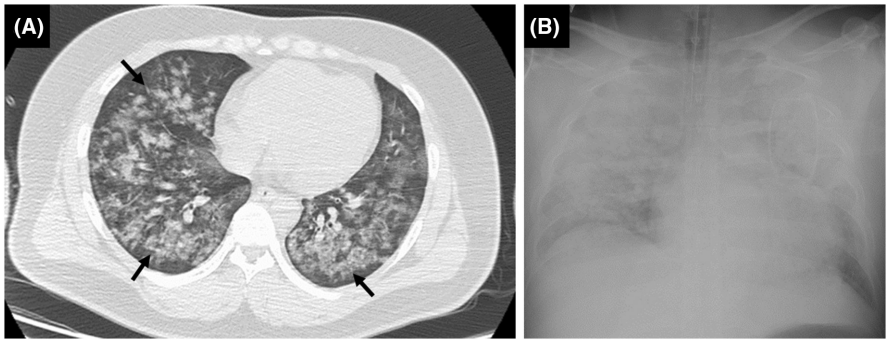

FIGURE 1 Chest computed tomography image (A) and chest X-rays (B) before the introduction of extracorporeal membrane oxygenation. (A) Bilateral ground-glass opacities (arrow) are shown, indicating pulmonary edema. (B) The diffuse infiltration throughout all lung fields is shown.

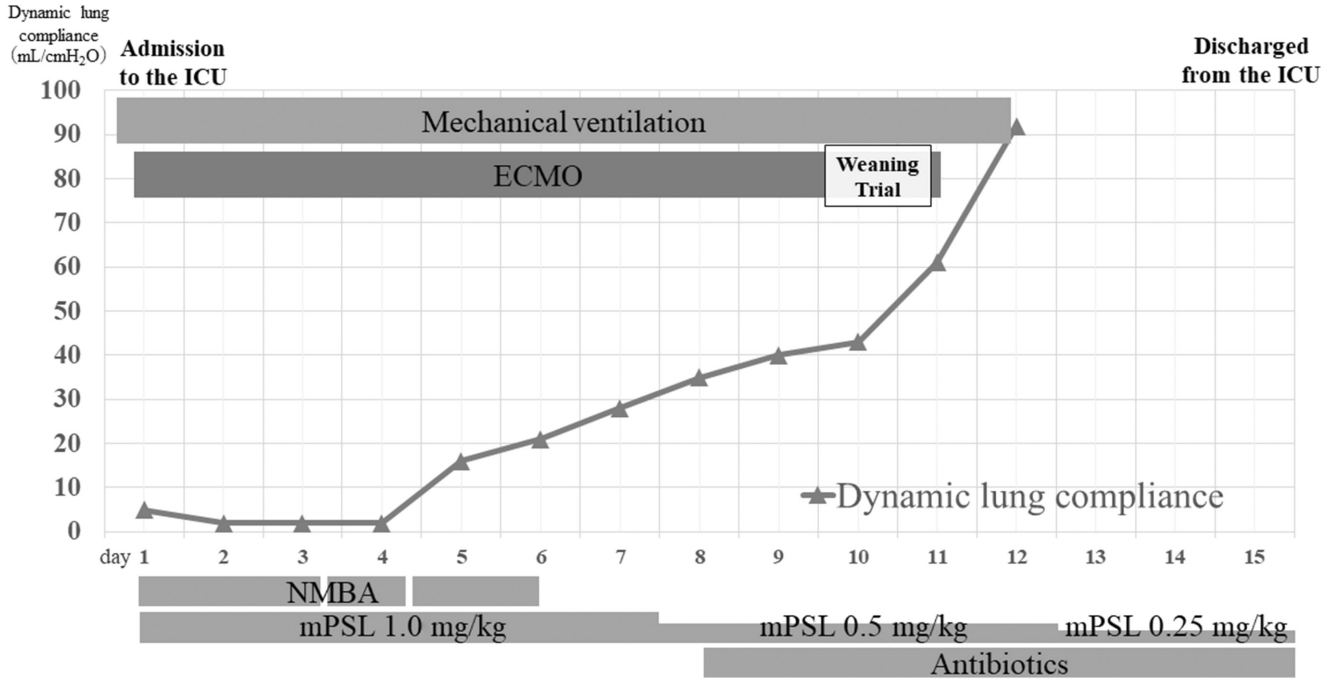

FIGURE 2 Clinical course and treatment process. Extracorporeal membrane oxygenation (ECMO) was introduced and a neuromuscular blocking agent (NMBA) and methylprednisolone (mPSL) were administered on day 1. With improvement in dynamic lung compliance and the chest X-ray, NMBA was finally discontinued on day 6. The dose of mPSL was gradually reduced. However, the patient developed ventilator-associated pneumonia (VAP) and antibiotics were started on day 8. After improvement in VAP, the ECMO was weaned off on day 11. ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; mPSL, methylprednisolone; NMBA, neuromuscular blocking agent.

TABLE 1 Previously reported cases of acute respiratory distress syndrome caused by nitrogen oxides inhalation with PaO_2/FIO_2 ratio less than 100.

Literature	Age/sex	$PaCO_2$	PaO_2	FIO_2	P/F ratio	MV	ECMO	Glucocorticoid	Other treatments	Outcome
Hajela et al. (1990) [5]	36/M	30	50	1	50	+	–	–	–	Death
Hajela et al. (1990) [5]	44/M	29	45	1	45	+	–	–	–	Death
Hajela et al. (1990) [5]	21/M	45	43	1	43	+	–	–	–	Death
Shin et al. (2007) [1]	37/M	85	54	1	54	+	–	–	–	Death
Murphy et al. (2010) [4]	66/M	52	74	1	74	+	–	mPSL 125 mg	Inhaled NO therapy, sodium thiosulfate, disulfiram	Death
Bur et al. (1997) [2]	56/M	79	50	1	50	+	+	mPSL 60 mg PSL 1000 mg	Aminophylline, terbutaline, piritramid, budesonide	Death
Shin et al. (2007) [1]	43/M	105	51	1	51	+	+	–	N-acetylcysteine, calcium gluconate	Alive
Lee et al. (2012) [6]	42/M	108	43	1	43	+	+	–	–	Alive
Yu et al. (2021) [3]	41/M	No data	50	0.8	63	+	+	mPSL (dose no data)	N-acetylcysteine, pirfenidone	Alive
Wang et al. (2022) [7]	40/M	78	52	1	52	+	+	mPSL 200 mg	N-acetylcysteine, sivelestat sodium	Alive

Abbreviations: ECMO, extracorporeal membrane oxygenation; mPSL, methylprednisolone; MV, mechanical ventilation; PSL, prednisolone; P/F ratio, PaO_2/FIO_2 ratio; NO, nitric oxide.

administration was effective in bronchopathy caused by nitrogen oxides. Although rapid improvement after glucocorticoid administration in lung injury caused by NO_2 inhalation indicates that glucocorticoids are effective, the reason for the efficacy is unclear. Although this case was severe, it was successfully treated using only mPSL and no other therapeutic agents. This suggests that glucocorticoids, rather than other therapeutic agents, may be effective against ARDS caused by NO_2 inhalation. In this case, mPSL 1.0 mg/kg/day was administered, but the specific type of glucocorticoid and the optimal dose remain unknown, and necessitating future investigation.

CONCLUSION

Lung injury caused by the inhalation of nitrogen dioxide can cause ARDS, and lung-protective ventilation with V-V ECMO induction, as well as glucocorticoid administration, may be effective for this condition.

FUNDING INFORMATION

No funding. The authors have no financial relationships relevant to this article to disclosure.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest for this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Approval of the research protocol: N/A.
Informed consent: Written informed consent was obtained from the patient for the publication of this case report and all accompanying images.
Registry and the registration no. of the study/trial: N/A.
Animal studies: N/A.

ORCID

Tomoya Nishimura https://orcid.org/0009-0003-1332-9139
Makoto Aoki https://orcid.org/0000-0001-8239-8822
Kenji Fujizuka https://orcid.org/0000-0003-2732-2774

REFERENCES

1. Shin JS, Lee SW, Kim NH, Park JS, Kim KJ, Choi SH, et al. Successful extracorporeal life support after potentially fatal pulmonary oedema caused by inhalation of nitric and hydrofluoric acid fumes. Resuscitation. 2007;75(1):184–8.
2. Bur A, Wagner A, Röggla M, Berzlanovic A, Herkner H, Sterz F, et al. Fatal pulmonary edema after nitric acid inhalation. Resuscitation. 1997;35(1):33–6.
3. Yu D, Xiaolin Z, Lei P, Feng L, Lin Z, Jie S. Extracorporeal membrane oxygenation for acute toxic inhalations: case reports and literature review. Front Med (Lausanne). 2021;8:745555.
4. Murphy CM, Akbarnia H, Rose SR. Fatal pulmonary edema after acute occupational exposure to nitric acid. J Emerg Med. 2010;39(1):39–43.
5. Hajela R, Janigan DT, Landrigan PL, Boudreau SF, Sebastian S. Fatal pulmonary edema due to nitric acid fume inhalation in three pulp-mill workers. Chest. 1990;97(2):487–9.
6. Lee YS, Lee SH, Kim WY, Kim JH, Park YC. Anesthetic management of a patient with nitric acid inhalation injury for extracorporeal membrane oxygenation. Korean J Anesthesiol. 2012;62(2):194–5.
7. Wang Q, Zhu J, Chen L, He Y, Li H, Lan Y, et al. Successful treatment of severe ARDS caused by accidental inhalation of nitric acid fumes with veno-venous ECMO: a case report and literature review. Medicine (Baltimore). 2022;101(30):e29447.
8. Ogura T, Ohshimo S, Liu K, Iwashita Y, Hashimoto S, Takeda S. Establishment of a disaster management-like system for COVID-19 patients requiring Veno-venous extracorporeal membrane oxygenation in Japan. Membranes (Basel). 2021;11(8):625.
9. Kido Y, Mitani A, Isago H, Takeshima H, Narumoto O, Tanaka G, et al. Successful treatment of pulmonary injury after nitrogen oxide exposure with corticosteroid therapy: a case report and review of the literature. Respir Med Case Rep. 2017;20:107–10.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Nishimura T, Aoki M, Suzuki H, Hagiwara H, Kawauchi A, Fujizuka K, et al. Veno-venous extracorporeal membrane oxygenation for acute respiratory distress syndrome caused by nitrogen dioxide inhalation: A case report. Acute Med Surg. 2024;11:e957. https://doi.org/10.1002/ams2.957