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Sevoflurane administration from extracorporeal membrane oxygenation via the AnaConDa device for a patient with COVID-19: A breakthrough solution for the shortage of intravenous anesthetics

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ABSTRACT

One of the major issues encountered during the coronavirus disease 2019 (COVID-19) pandemic has been the shortage of intravenous anesthetics. Moreover, patients undergoing extracorporeal membrane oxygenation (ECMO) need large quantities of intravenous anesthetics for sedation. We report the case of a 52-year-old man who was admitted to our hospital due to acute respiratory distress syndrome by COVID-19 and treated with ECMO. As controlling sedation with intravenous anesthetics was challenging, we attempted to administer inhaled anesthetics via the gas flow of ECMO. We decreased the quantity of intravenous anesthetics and opioids. This method might help overcome the shortage of intravenous anesthetics.

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Introduction

Coronavirus disease (COVID-19), caused by a novel virus called severe acute respiratory syndrome coronavirus 2, is widespread. COVID-19 is known to cause acute respiratory distress syndrome (ARDS). Due to the severity of this illness, some patients require mechanical ventilation and venovenous extracorporeal membrane oxygenation (ECMO). The patients often need to be sedated using intravenous anesthetics to reduce oxygen consumption. However, patients undergoing ECMO require a large quantity of intravenous anesthetics because of the loss of these drugs via the ECMO circuit.^{1,2} With the worldwide shortage of intravenous anesthetics,³ the sedation of ECMO patients is one of the major problems requiring attention.

The use of volatile drugs is one of the solutions to overcome the shortage of intravenous anesthetics. Sevoflurane is one of the

frequently used volatile anesthetics; when it is compared with midazolam, it has been proven to improve oxygenation.⁴ However, patients undergoing ECMO are often managed using ultra-lung protective ventilation. Therefore, it might be difficult to use volatile anesthetics for sedation because of the limited minute volume. Andreas et al. reported on the use of inhaled sedation in patients with ARDS undergoing ECMO.⁵ However, their results indicated that the patients' tidal volume had more than doubled. This change might impair the lung protective ventilation and increase mechanical power. Herein, we report the case of a patient to whom we administered inhaled anesthetics directly via ECMO without increasing the minute volume of mechanical ventilation. We obtained consent from the patient's family to publish this paper.

Case description

A 52-year-old man with a body mass index of 40 kg/m² and a weight of 127 kg was admitted to our hospital for dyspnea. He was diagnosed with ARDS caused by COVID-19 and was treated with venovenous ECMO from Day 2. Long-term ECMO was administered to this patient. Given his obese nature and drug adsorption by the artificial lung, we administered a large dose of sedatives. It became progressively difficult to regulate sedation control due to his drug

Abbreviations: ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation

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tolerance. Although we administered 5 mg/h of morphine, 100 μ g/h of fentanyl, 160–200 mg/h of propofol, 4 mg/h of midazolam, and 32 mg/h of dexmedetomidine to the patient, it was difficult to regulate his tachypnea and sedation level. Moreover, we had to administer large quantities of norepinephrine due to drug-induced hypotension and to stop eternal nutrition. To utilize the different type of sedatives, we tried to administer inhaled anesthetics through the ventilator using the Anaesthetic Conserving Device (AnaConDa; BOMImed, Winnipeg, Manitoba, Canada); however, it failed because the minute volume in this case was less than 0.5 L/minute due to the low compliance. Therefore, we attempted to administer inhaled anesthetics via gas flow of ECMO from Day 53.

Fig. 1 illustrates the procedure of administration of the inhaled anesthetic from ECMO. The AnaConDa device was inserted into the oxygen airline (Fig. 1A, red arrow). We chose sevoflurane as the inhaled anesthetic to be administered. The artificial membrane and gas outlet were covered with plastic bags to collect the exhaust gas from the gas outlet that contained

sevoflurane. The exhaust gas was collected using a pollution control system via a polyvinyl chloride tube. We also collected expiratory gas from the mechanical ventilator in case sevoflurane was emitted via the patient's native lung. The ECMO settings were as follows: fraction of delivered oxygen in the sweep gas, 100%; sweep gas, 5.5 L/minute; and flow, 4.3 L/minute. We determined the dose of sevoflurane by using the original dosage adjustment table based on the calculation of volatile anesthetics consumption (Table 1),⁶ and started administering sevoflurane at 5 ml/h and increased it to up to 8 ml/h, which was estimated to be equivalent to a constant flow of 0.44% sevoflurane. We then decreased the quantity of intravenous anesthetics and opioids as follows: 4 mg/h of morphine, 50 μ g/h of fentanyl, and 80 mg/h of propofol. We discontinued midazolam, dexmedetomidine, and norepinephrine, and restarted eternal nutrition. We confirmed that the patient was fully conscious and lightly sedated; his Richmond Agitation-Sedation Scale was –1 to –2. After sevoflurane was initiated, there was no change in the patient's laboratory examination findings until Day 70 (Table 2), and

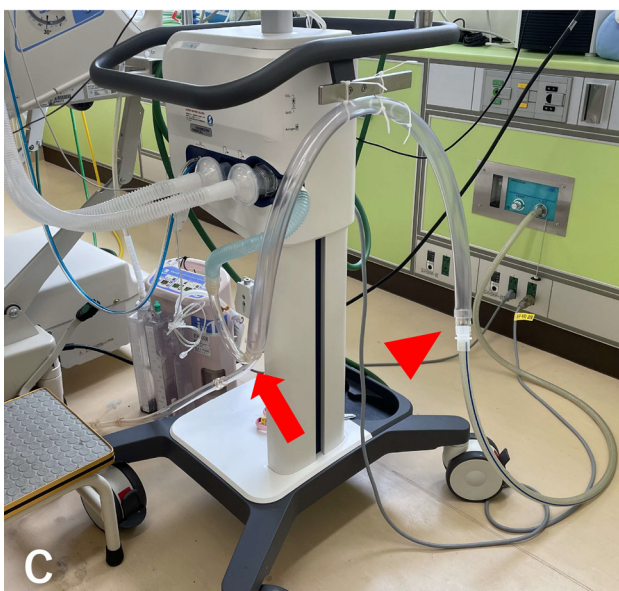
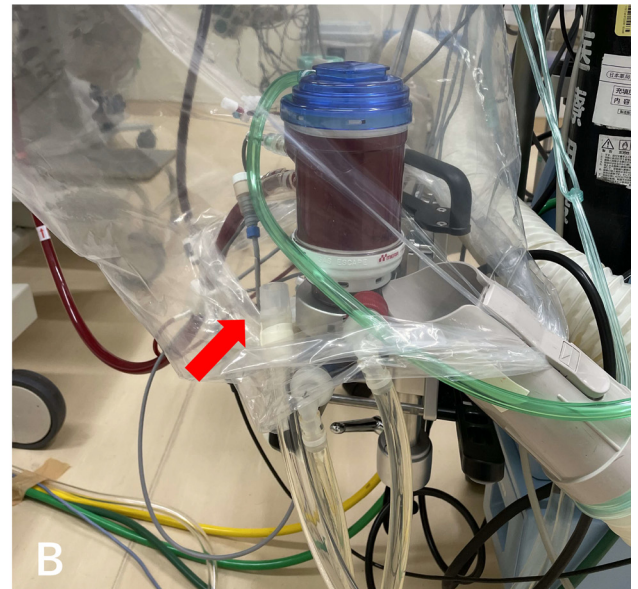
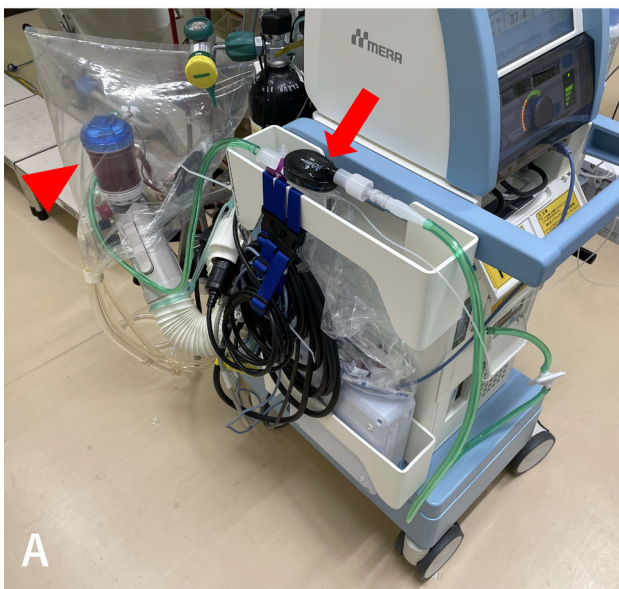


Fig. 1. Procedure for administration of the inhaled anesthetic from extracorporeal membrane oxygenation. The Anaesthetic Conserving Device (AnaConDa; BOMImed, Winnipeg, Manitoba, Canada) was inserted into the oxygen airline (Fig. 1A, red arrow). The artificial membrane and gas outlet were covered with plastic bags to collect the exhaust gas from the gas outlet (Fig. 1A, red arrowhead). This exhaust gas from the gas outlet was collected via a polyvinyl chloride (PVC) tube (Fig. 1B, red arrow). Expiratory gas from the mechanical ventilator was also collected via a PVC tube (Fig. 1C red arrow), and two PVC tubes were connected to the pollution control system (Fig. 1C red arrow and red arrowhead).

Table 1
Dosage adjustment table of sevoflurane.

Sweep gas of ECMO (L/minute)	Target SEV in constant gas flow (%)		
	0.5	1	1.5
1	1.7	3.3	5.0
2	3.3	6.6	9.9
3	5.0	9.9	14.9
4	6.6	13.2	19.8
5	8.3	16.5	24.8
6	9.9	19.8	29.7
7	11.6	23.1	34.7
8	13.2	26.4	39.6
9	14.9	29.7	44.6
10	16.5	33	49.5

The numbers in the table represent the flow rate of sevoflurane administered by the syringe pump (unit: ml/h). ECMO, extracorporeal membrane oxygenation; SEV, sevoflurane.

there was no excessive increase in urine volume. However, he developed sepsis-associated multiple organ failure and died on Day 75.

Discussion

To our knowledge, this is the first report on the administration of inhaled anesthetics via venovenous ECMO rather than mechanical ventilation. Although the patient eventually died, we could sedate this patient by using inhaled anesthetics, which have a different mechanism of action from intravenous anesthetics. We believe that this report provides a new method for using volatile anesthetics, instead of the usual intravenous anesthetics for ECMO patients with decreased minute ventilation.

A similar method was established for cardiovascular anesthesia.⁷ In some institutes, anesthesia during cardiopulmonary bypass was conducted by using inhaled anesthetics from the oxygenator fresh-gas supply. Similarly, we established sevoflurane administration from ECMO using the AnaConDa device. Unlike in cardiovascular surgery, patients with ARDS do not need to be immobilized. One narrative review suggested that a minimum alveolar concentration of sevoflurane of 0.2–0.5 was the adequate sedation goal.⁸ Therefore, we used a lower concentration of sevoflurane compared to that used in cardiovascular anesthesia and succeeded in achieving light sedation under ECMO, according to the original dosage adjustment table (Table 1). By using this method, we reduced the quantity of intravenous anesthetics; this could explain the stability of the patient's blood pressure. This new method was used in this patient with obesity. This method can also be used in patients with a normal BMI or

patients with emaciation, if the appropriate dosage of sevoflurane based on the sweep gas setting of ECMO is set.

This patient finally died from multiple organ dysfunction, and it is unknown whether long-term sevoflurane use was associated with the patient's outcome. A previous study reported the safety considerations of long-term use of sevoflurane,⁹ and sevoflurane was used for 12 days in some clinical trials. Polyuria and nephrogenic diabetes insipidus (NDI) are associated with long-term use of sevoflurane.¹⁰ In our patient, sevoflurane was used for a longer duration than has been reported in previous studies. However, he did not develop NDI, suggesting that the long-term use of inhaled anesthetics did not lead to the development of complications. Further studies are needed to prove the safety of long-term use of sevoflurane.

This method has some limitations. First, we could not measure the actual sevoflurane concentration in this patient. Although we used a multigas monitoring unit (Multigas Unit GF-220R, Nihonkoden), we could not detect the sevoflurane concentration. The threshold for the initial sevoflurane measurement of this device is 0.3%. Therefore, there is a high possibility that the concentration of anesthetic gas in the gas inhaled by the sampling tube was less than 0.3%. However, it is possible to estimate the administered sevoflurane concentration by calculating the volatile anesthetic consumption based on the sweep gas flow of ECMO.⁶ If we use neuromuscular blockers for the patients, the adjustment of volatile anesthetics based on the bispectral index might be useful.⁷ However, the dosage adjustment table of sevoflurane is our original creation, and external validation is needed in further studies. Second, it is unclear whether this method guarantees the effectiveness of sevoflurane for patients with ARDS. One previous research proved the effectiveness of sevoflurane for ARDS in terms of oxygenation,⁴ and another research revealed the bronchodilatory and anti-inflammatory effects of sevoflurane.¹¹ Some researchers reported on the antibacterial effect of this drug¹²; however, these effects were proven under the administration via the respiratory system. It is unknown whether these effects remain under the administration via the ECMO gas flow, and further studies are needed to prove it. Third, this method can only be used in intensive care units having a pollution control system or scavenging system. Using these systems correctly, volatile anesthetics can be administered safely in intensive care units.¹³ However, care needs to be taken to avoid inhalant anesthetic exposure in health care workers.

In conclusion, this sevoflurane administration method from ECMO via the AnaConDa device was effective for a patient with COVID-19 undergoing ECMO. This method might be able to help overcome the shortage of intravenous anesthetics. More experience in the use of this method and clinical studies are needed. This case report has been written following the CARE (Consensus-based Clinical Case Reporting) guidelines.

Table 2
Patient's laboratory examination findings.

	Day 52	Day 53	Day 58	Day 63	Day 68	Day 73
Total bilirubin (mg/dl)	0.8	0.7	0.9	0.8	1	4.8
Direct bilirubin (mg/dl)	0.4	0.3	0.4	0.4	0.5	4.2
Alkaline phosphatase (IU/l)	146	137	130	115	139	263
Γ-glutamyl transpeptidase (IU/l)	188	195	180	145	169	172
Aspartate aminotransferase (IU/l)	69	73	70	71	62	2364
Alanine aminotransferase (IU/l)	98	95	71	41	37	1171
Lactate dehydrogenase (IU/l)	737	653	804	752	797	3581
Blood urea nitrogen (mg/dl)	36	34	27	36	31	43
Creatinine (mg/dl)	0.71	0.69	0.53	0.62	0.67	1.52
Sodium (mmol/l)	147	145	143	135	132	135
Potassium (mmol/l)	3.7	3.6	3.5	3.9	4.6	5.9
Chloride (mmol/l)	103	101	94	90	91	102
White blood cell ($10^3/\mu\text{l}$)	25.7	20.9	12.2	15.1	25.2	25
Hemoglobin(g/dl)	9.6	9.4	11.3	9.7	10.1	9.1
Platelet count($10^3/\mu\text{l}$)	208	201	184	142	231	130

"Day" shows the admissions to the intensive care units.

Ethics approval

Approval from the hospital ethics committee was not required because this was a case report. Since we documented an off-label use of an unapproved device, permission to use the AnaConDa device in ECMO was obtained from the medical safety section of our hospital.

Consent to participate

Informed consent was obtained.

Consent for publication

One of the patient's family member provided written informed consent for the publication of this report.

Author contributions

All authors contributed to the writing of the manuscript. DK, TS, and KS supervised the investigation. NH, HS, and DI were involved in the patient management. All authors assessed the patient's condition and participated in discussions. YI contributed to the first draft of this manuscript, and all authors revised the manuscript. The final version of the manuscript has been approved by all authors. YI takes primary responsibility for this paper.

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Declarations of Competing Interest

none

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