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Extracorporeal Membrane Oxygenation and Perfluorocarbon in a Therapy Refractory Case of Acute Respiratory Distress Syndrome

Maria Theresa Voelker, MD, Sven Laudi, MD, Jeanette Henkelmann, MD, and Sven Bercker, MD

Department of Anesthesiology and Intensive Care Medicine, University Hospital Leipzig, Leipzig, Germany; and Department of Diagnostic and Interventional Radiology, University Hospital Leipzig, Leipzig, Germany

Perfluorocarbons are oxygen-carrying, dense liquids initially intended for the use in partial or total liquid ventilation of patients with severe acute respiratory distress syndrome but which did not show beneficial effects in clinical studies. However, perfluorocarbons may be used for lung lavage in severe alveolar proteinosis. In acute respiratory distress syndrome, oxygenation may be so severely compromised that the use of nonoxygenated perfluorocarbons may not be possible. We report a case of severe, nonresolving acute respiratory distress syndrome treated with extracorporeal membrane oxygenation to secure oxygenation, using perfluorocarbon in a single instillation to aid the clearance of debris and proteinacous edema.

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We report a case of severe acute respiratory distress syndrome (ARDS) in a young patient. Venovenous extracorporeal membrane oxygenation (ECMO) had to be initiated. Despite adequate and extensive supportive treatment, the ARDS was not resolving. Perfluorocarbon (PFC) was used in a single instillation technique to help clear debris from the lung. That was possible only by the simultaneous use of ECMO to ensure oxygenation as perfluorocarbon was not used for ventilation but only instilled once. As perfluorocarbon evaporated from the lung, bilateral infiltrations and, consequently, oxygenation improved. This case report displays a feasible and practical way to use perfluorocarbon to clear debris from lungs in cases of persistent ARDS without the danger of hypoxemia by the simultaneous application of ECMO.

A 20-year-old male refugee from Iraq, a nonsmoker with a history of type 1 diabetes mellitus, presented with cough and fatigue to a tertiary care hospital 9 days after arriving in Germany. Calculated antibiotic treatment was started with meropenem. The patient's condition worsened quickly, and he was admitted to the intensive care unit and intubated 2 days after admittance. Despite lung-protective ventilation, fluid restriction, and intermittent prone positioning, gas exchange deteriorated rapidly (Pa_{O_2} 40 mm Hg at fraction of inspired oxygen [Fi_{O_2}] of 1.0) and he was presented for transfer to our center 2 days later. With a Pa_{O_2} of 40 mm Hg at Fi_{O_2} 1.0 and aggressive ventilation, our ARDS retrieval team decided on an on-site initiation of ECMO before transportation. The patient received a 21F multistage draining cannula into the right femoral vein and a 19F returning cannula into the right jugular vein. The ECMO was started (blood flow 4 L/min, gas flow 3 L/min) and ventilation could be deescalated (peak pressure 30 mm H_2O; positive end-expiratory pressure 15 mm H_2O; respiratory rate 20 breaths per minute; tidal volumes less than 100 mL) resulting in a Pa_{O_2} of approximately 70 mm Hg.

Initial computed tomography scan at our center revealed massive pulmonary infiltration and pleural effusions (Figure 1A). Bronchoscopy showed no obstructions but excessive pus and proteinaceous edema. Cultures of bronchial and tracheal secretions were obtained but showed no growth. Acid fast staining and polymerase chain reaction for *Mycobacterium tuberculosis* came back negative. Urinary antigen testing for *Legionella pneumophila* serogroup 1 antigen and pneumococcal antigen were negative. Immunoglobulins showed no acute infections with *Chlamydophila pneumoniae* and *Mycoplasma pneumoniae*. Excessive diagnostic testing for autoimmune pathologies were negative. We found no viral infections with HIV or *Hepadna viridae*, but polymerase chain reaction for influenza A/H1N1 was positive. Antibiotics were stopped consequently.

The patient received a percutaneous dilational tracheostomy at day 15, sedation was weaned to a Richmond Agitation Scale Score (RASS) of −1/−2 to promote spontaneous breathing but allow for prone positioning. Despite further deescalation of the ventilation on ECMO, strict fluid restriction, and continuing intermittent prone positioning, there was no clinical or radiographic improvement after 18 days (Figure 1B).

The Video can be viewed in the online version of this article [https://doi.org/10.1016/j.athoracsur.2021.07.045] on http://www.annalsthoracicsurgery.org.

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Address correspondence to Dr Voelker, Department of Anesthesiology and Intensive Care Medicine, University Hospital Leipzig, Liebigstrasse 20, Leipzig 04103, Germany; email: theresa.voelker@medizin.uni-leipzig.de.

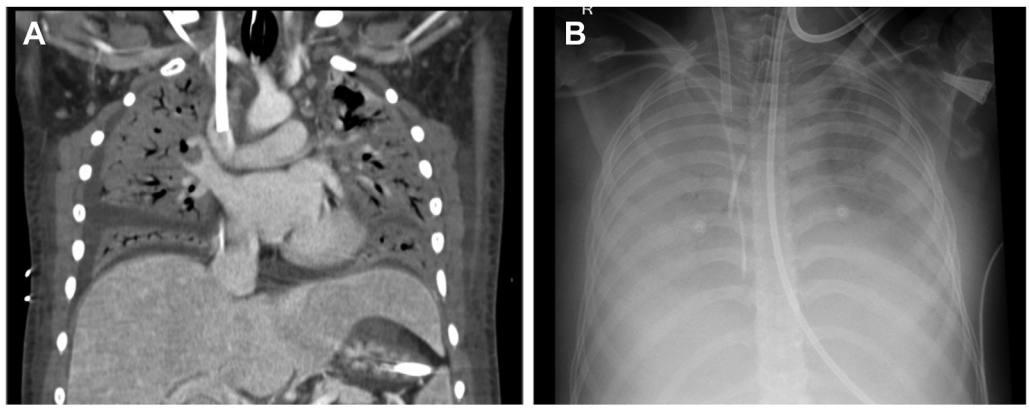

FIGURE 1 (A) Computed tomography scan on admission (coronal axis mid-cardiac); bilateral consolidation of the lung with air bronchogram and pleural effusions. (B) Chest radiograph just before instillation of perfluorocarbon showing diffuse lung white-out with consolidation and air bronchogram.

At this point, the team and family of the patient decided on the off-label use of perfluorocarbon (perflubron [LiquiVent; OriGen Biomedical, Austin, TX] for research use only in the United State; CE marked) for the displacement of intraalveolar debris and fluids. Sedation was increased slightly (RASS −3/−4) to tolerate the

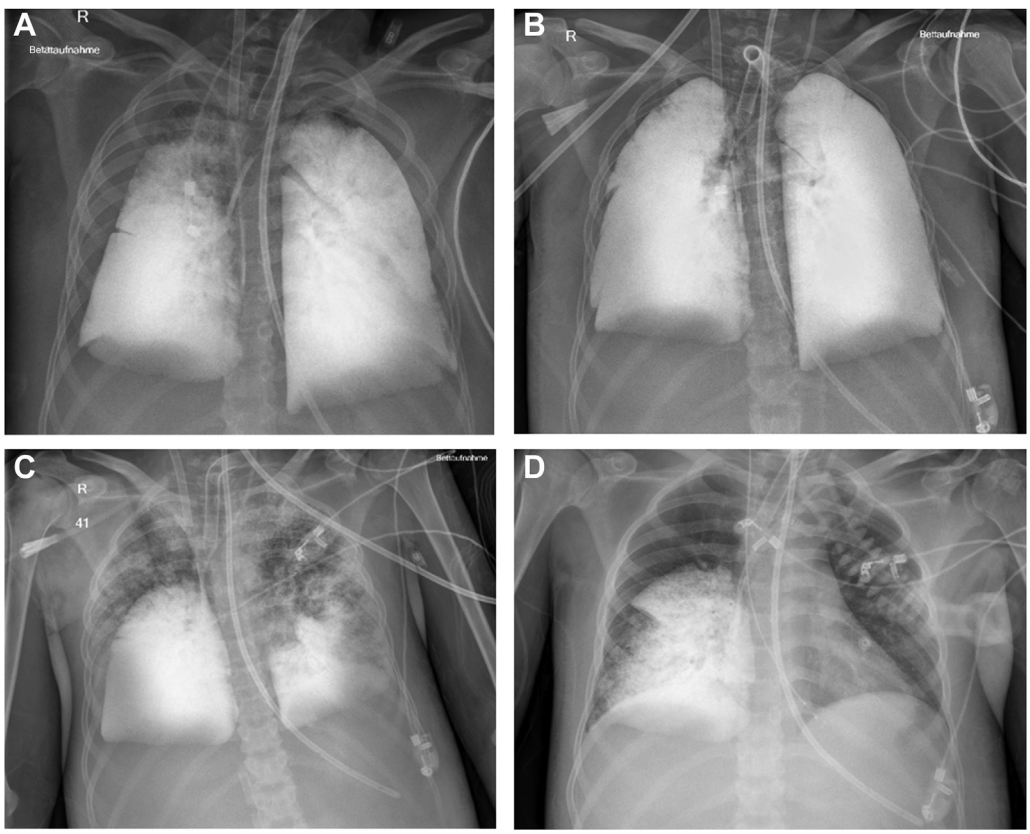

FIGURE 2 Chest radiographs. (A) One hour after instillation of perfluorocarbon (PFC). Radio-opaque PFC results in opacification notably in the basal parts of the lungs with bilateral pleural effusions. (B) Two days after instillation, distribution of PFC homogenizes in both lungs. (C) Six days after instillation, re-aeration of upper pulmonary sections. (D) Eleven days after instillation, significant re-aeration of both lungs.

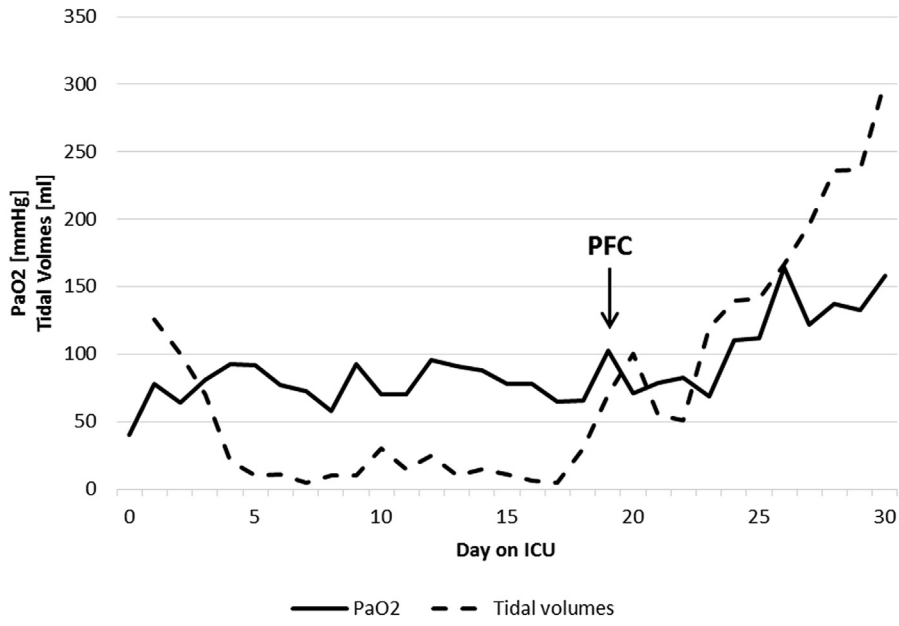

FIGURE 3 Tidal volumes (broken line) and Pa_{O_2} (solid line) from admittance to termination of extracorporeal membrane oxygenation. (ICU, intensive care unit; PFC, perfluorocarbon.)

procedure. By bronchoscopy, 550 mL PFC was instilled until fluid level was approximately 3 cm above the bifurcation (Video). Ventilation was continued with peak pressure of 25 cmH_2o, Fi_{O_2} of 0.4, and a respiratory rate of 20 breaths per minute, resulting in tidal volumes of less than 50 mL. Gas exchange was secured with the ongoing ECMO support. A chest radiograph immediately after instillation showed a concentration of perflubron notably in the basal parts of the lungs (Figure 2 A). The pleural effusions are still visible. Only 2 days later, the distribution has clearly homogenized and the pleural effusion seems to be dissolved (Figure 2B). The ECMO settings, tidal volumes, and gas exchange were stable at this time (Figure 3). The ECMO blood flow was between 4.6 and 6 L/min. Sedation depth was kept at a RASS of −3.

During the next 6 days, we noticed a significant increase in proteinaceous secretion to be suctioned from the upper airways, presenting as a supernatant above the perflubron. As the perflubron slowly evaporated, tidal volumes increased continuously, gas exchange improved, and chest radiograph showed a marked increase of aeration (Figures 2C and 3). Eleven days after PFC, ECMO therapy could be stopped (Figure 2D). After a further course, sedation was altogether stopped and the patient started nonverbal communication with his family.

Two days after the stopping of ECMO and the removal of the cannulas, and 13 days after PFC treatment, the patient suddenly had a cardiac arrest. Return of spontaneous circulation was achieved quickly, and diagnostics revealed a sinus arrest to be treated with a pacemaker. However, somnolence progressed to coma after the events, and a cerebral scan showed multiple disseminated infarctions. He died 20 days later of cerebral herniation. The family did not give consent for autopsy.

COMMENT

Perfluorocarbons are oxygen-carrying, dense liquids that were initially intended for use in partial or total liquid ventilation in patients with severe ARDS. It reduces surface tension thereby improving lung compliance, potentially clearing debris, and opening collapsed alveoli. It has antiinflammatory effects mediated by reduction of the adhesive interaction of neutrophils and epithelial cells, reducing target cell injury in the lung.[1-3] However, clinical studies were not able to show beneficial effects on survival.[4,5] Ultimately, PFC may be used as rescue therapy for nonresolving ARDS to aid clearance of cell debris and edema.[6]

Total liquid ventilation is technically challenging and expensive, as adequate circulation of oxygenated PFC must be provided to ensure oxygen delivery into the lung. However, in patients with severe hypoxemia due to ARDS, partial liquid ventilation cannot be used safely without risking hypoxemia owing to the reduced tidal volume immediately after instillation. In this case, we saw a completely opaque lung. After the use of PFC,

aeration was restored quickly. We postulate that this was induced by supporting alveolar clearance of cell debris and proteinaceous secretion, leading to supernatant above the PFC.

In this unfortunate course of the patient presenting with disseminated cerebral infarctions 2 days after the removal of the ECMO cannulas and 13 days after the application of PFC, we cannot exclude that these infarctions were a thromboembolic complication of ECMO or caused by PFC therapy. However, that the patient was fully awake between ECMO and infarction and the long interval between PFC treatment and infarction provide some arguments against this hypothesis. From a pathophysiologic point of view, PFC as a cause at least seems implausible. Unfortunately, the definite reason remains unclear.

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