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Inhaled nitric oxide in patients with acute respiratory distress syndrome caused by COVID-19: treatment modalities, clinical response, and outcomes

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Abstract

Background: Inhaled nitric oxide (iNO) has been widely used in patients with COVID-19-related acute respiratory distress syndrome (C-ARDS), though its physiological effects and outcome are debated in this setting. The objective of this cohort study was to describe the modalities of iNO use, clinical response, and outcomes in a large cohort of C-ARDS patients.

Methods: Multicentre, retrospective cohort study conducted in France.

Results: From end February to December 2020, 300 patients (22.3% female) were included, 84.5% were overweight and 69.0% had at least one comorbidity. At ICU admission, their median (IQR) age, SAPS II, and SOFA score were 66 (57-72) years, 37 (29-48), and 5 (3-8), respectively. Patients were all ventilated according to a protective ventilation strategy, and 68% were prone positioned before iNO initiation. At iNO initiation, 2%, 37%, and 61% of patients had mild, moderate, and severe ARDS, respectively. The median duration of iNO treatment was 2.8 (1.1-5.5) days with a median dosage of 10 (7-13) ppm at initiation. Responders (PaO₂/FiO₂ ratio improving by 20% or more) represented 45.7% of patients at 6 h from iNO initiation. The severity of ARDS was the only predictive factor associated with iNO response. Among all evaluable patients, the crude mortality was not significantly different between responders at 6 h and their counterparts. Of the 62 patients with refractory ARDS (who fulfilled extracorporeal membrane oxygenation criteria before iNO initiation), 32 (51.6%) no longer fulfilled these criteria after 6 h of iNO. The latter showed significantly lower mortality than the other half (who remained ECMO eligible), including after confounder adjustment (adjusted OR: 0.23, 95% CI 0.06, 0.89, p = 0.03).

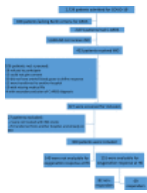
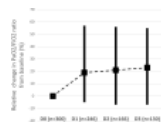
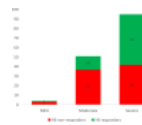
Conclusions: Our study reports the benefits of iNO in improving arterial oxygenation in C-ARDS patients. This improvement seems more relevant in the most severe cases. In patients with ECMO criteria, an iNO-driven improvement in gas exchange was associated with better survival. These results must be confirmed in well-designed prospective studies.

Keywords: Acute respiratory distress syndrome; COVID-19; ECMO; Inhaled nitric oxide; Refractory hypoxaemia.

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Figures

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