Acute ischemic optic neuropathy with extended prone position ventilation in a lung transplant recipient

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ABSTRACT
Prone position ventilation (PPV) improves mortality in severe acute respiratory distress syndrome (ARDS), but outcomes following its use in lung transplant recipients are not known. We report the case of a 42-year-old Caucasian man who presented with severe ARDS from Bordetella pertussis, 5 years after bilateral sequential lung transplant for cystic fibrosis. He was managed with PPV for 22 days and had a prolonged ICU stay complicated by hypoxic ischemic optic neuropathy leading to blindness. Since his discharge from the ICU 6 months ago, his FEV₁ has recovered to 47% predicted compared to his pre-ICU peak FEV₁ of 85% predicted, suggesting recovery of lung function. This is the first report of optic nerve damage and vision loss in patients undergoing PPV. Our report also suggests that, in appropriately selected lung transplant recipients, severe hypoxemia could potentially be managed with prone ventilation.

Key Words: ARDS, complications of prone position ventilation, lung transplantation, rescue modes of mechanical ventilation, severe hypoxemia

INTRODUCTION
The outcomes of prone position ventilation (PPV) in lung transplant recipients remain to be defined, despite the increasing popularity of earlier PPV following the recent Proning Severe ARDS Patients (PROSEVA) study and the meta analyses thereof. In the immediate post-lung transplant period, the management of severe hypoxemia in the setting of a recent surgical incision and multiple chest drains preclude prone ventilation. Non-invasive ventilation in prone position has been reported in this peri-operative period. However, outcomes of PPV in patients with severe acute respiratory distress syndrome (ARDS) in the late post-transplant period have not been described. We present a case of severe ARDS (PaO₂/FiO₂ ratio < 100) secondary to Bordetella pertussis pneumonia in a bilateral lung transplant recipient. This patient was managed with prone ventilation for 22 consecutive days experienced an unusual and thus far unreported complication of ischemic optic neuropathy (ION).
Within 24 hours of ICU admission his clinical condition deteriorated, necessitating mechanical ventilation with a low tidal volume and positive end-expiratory pressure. Shortly thereafter, septic shock and refractory hypoxemia required neuromuscular blockade with cisatracurium, pulmonary vasodilator therapy with inhaled epoprostenol, and vasopressor support. Immunosuppression was curtailed, and broad-spectrum antimicrobial therapy including vancomycin, piperacillin-tazobactum, azithromycin, and voriconazole was initiated. PPV was initiated after escalating medical therapy and different ventilator strategies proved unsuccessful.

Manual proning was initiated on day 1 with significant improvement in hypoxemia from PaO$_2$ of 81 mmHg to 168 mmHg. Bronchoscopic sampling (broncho-alveolar lavage) was deferred in view of severe hypoxemia. On day 8 of PPV the patient’s daughter tested positive for *Bordetella pertussis*. On day 9, the patient himself tested positive for *Bordetella pertussis*. Levofloxacin was added to his antimicrobial regimen and he was transitioned to a mechanically rotating bed in anticipation of prolonged PPV needs. PPV was initiated for approximately 16 hours a day until day 22 of hospital admission, when he finally tolerated supine ventilation. However, ventilator dyssynchrony necessitated deep sedation and intermittent neuromuscular blockade. He underwent a tracheostomy on day 27 and was liberated from mechanical ventilation on day 64. His ICU course was complicated by severe neuromuscular weakness (critical illness neuropathy/myopathy) and ICU delirium.

On day 31, the patient was noted to have non-reactive pupils, prompting cessation of neuromuscular blockade resulting in a thorough neurological work-up. Magnetic resonance (MR) imaging of the brain was consistent with multifocal lesions, especially within the left occipital lobe, with central and peripheral enhancement suggesting septic emboli. An extensive work-up including lumbar puncture, MR imaging, MR angiography, trans-esophageal echocardiogram, and serial blood cultures failed to reveal a septic etiology. Fundoscopic examination revealed bilateral visual loss with optic nerve pallor inconsistent with the lesions noted on brain imaging and suggesting optic nerve injury. In consultation with neurologists and ophthalmologists, we concluded that hypoxia-induced cerebral infarction was the probable etiology of the brain lesions. In addition, increased intraocular pressure with resultant decrease in ocular perfusion pressure secondary to PPV was thought to be the most likely mechanism for the optic nerve injury. This hypothesis was supported by profound optic nerve pallor detected on fundoscopic examination as shown in Figure 2 and severe bilateral optic atrophy noted on subsequent outpatient visits.

This patient had a fairly uncomplicated course with a single ABO rejection after his transplant 5 years earlier. His peak FEV$_1$ post-transplant was 3.32 liters (88% predicted) and pre-ICU FEV$_1$ was 3.17 liters (85% predicted). Six months after discharge from the ICU he has regained some of his lung function to an FEV$_1$ of 1.74 liters (47% predicted). However, he has remained legally blind from bilateral optic atrophy with retinal vascular attenuation [Figure 2].

**DISCUSSION**

This is the first reported case of extended PPV resulting in loss of vision from ION. While prone ventilation for 22 days proved to be a lifesaving measure for our patient, it also brought to light the potential complication ION, which may lead to severe vision impairment (i.e., legal blindness) from bilateral optic atrophy with retinal vascular attenuation [Figure 2]. Follow-up studies in ARDS survivors have reported near-normal lung function assessed by pulmonary function tests at 3 and 5 years; the decline in lung function in this case is probably related to the previous lung transplant. This case also
highlights the use of PPV in lung transplant recipients, which has been infrequently reported in the literature.

Although ION has been attested in patients on PPV while under general anesthesia for spinal surgery, it has not been reported after PPV in patients with ARDS.[5,6] The pathophysiological mechanism for ION in patients in the prone position is mainly due to increased intra-ocular pressure (IOP) in the prone position.[5] Blood supply to the optic nerve is auto-regulated by changes in the terminal arteriolar resistance.[5] Auto-regulation breaks down at the extreme end of the mean arterial pressure (MAP) spectrum, and the blood flow to the optic nerve becomes solely dependent on the difference between the MAP and the IOP. Prone positioning has been reported to increase IOP and effectively decrease ocular perfusion in patients undergoing spinal surgery.[7] Changes in volume status and blood pressure could also offset the balance of ocular blood flow.

Intensivists need to be aware of potentially modifiable risk factors that could prevent rare complications of PPV (e.g., ION), as PPV is now frequently used as rescue therapy for severe hypoxemia. Such strategies should include positioning with the head level with or above the heart, minimizing anesthetic duration and blood loss, the use of both colloids and crystalloids for intravascular volume replacement, periodic hemoglobin monitoring during cases associated with significant blood loss, and optimization of hemodynamics with maintenance of blood pressure within 20% of baseline.[8] Reverse Trendelenburg position limits hypercapnia, optimizes hemodynamics, and maintains blood pressure within 20% of baseline, and judicious volume replenishment could prove to be important.[8-10] In addition, families of patients undergoing PPV should be informed of the small but increased risk of ION. This report gives credence to the use of PPV as a therapeutic option for managing refractory hypoxemia in lung transplant recipients, but clinicians must remain vigilant to the possibility of unusual associated complications such as ION. Further studies of this ventilation mode to treat ARDS in lung transplant patients are needed to provide outcomes data.

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Conflicts of interest
There are no conflicts of interest.

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