



## Case report

# Partial neuromuscular blockage to promote weaning from mechanical ventilation in severe ARDS: A case report

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## ABSTRACT

Spontaneous breathing efforts during mechanical ventilation can lead to patient self-inflicted lung injury (P-SILI). In order to prevent P-SILI, patients are generally heavily sedated and receive muscle relaxation, resulting in a slower weaning process. We present a case in which we applied partial neuromuscular blockage in order to prevent P-SILI while allowing spontaneous breathing but with limited efforts during assist mechanical ventilation.

## 1. Introduction

Protective ventilation with low tidal volumes and airway plateau pressure ( $P_{plat}$ ) limitation is advocated especially in patients with severe acute respiratory distress syndrome (ARDS) [1]. Guérin et al. [2] showed that prone positioning reduces mortality in severe ARDS if applied immediately after diagnosis and during the first five days of mechanical ventilation. Also, neuromuscular blocking agents (NMBAs) were given during prone positioning. Earlier, it was shown that NMBAs improve outcome in early severe ARDS if applied during the first 48 hours [3].

Recently, Yoshida et al. [4] showed that spontaneous breathing efforts during mechanical ventilation can induce tremendous pressure ( $P_L$ ) due to very low pleural pressure as a result of extreme effort of the diaphragm. This so-called P-SILI indicates additional injury that is a result of high local stress.

Doorduyn et al. [5] showed the use of NMBAs can be used for partial neuromuscular blockage in patients with ARDS, reducing the tidal volume during pressure control ventilation or neurally adjusted ventilatory assist, thus reducing the risk of developing P-SILI. This was a proof-of-concept study in which partial neuromuscular blockage was applied only for two times one hour.

We report a case where we applied partial neuromuscular blockage as an escape strategy during assist mechanical ventilation after three weeks of mechanical ventilation for severe ARDS, in order to prevent high tidal volumes and promote the weaning process, resulting in significant and rapid patient improvement.

## 2. Case report

The patient was a man of eastern European origin in his late twenties with a medical history of depression for which he received antidepressant medication, and a history of Hepatitis B during his childhood for which he received Interferon type II (INF- $\gamma$ ). He recently travelled to the Netherlands for work. He presented himself to a general practice center with general malaise and dyspnea. He had a dry cough and a temperature of 40.4 °C. He received antibiotic treatment (augmentin) for a suspected pneumonia and was sent home. The next day he returned and was sent to the emergency room of a general hospital due to a low  $Sp_{O_2}$  of 83%. He was immediately admitted to the Intensive Care Unit (ICU) and intubated.

X-ray imaging (Fig. 1) showed bilateral patchy consolidations. Later, a polymerase chain reaction test would confirm the diagnosis of respiratory failure due to Influenza A infection. With a lowest measured ratio between  $Pa_{O_2}$  and  $Fi_{O_2}$  the of 76 mmHg and in absence of a suspicion of cardiac failure the patient satisfied the conditions for the diagnosis of severe ARDS [6]. The patient was transferred to our hospital with a possible indication for extra-corporeal membrane oxygenation. The following days the patient was treated with antibiotics (doxycycline, ciproxin, cefotaxim), anti-viral medication (oseltamivir) and active cooling. The patient was sedated, received muscle relaxation and was mechanically ventilated in prone positioning for approximately 16 h per day with a tidal volume ( $V_T$ ) of 6 mL/kg $_{IBW}$ , 20 cmH $_2$ O of positive end-expiratory pressure (PEEP) and a peak airway pressure ( $P_{peak}$ ) of 32 cmH $_2$ O.

The esophageal pressure ( $P_{es}$ ) and the intra-tracheal pressure ( $P_{trach}$ ) were simultaneously measured to calculate the  $P_L$ . The  $P_L$  was 7 cmH $_2$ O

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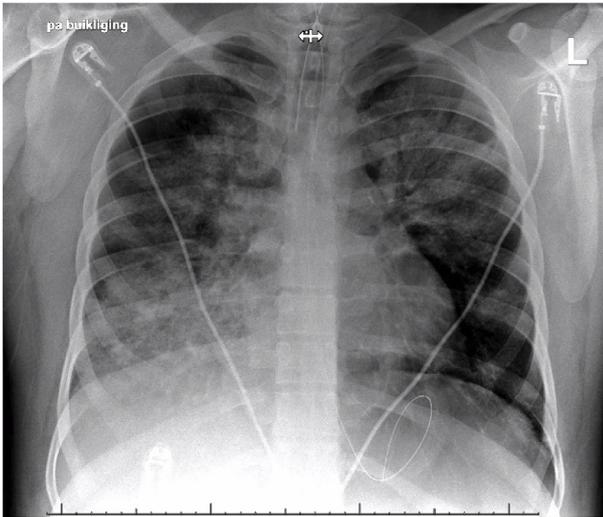


Fig. 1. X-ray imaging of the chest in supine position after transfer to our hospital on second day of admission, showing bilateral patchy opacities.

at end of expiration and 14 cmH<sub>2</sub>O at end of inspiration. As the P<sub>L</sub> during inspiration was well below the threshold of 25 cmH<sub>2</sub>O [7], PEEP was increased 20 to 28 cmH<sub>2</sub>O resulting in a P<sub>peak</sub> of 40 cmH<sub>2</sub>O and a P<sub>L</sub> of 19 cmH<sub>2</sub>O during inspiration. As a result, oxygenation improved significantly.

During the first week the patient was kept sedated, given muscle relaxation and the patient's position was switched between prone and supine approximately every 12 hours. After six days on mechanical ventilation, rocuronium infusion was stopped and the patient was kept in supine position. The patient improved slowly but had multiple periods of discomfort with increased blood pressure, increased respiratory rate, patient-ventilator asynchrony, deterioration of SpO<sub>2</sub>, restlessness and grimacing. Therefore, clonidine (0.85 μg/kg/h) was started and remifentanyl was increased 10–17 μg/kg/h to keep the patient comfortable.

On day 10 of admission the sedation levels were reduced in an attempt to switch from controlled mechanical ventilation to pressure support ventilation. However, the patient became restless again and the tidal volume increased 500–870 mL (11 mL/kg<sub>IBW</sub>) and respiratory rate increased 25 to 34/min. We had to increase sedation levels again and kept the patient on controlled mechanical ventilation. On day 18 we tried to stop the muscle relaxation again, again resulting in discomfort and ventilator asynchrony. Therefore, esketamine (53 μg/kg/h) was started and remifentanyl was switched to sufentanil (0.66 μg/kg/h), whereby the patient became more comfortable.

On day 21 we tried again to switch the patient from controlled mechanical ventilation to pressure support ventilation. Tidal volumes increased up to 1200 mL (15 mL/kg<sub>IBW</sub>). Therefore, we decided to apply partial neuromuscular blockage. A bolus of 10 mg of rocuronium was repeatedly administered intravenously until 50 mg was infused in 45/min. Tidal volume decreased 850 to 550 mL on average (10.6 to 6.9 mL/kg<sub>IBW</sub>) while the respiratory rate increased 15 to 23/min. Without NMBAs the patient created a negative pressure swing of around 38 cmH<sub>2</sub>O in the esophagus during inspiration (ΔP<sub>es</sub>), which decreased to 21 cmH<sub>2</sub>O with partial neuromuscular blockage. Fig. 2 shows tracings of ventilator waveforms, the P<sub>trach</sub>, P<sub>es</sub> and P<sub>L</sub> right before and after the first bolus of rocuronium. Thereafter, we started a continuous infusion of rocuronium (48 mg/h) titrated to target a tidal volume of around 500 mL (6.3 mL/kg<sub>IBW</sub>). After 18 h the rocuronium infusion was stopped while tidal volumes remained stable.

Thereafter, sedation and ventilatory parameters could be quickly reduced. Four days after the start of partial neuromuscular the patient was extubated and put on high-flow nasal cannula oxygen therapy

(HFNC). Another two days later the HFNC was replaced by a non-rebreathing mask and the patient was moved back to the referring hospital just within a month after transfer to our ICU.

### 3. Discussion

In this case report we described the successful application of partial neuromuscular blockage after three weeks of mechanical ventilation in a patient with severe ARDS in order to facilitate pressure support ventilation and weaning. Tidal volume decreased 15 to ± 6.5 mL/kg<sub>IBW</sub>, while the ΔP<sub>es</sub> significantly decreased 38 to 21 cmH<sub>2</sub>O during an inspiratory effort.

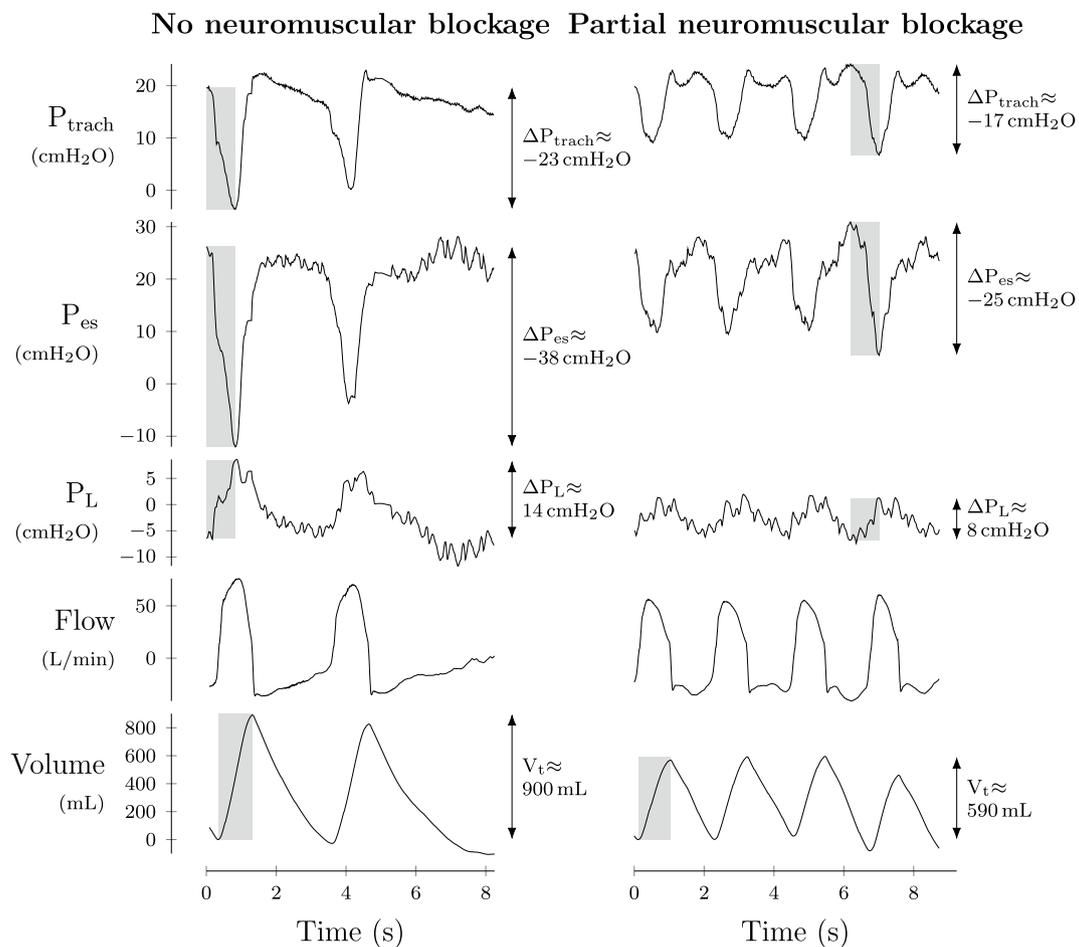
The patient showed a classic case of severe ARDS due to Influenza A infection with a possible superimposed bacterial infection. Recent guidelines on the treatment of severe ARDS [8] recommend the application of low tidal volumes, P<sub>plat</sub> ≤ 30 cmH<sub>2</sub>O, prone positioning in the early phase and higher PEEP levels. The patient in this case was successfully ventilated with low tidal volumes, prone positioning and higher PEEP levels during the initial treatment. Our protocol states the P<sub>L</sub> should stay below the suggested physiological limit of 25 cmH<sub>2</sub>O [7] at end of inspiration. We accepted P<sub>peak</sub> > 30 cmH<sub>2</sub>O based on the P<sub>L</sub> and increased PEEP to improve oxygenation.

The usage of NMBAs is frequently used in the early phase of the disease in order to control ventilator synchrony. We have reported a previous case where full paralysis by NMBAs proved to be an important part of the treatment in a patient with a high respiratory drive [9]. In the current case, breathing effort, patient-ventilator asynchronies and coughing could not be mitigated by sedatives alone, thus requiring prolonged muscle relaxation. Since the patient had been on mechanical ventilation for three weeks already and the status did not seem to change for the last ten days, we thought to do well by trying the experimental application of partial neuromuscular blockage in order to allow the patient to wake up and allowing for spontaneous efforts and partial ventilatory support. The patient in the current case would fit the inclusion criteria of Doorduyn et al. [5]: an adult patient with ARDS developing high V<sub>i</sub> during pressure support ventilation. That study showed that V<sub>i</sub> was significantly reduced 9.3 to 5.6 mL/kg<sub>IBW</sub> during partial neuromuscular blockage. In the current case, the V<sub>i</sub> before was much higher, but we were able to reduce V<sub>i</sub> almost to 6 mL/kg<sub>IBW</sub>.

Doorduyn et al. [5] studied partial neuromuscular blockage for only two times one hour, and we are not aware of any case reports in which prolonged partial neuromuscular blockage has been tried. In this case, we tried the strategy of titrating rocuronium infusion by infusion of boluses of 10 mg and subsequently a continuous infusion, allowing us to titrate the V<sub>i</sub> between 6 and 8 mL/kg<sub>IBW</sub>. We had no expectations as to how long to apply partial neuromuscular blockage and were surprised by the rapid improvement of patient comfort and patient-ventilator synchrony. The subsequent weaning from the ventilator took only four days.

Normally, NMBAs are only applied in deeply sedated patients because of the inability to adequately assess pain and anxiety during muscle relaxation [10]. It is not surprising that physicians and nursing staff questioned the method as we were preparing the infusion of boluses of rocuronium after reducing sedation levels. This resulted in a healthy discussion on the possible merits and disadvantages of partial neuromuscular blockage in the current case.

In summary, the application of partial neuromuscular blockage allowed for spontaneous efforts and partial ventilator support in a patient with high respiratory effort after severe ARDS. Patient-tailored treatment and extensive monitoring is required in such complex cases. Partial neuromuscular blockage is experimental and should be used to the discretion of the caretaker. We do not recommend partial neuromuscular blockage as part of standard treatment of ARDS.



**Fig. 2.** Tracings of the intra-tracheal pressure ( $P_{trach}$ ), esophageal pressure ( $P_{es}$ ) and trans-pulmonary pressure ( $P_L$ ), flow and volume without neuromuscular blockage (left) and with partial neuromuscular blockage (right). The arrows indicate the pressure swings during inspiration ( $(\Delta P_{trach})$ ,  $(\Delta P_{es})$  and  $(\Delta P_L)$ ) and the ( $V_t$ ).

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