

# Swift recovery of severe acute hypoxemic respiratory failure under non-invasive ventilation

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## Abstract

**Background:** In the setting of severe acute respiratory distress syndrome ( $\text{PaO}_2$  to  $\text{F}_i\text{O}_2$  ratio  $< 100$ ), the cut-off point for switching from non-invasive ventilation to tracheal intubation combined with mechanical ventilation is poorly defined.

**Results:** The swift resolution over 10 h of a severe acute hypoxemic respiratory failure ( $\text{PaO}_2/\text{F}_i\text{O}_2 = 57$ ) caused by aspiration following heroin overdose, using non-invasive ventilation with high positive end expiratory pressure 15–20 cm  $\text{H}_2\text{O}$  along with low pressure support (8 cm  $\text{H}_2\text{O}$ ) is reported. The success in treating non-invasively severe hypoxia was presumably linked to a highly restricted subset: healthy young patient, minimal alteration of consciousness, non-combativeness, absence of severe metabolic acidosis, quick resolution of supraventricular arrhythmia, one-to-one supervision by the intensivist in the critical care unit.

**Conclusion:** Given the complications associated with tracheal intubation and mechanical ventilation on the one hand, and with delayed intubation on the other hand, high PEEP-NIV may warrant study in a restricted set of patients closely monitored in a critical care environment.

**Key words:** heroin overdose, aspiration, severe acute respiratory distress syndrome, non-invasive ventilation, high PEEP, pressure support

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Severe acute respiratory distress syndrome (ARDS,  $\text{PaO}_2$  to  $\text{F}_i\text{O}_2$  ratio =  $\text{P}/\text{F} < 100$ ) [1] is managed with up-front tracheal intubation and controlled mechanical ventilation (CMV). The cut-off point between non-invasive ventilation (NIV) and intubation used along with CMV is poorly defined: a) the French Society of Critical Care Medicine (SRLF) considers  $\text{P}/\text{F} < 150$  as the cut-off point to switch from NIV to invasive ventilation [2]; b) a cut-off point of  $\text{P}/\text{F} < 175$  requires close monitoring and a low threshold for intubation [3]; c) 84% of patients presenting with severe ARDS require tracheal intubation [4]. Nevertheless, NIV has been successfully used upon  $\text{P}/\text{F} = 116$  [5] or 100 [6]. Accordingly,

patients were randomized to NIV with a  $\text{P}/\text{F} = 102 \pm 21$  (SD) [7] or  $104 \pm 42$  [8] upon inclusion. The lower limit may be  $\text{P}/\text{F} \sim 70\text{--}85$  ( $\text{P}/\text{F} = 85$  by design [9];  $\text{P}/\text{F} = 70$  ending to NIV failure [10]). Finally,  $\text{P}/\text{F} < 55$  appears as a cut-off point to consider extra-corporeal membrane oxygenation (ECMO), following optimization of intubation + CMV [11].

Given this continuum from NIV to ECMO, the present observation appears unique: a) a patient presenting with severe hypoxemic respiratory failure (AHRF;  $\text{P}/\text{F} \sim 57$ ) was treated using NIV up to the discontinuation of mechanical ventilation b) the  $\text{P}/\text{F}$  increased from 57 to 240 over  $\sim 10$  h, following the use of high PEEP (15–20 cm  $\text{H}_2\text{O}$ ).

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## CASE REPORT

A male patient, 24 years old (height 180 cm, body mass 70 kg), was brought from home to hospital (~ 21:45pm, day 1 = D1), unconscious and suspected of cocaine intake. In the emergency department (ED), as soon as naloxone ( $0.04 \text{ mg h}^{-1}$ ) evoked return to consciousness, he presented with acute respiratory distress ( $\text{O}_2$  peripheral saturation:  $\text{SpO}_2$ ) ~ 70%,  $\text{O}_2$  flow =  $15 \text{ L min}^{-1}$  via high oxygen concentration mask). The intensivist observed a supine young Caucasian male, with a history of smoking (~ 10 packs per year), presenting drowsiness (Glasgow Coma Scale 13 points) but able to answer questions following continuous naloxone infusion. Additional findings were: bilateral myosis, no functional neurological deficit, scant particulate vomitus at the corner of the mouth, very severe unguis and lips cyanosis, major peripheral vasoconstriction with minor knee mottling, severe dyspnea, bilateral heavy wheezing without rales, no ronchi, thoraco-abdominal discoordination, sternal notch retraction, dilatation of the *nares*, tachypnea ( $30 \text{ min}^{-1}$ ). Arterial blood pressure (ABP) was determined as 141/71 mm Hg, heart rate (HR) was 171 beats per min — presumably supraventricular arrhythmia, neither jugular overdistension, hepato-jugular reflux, ankle or tibial edema, nor abdominal tension were observed. Body temperature was  $35^\circ\text{C}$  while a chest X-ray (taken immediately upon arrival to ED) was unremarkable. Immediately after admission the oxygen flow was increased to  $\sim 30 \text{ L min}^{-1}$ ,  $45^\circ$  head up position was set and naloxone infusion was increased to  $0.24 \text{ mg h}^{-1}$ . An arterial blood gas analysis (ABG) revealed:  $\text{pH} = 7.19$ ,  $\text{PaCO}_2 = 69 \text{ mm Hg}$ ,  $\text{PaO}_2 = 57 \text{ mm Hg}$ ,  $\text{SaO}_2 = 84\%$ ,  $\text{BE} = -5 \text{ mmol L}^{-1}$ , lactates level —  $3.55 \text{ mmol L}^{-1}$ , carboxyhaemoglobin concentration was 6.8%. The patient received intravenously magnesium 3 g over 15 min, then amiodarone 450 mg over 20 min. ABP and HR normalized ( $102/57 \text{ mm Hg}$  and  $\sim 100$  per min respectively) over approximately 45 min.

Given the acute distress, NIV was started as a bridge to intubation [12]. As soon as NIV was set (sitting position,  $\text{F}_i\text{O}_2 = 1.0$ , PEEP =  $10 \text{ cm H}_2\text{O}$ , pressure support (PS) =  $10 \text{ cm H}_2\text{O}$ , trigger to the lowest value =  $0.3 \text{ L min}^{-1}$ , slope = 0.2), the ventilator was fully synchronized to the patient with immediate reduction of thoraco-abdominal discoordination and sternal notch retraction. By contrast,  $\text{SpO}_2$  remained ~ 70–80% with major peripheral and unguis cyanosis.

A re-examination of the patient's file showed the occurrence of vomiting at home. Given a low temperature, an unremarkable chest X-ray, and wheezing, the diagnosis of unconsciousness linked to heroin overdose followed by aspiration causing severe acute hypoxemic respiratory failure (AHRF) was raised. Meanwhile, the patient repeatedly denied taking intravenous heroin, only intranasal cocaine. Only opiates were found in blood and urine. The patient

was admitted to the critical care unit (CCU, 22/45, D1). Pending intubation, NIV was set (reverse Trendelenburg at  $45^\circ$  head-up position,  $\text{F}_i\text{O}_2 = 1.0$ , PEEP =  $15 \text{ cm H}_2\text{O}$ , PS =  $8 \text{ cm H}_2\text{O}$ , slope = 0.2, trigger :  $0.3 \text{ L min}^{-1}$ . Drager Evita 4XL respirator (Lubeck, Germany) was used. Antibiotics (amoxicillin  $3 \times 2 \text{ g}$  with clavulonic acid  $3 \times 200 \text{ mg}$  and metronidazole  $3 \times 500 \text{ mg}$ ) were administered. The following clinical signs further improved: near suppression of respiratory distress; thorough reduction of wheezing; near-perfect synchronization of NIV with the patient;  $\text{SpO}_2$  ~ 80%; near-total suppression of peripheral vasoconstriction; suppression of knee mottling; persistence of major unguis cyanosis. An arterial line was inserted. The ABG showed a P/F = 73 (00:30 at D2,  $\text{F}_i\text{O}_2 = 1.0$ , PEEP =  $15 \text{ cm H}_2\text{O}$ , PS =  $8 \text{ cm H}_2\text{O}$ ) increasing to 225 (5:30 D2,  $\text{F}_i\text{O}_2 = 0.8$ , PEEP =  $15 \text{ cm H}_2\text{O}$ , PS =  $8 \text{ cm H}_2\text{O}$ ; lactate concentration was  $3.4 \text{ mmol L}^{-1}$ ) then 240 (8:45 D2,  $\text{F}_i\text{O}_2 = 0.4$ , PEEP =  $15 \text{ cm H}_2\text{O}$ , PS =  $8 \text{ cm H}_2\text{O}$ ). Between 00:30 and 3:00 at D2, PEEP was set to  $20 \text{ cm H}_2\text{O}$  aiming at  $\text{SpO}_2 \geq 90\%$  with the intensivist present. The base excess remained stable between  $-5$  and  $-7 \text{ mmol L}^{-1}$  throughout the evolution.  $\text{PaCO}_2$  lowered from 69 (~ 22:00 at D1) to 46 mm Hg (8:45 at D2) under continued naloxone infusion. Wheezing, peripheral vasoconstriction and major unguis cyanosis waned off between 22:00 at D1 and early morning of D2. The intensivist in charge of the CCU on D2 felt that the patient was no longer in need of NIV: the patient was switched to high  $\text{O}_2$  concentration mask on D2 and discharged on room air (D3).

## DISCUSSION

We presented the case of patient with a severe AHRF (P/F ~ 57 under  $30 \text{ L min}^{-1}$  of  $\text{O}_2$  later documented to P/F = 73 after > 2 h of NIV, PS =  $8 \text{ cm H}_2\text{O}$ , PEEP =  $15 \text{ cm H}_2\text{O}$ ,  $\text{F}_i\text{O}_2 = 1.0$ ) who was cured over 10 h, without intubation and CMV.

## DIAGNOSIS

The toxicology data fitted with a near-normal chest X-ray, major wheezing, response to an increasing naloxone dose, establishing intranasal heroin overdose complicated by aspiration. This diagnosis could be substantiated neither by plasma opioids determinations nor with fiberoptic bronchoscopy, neither of relevance here, given the swift improvement under naloxone-NIV management. As the patient stated repeatedly having used no i.v. injection, the possibility for small occluding particles of unclean i.v. heroin causing increased pulmonary impedance and re-opening a foramen ovale was to be excluded. By contrast, a normal chest X-ray combined with no response to  $\text{F}_i\text{O}_2 = 1.0$  suggest lung collapse. The absence of urinary cocaine does not suggest the possibility of elevated pulmonary impedance evoked by cocaine. Indeed, the present distress fits with the

established ARDS (30 min,  $F_{iO_2} = 1.0$ , PEEP = 10 cm H<sub>2</sub>O) [13]. Despite >2h under NIV ( $F_{iO_2} = 1.0$ , PEEP up to 15 cm H<sub>2</sub>O), the patient exhibited a P/F = 73 and a SpO<sub>2</sub> < 90%. The definition of ARDS requires bilateral opacities ≥ 3 quadrants [1], not observed here: the interval between hypoxic distress and the chest X-ray was minimal. Therefore, as the criteria for severe ARDS are not met, severe AHRF will be considered.

### INTUBATION?

Firstly, should drowsiness have led to intubation to protect the airway from further aspiration? Is it relevant to intubate the trachea of a patient fully responsive to command and able to discuss heroin vs. cocaine intake, under naloxone infusion, when the patient is under constant supervision by the intensivist in a CCU? The reader will decide whether the absence of intubation is malpractice or whether intubation would have exposed this patient to complications (see below). Secondly, should severe hypoxia have led to intubation? Given the margin of safety (ECMO: P/F < 55 [11]; intubation: P/F < 150–175 [2, 3]), the answer should have been positive in the affirmative. Nevertheless, the immediate improvement in the thoraco-abdominal discoordination and sternal notch retraction, the absence of hypercapnic encephalopathy from ~ 22:00 to ~ 3:00, the absence of combativeness and the perfect synchronization of NIV to the patient argued against our initial rush to intubate the trachea. Indeed, the decision was a *clinical* decision, taken on a minute-to-minute basis, based on fatigue and ventilatory discoordination to prevent cardiorespiratory arrest (figure 1 in [14]). The issue is to treat a patient, not numbers (P/F < 150 [2, 3]). Failure of NIV rests on a frank worsening of respiratory distress under NIV, RR > 40 min<sup>-1</sup>, dependence of NIV for > 12 h, pH < 7.35, SpO<sub>2</sub> < 90% despite  $F_{iO_2} = 1.0$  [4]. Here, only the last criterion of failure was met. On the spot, four elements were considered: a) a young healthy patient b) a “pure” ventilatory disease without major circulatory (no low PvO<sub>2</sub> effect [15]) nor renal impairment. c) the initial respiratory acidosis was of no concern, once naloxone and NIV had been implemented d) failure of NIV is observed upon shock or metabolic acidosis [10]. In the setting of severe metabolic acidosis, the H<sup>+</sup> stimulus mandates muscle relaxation to lower RR and energy requirements, up to the correction of acidosis [16]. Here, metabolic acidosis was no threat. At a distance, tracheal intubation and mechanical ventilation are associated with muscle weakness [17, 18], and nosocomial infections. This has led one to “avoid tracheal tubes, minimize sedation, prevent ventilator-induced lung injury and nosocomial infections” [19]. In the setting of ARDS, irrespective of P/F after NIV trial, the avoidance of intubation is associated with lower mortality [3]. Nevertheless, after NIV trial, P/F < 175 requires intubation [3]. Given P/F < 100, most intensivists would have chosen intubation,

possibly with muscle relaxation and prone positioning; differentiating malpractice (84% of patients presenting with severe ARDS need intubation [4]) vs. overtreatment (16% of the patients presenting with severe ARDS do not need intubation [4]) is exacting: a minute-by-minute observation by an intensivist in a CCU was key to avoid disastrous consequences, should the NIV trial have failed.

### EXPIRATORY SET UP

The first remarkable feature is the near total suppression of respiratory distress, *immediately* following the implementation of NIV, despite increased RR (~ 30 min<sup>-1</sup> acceptable in a young healthy patient for a short period of time). Indeed, the unloading of respiratory muscles, improved dyspnea and reduced respiratory drive have been documented in patients presenting with P/F < 300 under PS = 15 cm H<sub>2</sub>O + PEEP = 5 cm H<sub>2</sub>O [20]. Presumably, aspiration evokes a high resistive work: the need to develop a high transpulmonary pressure generates thoraco-abdominal discoordination. However, despite the reduced work of breathing, the continued major unguet cyanosis and low SpO<sub>2</sub> ~ 70–80% suggest that the intrapulmonary shunt was still important upon low PEEP levels: the initial PEEP (10 cm H<sub>2</sub>O) set in the ED may have been too low to set the lung in proper end-expiratory position [21] on its *decremental* [22] pressure-volume (P-V) curve i.e. above the critical *closing* pressure [23]. The high PEEP set in CCU (15 cm H<sub>2</sub>O; 20 cm H<sub>2</sub>O between 0:30 and 3:00) to increase SpO<sub>2</sub> > 90% fits with this hypothesis. Experienced investigators set 10 ≤ PEEP ≤ 16 cm H<sub>2</sub>O [24–27] when an inflexion point cannot be delineated on a P-V curve [24, 25] or before a CT scan to differentiate focal vs. diffuse ARDS [26, 27]. When our observation is contrasted to the literature, the high PEEP used here (15–20 cm H<sub>2</sub>O) contrasts with the maximum PEEP = 12 cm H<sub>2</sub>O [3] (range 4–12 cm H<sub>2</sub>O [7]) or from PEEP ~ 5 cm H<sub>2</sub>O (NIV failure: 4.4 ± 1.3; NIV success: 4.8 ± 1) [4]. Therefore, success was linked to little leaks+good tolerance or persistency+high PEEP, or both.

### INSPIRATORY ASSISTANCE

Initially, a low PS (10 cm H<sub>2</sub>O) was set to avoid adding discomfort to acute respiratory distress in a drowsy, non-combative, patient. To avoid the genesis of high transpulmonary pressure [28, 29], the PS was quickly lowered to 8 cm H<sub>2</sub>O. Although high PEEP along with low PS has been reported in intubated patients [30], this is at variance with the usual settings (e.g. low PEEP = 5 cm H<sub>2</sub>O + high PS = 15 cm H<sub>2</sub>O [9, 20]): a) schematically, the alveolus functions like a child’s balloon and is inflated over the critical *opening* pressure, at once, and kept open by end-expiratory positive pressure above the critical *closing* pressure [22, 23], b) then, the pressure gradient necessary to generate the next tidal volume into the already open alveolus is minimal [31–33]. As the

lung is open at end-expiration, the next tidal volume operates along the *incremental* limb of the P-V curve with the *highest slope* [33] (“best compliance”) in position of optimal function” [21]. Given this high slope, a low resistive work overcomes the load of the valves and circuit (i.e. 3–5 cm H<sub>2</sub>O under NIV [20]): thus the low PS. Nevertheless, this high PEEP + low PS setting [30, 34] awaits evidence-based documentation.

### TIME COURSE

The second remarkable feature is the resolution of severe AHRF (P/F = 57 to 240) over 10 h, faster than observed earlier (P/F ~ 100 to ~ 175 over 12 h [7]). The present time course fits with data in intubated patients (~ 2–3 h, high PEEP: P/F = 48 to 220 [35]; ~ 30 min, high transpulmonary end-inspiratory pressure : P/F = 67 to 180 [36]). A swift improvement was reported in the setting of ARDS treated by NIV ([37]: P/F from 116 to 230 over 60 min with PEEP ~ 10 cm H<sub>2</sub>O). Interestingly, a) a larger increase in P/F was observed when NIV was opposed to tracheal intubation+CMV [8, 37] b) hypoxemia and RR improved when tracheas were extubated to NIV with similar settings [38]: thus, does spontaneous ventilation improve the ventilation/perfusion ratio (VA/Q) more than CMV in a sedated patient under muscle relaxant [8]?

Given a highly restricted subset (“pure” ventilatory disease, healthy young patient, minimal alteration of consciousness, non-combattiveness, absence of severe metabolic acidosis, quick resolution of supraventricular arrhythmia), severe hypoxia, treated in a CCU under *close* supervision, may quickly respond to very high PEEP levels (≥ 15 cm H<sub>2</sub>O). Nevertheless, in the setting of severe ARDS, intubation + CMV coupled to myorelaxation (48 h only) [39] and a prone position [40] remains the standard of care.

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3. Guldner, Pelosi and Gama de Abreu recently published a schema on ventilation using high PEEP-low PS in animals very similar to our high PEEP-low PS setting in humans: Spontaneous breathing in mild and moderate versus severe acute respiratory distress syndrome. *Curr Opin Crit Care* 2014; 20: 69–76, Figure 1.

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