



CASE REPORT

Clinical experience with a pumpless extracorporeal lung assist device

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Summary

We present three patients with respiratory failure in whom conventional mechanical lung ventilation resulted in unacceptably high levels of carbon dioxide, severe acidosis and high vasopressor requirements. A pumpless arteriovenous extracorporeal carbon dioxide removal device (NovalungTM) was inserted. Arterial carbon dioxide levels were reduced rapidly with a corresponding increase in pH, reduction in vasopressor requirements and reduction in inspiratory pressures. One patient required the additional use of high frequency oscillatory ventilation. There were no complications associated with use of the device. We conclude that use of extracorporeal carbon dioxide removal devices should be considered at an early stage in the management of respiratory failure refractory to conventional ventilatory techniques.

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Mortality in acute respiratory distress syndrome (ARDS) is influenced by ventilation technique. An 'open lung' strategy is associated with a reduction in ventilator-induced lung injury and an improved outcome [1]. This commonly results in moderate hypercapnia which is well tolerated in most patients but which may lead to severe acidosis and profound cardiovascular instability in a minority. Management of this situation remains challenging. Conventional extracorporeal membrane oxygenation (ECMO) can be used to remove carbon dioxide [2], but this treatment is not readily available and may involve a challenging patient transfer. The results of a national trial of its use are awaited [3]. Despite good anecdotal evidence previous trials have failed to show an outcome benefit of ECMO when compared with conventional ventilation [4]. A simpler, and potentially safer, pumpless extracorporeal lung assist device (NovalungTM; Inspiration Healthcare Ltd, Leicester, UK) has recently been developed which has been shown to eliminate carbon dioxide in mechanically ventilated patients [5]. Initial reports of its use have been promising.

We present our experience of using the Novalung device in three mechanically ventilated patients in whom conventional ventilatory techniques had failed

resulting in severe hypercapnia, acidosis and cardiovascular instability.

Case 1

A 24 year-old female with no previous medical history was admitted to hospital with a community-acquired pneumonia. Antibiotic therapy was commenced but within 6 h of admission she required tracheal intubation and mechanical lung ventilation because of hypoxaemia (P_{aO_2} 8.5 kPa). Oxygenation and ventilation were difficult due to poor lung compliance. Pressure-controlled, inverse ratio ventilation (inspiratory pressure 38 cmH₂O and positive end expiratory pressure (PEEP) 15 cmH₂O) achieved tidal volumes of approximately 250 ml. Despite an atracurium infusion and prone ventilation she deteriorated, becoming increasingly hypercapnic and acidotic and requiring increased vasopressor support. Five hours after intubation her P_aCO_2 was 16.5 kPa and pH 6.95. She was turned supine and treatment with a Novalung was started for extracorporeal removal of carbon dioxide. The left femoral vessels were cannulated with a 13 Fr venous line and a 15 Fr arterial line. Due to a confirmed venous thrombosis in the opposite leg a heparin infusion was

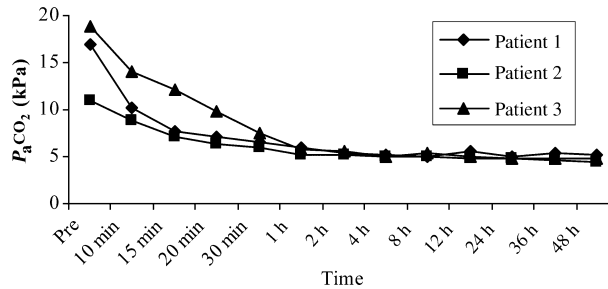


Figure 1 Changes in P_{aCO_2} following commencement of Novalung™ therapy.

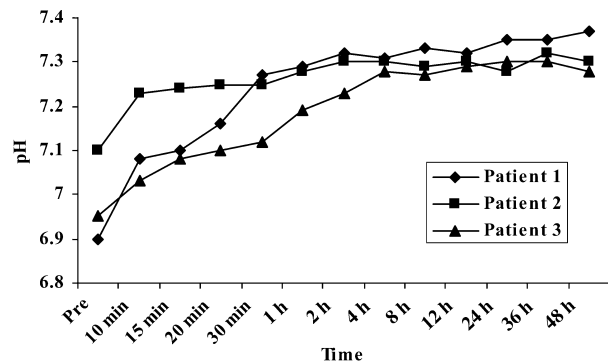


Figure 2 Changes in pH following commencement of Novalung™ therapy.

commenced after insertion of the cannulae aiming to maintain an activated partial thromboplastin time (APTT) ratio of 2. This was continued for the duration of therapy with the Novalung. Oxygen flow at $6 \text{ l}\cdot\text{min}^{-1}$ was commenced across the membrane and increased to $10 \text{ l}\cdot\text{min}^{-1}$ after 15 min when the P_{aCO_2} had fallen to 10.5 kPa. Her P_{aO_2} remained between 9–10 kPa. Within 2 h the P_{aCO_2} and pH had returned to normal levels (Figs 1 and 2). She remained on Novalung therapy for the next 6 days until oxygenation and lung compliance had improved. The oxygen flow rate was then reduced with the aim of stopping the device but due to persistent hypercapnia it was continued for a further 48 h. The vascular sheaths were removed on day 9. She was weaned from the ventilator in a conventional manner and was discharged to the ward 25 days after admission where she made a full recovery.

Case 2

A 62 year-old previously fit male underwent L5-S1 anterior discectomy and fusion. Three days after surgery he developed bi-basal pneumonia, requiring tracheal intubation and mechanical lung ventilation. He

responded well to initial treatment and underwent percutaneous dilatational tracheostomy on day 4. Subsequent weaning was complicated by a myocardial infarction on day 7 and a large rectal bleed on day 11 requiring laparotomy and bowel resection. Postoperatively his respiratory function deteriorated significantly. Lung compliance was poor resulting in inspiratory pressures of greater than $35 \text{ cmH}_2\text{O}$. Chest radiography revealed severe bilateral consolidation. Despite high levels of PEEP, inverse ratio ventilation and neuromuscular paralysis there was no improvement in his condition. Novalung therapy was started 18 h after the laparotomy when his P_{aCO_2} had risen to 10.9 kPa with a pH of 7.18 and a substantial increase in vasopressor requirements. Oxygen flow across the membrane was commenced at $6 \text{ l}\cdot\text{min}^{-1}$ and increased to $10 \text{ l}\cdot\text{min}^{-1}$ within 3 h. In view of the previous rectal bleeding and recent surgery unfractionated heparin was not commenced and he received prophylactic enoxaparin 20 mg daily only. The APTT remained around 30 s. There were significant improvements in the hypercapnia and acid base balance within 2 h (Figs 1 and 2) but his oxygen requirements remained high. He remained relatively stable for the next 6 days on Novalung therapy but then developed increasing vasopressor requirements as a result of sepsis. He continued to deteriorate and died 22 days after admission.

Case 3

A 39 year-old morbidly obese female was admitted to hospital as an emergency for investigation of a vulval swelling. She also had a one-week history of breathlessness. Her past medical history was unremarkable. Twenty four hours after admission she became tachypnoeic and hypoxaemic. Chest radiography revealed extensive nodular shadowing consistent with infection or possible malignancy and intravenous antibiotic therapy was commenced. Twelve hours later she required tracheal intubation and mechanical lung ventilation. Lung compliance was poor and oxygenation and ventilation were difficult. With a peak inspiratory pressure of $38 \text{ cmH}_2\text{O}$ and PEEP of $15 \text{ cmH}_2\text{O}$ a tidal volume of approximately 200 ml was achieved. Over the next 48 h neuromuscular paralysis and prone ventilation were attempted but gas exchange worsened. High frequency oscillatory ventilation (HFOV) was commenced on day four (Vision alpha, Inspiration Healthcare Ltd). Some improvement in oxygenation occurred but she became increasingly hypercapnic and acidotic. Novalung therapy was started 2 h after commencement of HFOV when the P_{aCO_2} was 18.1 kPa with a pH of 6.95. Unfractionated heparin was not commenced and she received prophylactic

enoxaparin 40 mg daily only. There was a substantial reduction in $P_a\text{CO}_2$ over the next 2 h with an increase in pH (Figs 1 and 2) and reduction in vasopressor requirement. HFOV at 8 Hz and a mean airway pressure of 28 cmH₂O maintained the $P_a\text{O}_2$ between 7.5–8.5 kPa. Both HFOV and Novalung therapy were continued for the next 48 h until the vulval biopsy results were available which showed a poorly differentiated carcinoma. Her oxygenation continued to deteriorate and in view of the clinical state and probable disseminated malignancy treatment was withdrawn. She died 7 days after admission to ICU.

Discussion

We have presented three cases in which use of the Novalung resulted in a rapid correction of severe hypercapnia and acidosis when conventional ventilatory techniques had failed. In the first two patients the device allowed a significant reduction in inspiratory pressures to be achieved whilst adequate oxygenation was maintained thus reducing the risk of ventilator-induced lung injury. A reduction in inspired oxygen was also achieved in the first patient although this was not the primary aim of the Novalung treatment. The third patient required the use of high frequency oscillatory ventilation due to hypoxaemia and poor lung compliance. All three patients had an initial reduction in their requirement for vasopressors despite the need to maintain a mean arterial pressure of 70–80 mmHg with the device in place.

Pump-driven extracorporeal carbon dioxide removal was first described in 1986 [6], however it was not until 2000 that the first reports of a pumpless system were published [7]. The Novalung utilises the arteriovenous pressure difference as the driving force for blood flow through a low resistance membrane oxygenator. Because it is a pumpless system the device is readily portable and reduces the need for systemic anticoagulation. The manufacturer suggests maintaining an APTT of 50 s, although the device has been successfully used in patients in whom anticoagulation is contra-indicated. Venous and arterial cannulae (ranging in diameter from 13 Fr to 21 Fr) are placed in the femoral vessels. The exact arteriovenous pressure difference depends upon the gauge of the cannulae inserted but typically there is a difference of 15 mmHg between inflow and outflow of the system producing a blood flow of 1–2.5 l.min⁻¹. Carbon dioxide exchange takes place by way of a heparin-bonded membrane whose surface area is 1.3 m². Oxygen at 4–12 l.min⁻¹ is connected to the inflow side of the membrane. Clearance of carbon dioxide is controlled by adjustment of the oxygen flow rate. The technique is attractive because of its relative simplicity and portability

and insertion and maintenance of the device are relatively straightforward.

Our first patient had the device in place for 8 days. Earlier cessation of treatment was not possible as carbon dioxide levels rose dramatically when the oxygen flow through the membrane was reduced. This duration of therapy is longer than previously reported and presumably reflects the severity of the underlying lung disease. Despite this we encountered no problems with its use. In particular, we did not experience any problems with impaired membrane function related to propofol sedation as previously reported [7], or due to blood clotting within the membrane or extracorporeal circuit. The first patient was heparinised for treatment of a confirmed venous thrombosis (in the opposite limb to where the Novalung cannulae had been inserted) but the remaining two patients received prophylactic doses of low molecular weight heparin only and had normal APTT and prothrombin times.

Despite its simplicity the Novalung has rarely been used in the UK. There are case reports of the device being used to control hypercapnia in acute severe asthma [8] and after craniotomy [9], but these have only required its use for 72–96 h. We have demonstrated that it is feasible and safe to use the Novalung for a longer time period allowing resolution of the underlying lung injury. The device is licensed for insertion for a maximum period of 29 days.

The timing of commencement of Novalung therapy appears crucial. Our first patient had a short period of conventional ventilation before the cannulae were inserted whereas their insertion was delayed in the second two patients. It has been demonstrated that a shorter period of mechanical ventilation prior to initiation of Novalung therapy is associated with a lower mortality rate [5]. As this is also the case for other adjuvant treatments in ARDS (such as HFOV [10]) it would suggest that early de-escalation of aggressive ventilatory techniques leads to improved outcomes in mechanically ventilated patients. After our experience with the Novalung it is now our policy to consider its insertion after 12 h of conventional ventilation if persistent hypercapnia results in a pH of < 7.2.

Our third patient concomitantly received high frequency oscillatory ventilation. The alternative therapy in such groups of patients is extracorporeal membrane oxygenation (ECMO). In the UK this treatment is not readily available, requires patient transfer to a national centre and may be associated with serious complications such as bleeding. Results of the CESAR trial comparing ECMO with conventional ventilation should soon be available [3]. Even if there is a benefit with the use of ECMO, this treatment is unlikely to be freely available due to limited resources and the requirement for a

possible lengthy transfer of a very unstable patient. The combination of Novalung and HFOV provide a simpler, more readily available alternative in situations when conventional ventilatory techniques have failed.

Recently concerns have been raised over the safety profile of arteriovenous extracorporeal carbon dioxide removal devices [11]. Episodes of lower limb ischaemia have been reported secondary to their use, although in the majority of patients these have been transient and have resolved with removal of the device. Measurement of foot temperature and lower limb pulse oximetry [9, 12] have been used as a means of detecting ischemic episodes. Cannula thrombosis was observed in the early phases of development of the Novalung [12] but has not been reported since 2001 when specially designed cannulae were introduced. Bleeding secondary to removal of the arterial cannulae has been reported in a very small number of cases. It is worth noting that these complications can occur with the use of any vascular access device and are not unique to Novalung cannulae.

In summary we have demonstrated that the Novalung is a feasible, effective and safe option in the management of hypercapnia during mechanical ventilation. Removal of carbon dioxide is rapid and predictable and is associated with reductions in vasopressor requirements. Use of the Novalung allows a less aggressive ventilatory strategy to be employed which is known to result in improved patient outcome. Further investigation of the device and its exact role are now warranted. Ideally multicentre randomised controlled trials are required comparing the Novalung with conventional treatment and ECMO. In the meantime a national register of its use would be beneficial to identify all episodes of insertion, patient outcome and associated complications.

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References

- 1 The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *New England Journal of Medicine* 2000; **342**: 1301–8.
- 2 Mielck F, Quintel M. Extracorporeal membrane oxygenation. *Current Opinion in Critical Care* 2005; **1**: 87–93.
- 3 *Conventional Ventilation or ECMO for Severe Adult Respiratory Failure (CESAR)*. ISRCTN 47279827 www.cesar-trial.org. Last accessed: 27 April 2008.
- 4 Zapol WM, Snider MT, Hill JD, et al. Extracorporeal membrane oxygenation in severe acute respiratory failure. A randomised prospective study. *Journal of the American Medical Association* 1979; **242**: 2193–6.
- 5 Bein T, Weber F, Philipp A, et al. A new pumpless extracorporeal interventional lung assist in critical hypoxaemia/hypercapnia. *Critical Care Medicine* 2006; **34**: 1372–7.
- 6 Gattinoni L, Pesenti A, Mascheroni D, et al. Low frequency positive pressure ventilation with extracorporeal carbon dioxide removal in severe respiratory failure. *Journal of the American Medical Association* 1986; **256**: 881–6.
- 7 Liebold A, Reng CM, Philip A, Pfeifer M, Birnbaum DE. Pumpless extracorporeal lung assist – experience with the first 20 cases. *European Journal Cardiothoracic Surgery* 2000; **17**: 608–13.
- 8 Elliot SC, Paramasivam K, Oram J, et al. Pumpless extracorporeal carbon dioxide removal for life threatening asthma. *Critical Care Medicine* 2007; **35**: 945–8.
- 9 Mallick A, Elliot S, McKinlay J, et al. Extracorporeal carbon dioxide removal using the Novalung in a patient with intracranial bleeding. *Anaesthesia* 2007; **62**: 72–4.
- 10 Dordak S. High frequency oscillatory ventilation for acute respiratory distress syndrome in adult patients. *Critical Care Medicine* 2003; **31**: S317–23.
- 11 *Arteriovenous Extracorporeal Membrane Carbon Dioxide Removal*. London: National Institute for Health and Clinical Excellence, 2008.
- 12 Walles T. Clinical experience with the iLA Membrane Ventilator pumpless extracorporeal lung assist device. *Expert Review of Medical Devices* 2007; **4**: 297–305.