Strategy for Difficult to Wean Sepsis or Severe Pneumonia Patients

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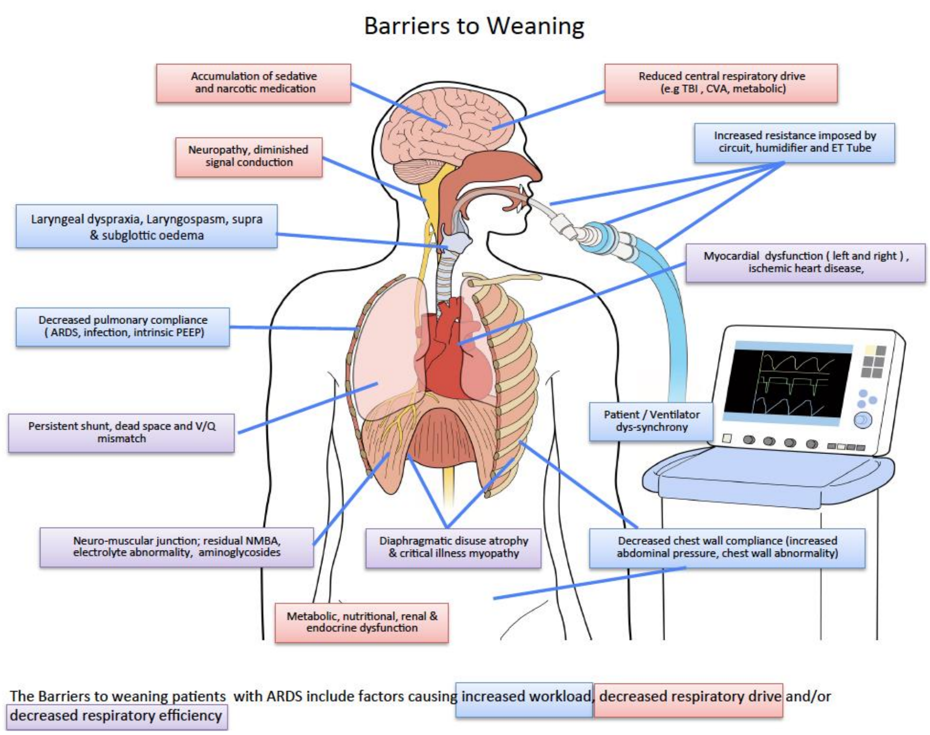
Introduction

As Mechanical ventilation (MV) is the mainstay of support for critically ill, commonly in those with Severe Sepsis and almost ubiquitous in those with severe pneumonia. It is also a driver of intensive care costs as the duration of MV directly affects the burden of the disease. (1) Ventilator dependent patients with severe sepsis and severe pneumonia result of the systemic insult to the body that is manifest in the respiratory system as ARDS. (2) Depending upon case mix, about one in ten ventilated in ICU has ARDS induced respiratory failure. (3)
MV, a necessity during ARDS induced respiratory failure, is associated with complications that pose risks to patients.(4) A risk that increases with duration of MV. (5). As respiratory function improves MV needs to be withdrawn at the earliest possible juncture. Very few randomised trials of MV weaning have had a primary focus on patients suffering from ARDS. For reasons outlined below substituting results acquired from general populations, or applying techniques developed in non ARDS patient groups may be flawed. (2)

In patients with ARDS reversal or control of the precipitant of the respiratory failure is essential before to the "weaning" can begin. This entails correction or attenuation of the precipitating cause of the ARDs as well restoring the respiratory systems to a stable, functional state. ARDS impact is not confined to the respiratory system, and thus weaning is not solely ventilator focused. Restoration of cardiovascular, neuromuscular, neurological and psychiatric homeostasis is required for successful weaning.(6, 7) Much of the problem in weaning are related to issues that are non-respiratory in origin. While much emphasis has been placed on routine protocols, these protocol s have not proven to be efficacious in mixed or non COPD populations

Barriers to Weaning

The barriers to immediate easy weaning are show nbelow. It is noteworthy that only a few are reversible directly by manipulation of the ventilation support, the primary focus on many early "weaning " attempts.



Increased Respiratory Load

With ARDS the residual shunt, increased dead space and ongoing poor ventilation-perfusion matching does not resolve immediately. (8) Weaning patients have requirements for supra normal minute ventilation, increased airway resistance, decreased pulmonary and or chest wall compliance changes and thus a greater work of breathing. (9). Decreased pulmonary compliance can arise from reversible causes like pleural effusions, and pulmonary oedema. Drainage or diuretics may improve compliance, oxygenation, decrease transpulmonary pressure and shorten weaning time. (10, 11)

Respiratory Drive

A central respiratory drive is necessary for ventilator activity to continue once the ventilator support is removed. Commonly there is a reduced respiratory drive with an inadequate response to either hypercarbia or hypoxemia. Carbon dioxide responsiveness is seldom tested formally, although ventilator response to reduction in pressure support is used as part of the weaning algorithm. Responsiveness to carbon dioxide assessed from the 100-ms occlusion pressure has been shown to predict weaning. (12)

Excess Sedation and Analgesia

The triad of adequate analgesia, control of delirium, and optimal sedation to facilitate tolerable MV is never more important than during weaning. (13). Early sedation depth predicts delayed extubation (14, 15) This association is confounded by severity of illness, and with neuromuscular blockade and prone positioning in severe ARDS, both precipitating deeper sedation, being recommended therapy for severe ARDS, it is not surprising that ARDS patients are deeply sedated. (16, 17) Kress demonstrated daily interruption of sedative infusions reduced the duration of MV, but less than a third of the studied group had ARDS or pulmonary oedema.(18) Protocol-directed sedation is controversial as results from the two randomized controlled trials were conflicting. (19, 20),

Prolonged weaning can be a complication of inappropriate dosing sedative/hypnotic medication, with delayed clearance in multi-organ failure a common feature of ARDS patients. (21) (7) Increased understanding of sedation goals by attending staff principles may further reduce ventilation duration (22). Change in sedation choice may contribute to shorter weaning periods. A five fold increase in propofol use, and a 70% reduction in midazolam use over eight years was associated with a decline in MV duration, tracheostomy rate, ICU and hospital length-of-stay. (23) Sedation techniques, particularly those that include the use of benzodiazepines may increase delirium, agitation, withdrawal and other neuro psychiatric conditions, which either directly or indirectly delay weaning. (24, 25).

Cardiac Load

Cardiac dysfunction is amongst the most common barriers to weaning.(26) The onset of ARDS respiratory failure may be precipitated by, exacerbate or importantly mask, congestive and right heart failure. Positive pressure reduces pulmonary oedema, provides increased alveolar pressures and reduces afterload. With weaning, spontaneous breathing is re-established, the process reverses and with a negative pleural pressure during inspiration.(27) This decrease in intrathoracic pressure increases the systemic venous return pressure gradient, the right ventricular (RV) preload, the central blood volume, and subsequently the LV preload.(28) A second effect is a decrease the LV ejection pressure gradient, increasing the LV afterload. (29) As a consequence respiratory and cardiac failure may occur, associated with increased work of breathing and hypoxemia.

Diagnosis and monitoring, augmented by echocardiography allows titration of treatment by diuretics, vasodilators, inotropes and coronary angioplasty when indicated. Using diuretics guided by brain natriuretic peptide (BNP) measurements shortens weaning suggesting that negative fluid balance using diuretics could hasten extubation. (30) The use of a conservative fluid strategy shortened MV in patients with acute lung injury although poor longer term cognitive outcomes are concerning. (10, 31)

Muscle Atrophy and Weakness

Early muscle changes are driven by inflammation and disuse, with atrophy from increased protein degradation. (32, 33) Late-phase muscle weakness persists in many despite resolution of lung injury and cessation of ongoing acute inflammation. (32) Late-phase muscle dysfunction may reflect a failure of the musculoskeletal system to regain homeostatic balance. These differences, may require different therapy. Electrical muscle stimulation for those that cannot exercise has been suggested although the for this novel technique in the ICU setting is scarce.(34) Denervation injuries, for which there are no specific therapies, may persist and delay weaning.

Metabolic Electrolyte and Endocrine Considerations

Metabolic alkalosis a common disorder in ICU impedes respiratory drive, and can be caused by diuretic use, hypernatremia and hypokalemia, all classically associated with ARDS management. (35) Increased serum bicarbonate is associated with increased ICU LOS, more days on MV and higher hospital mortality.(36) Chloride restricted buffered solutions theoretically could increase metabolic alkalosis, but in an interventional trial , chloride restriction did not increase in ventilation time (37, 38) Studies of "contraction alkalosis" and effect medications such as acetazolamide on weaning are needed.(39).

Serum calcium, phosphate, magnesium and potassium deficiency all cause muscle weakness.(40) Hypothyroidism, hypoadrenalism and relative or absolute cortisol efficiency also contribute to weaning difficulty. Endogenous and Exogenous corticosteroids are often used in critical illness for septic shock, directly for ARDS or for other indications may also contribute.(41) The corticosteroids and steroid based neuromuscular blocking agents are associated with muscular weakness but their overall effect on weaning remains unclear. (42). Avoidance and, when present, early correction of electrolyte abnormality as routine care is crucial to successful weaning. (40)

Psychological Dysfunction

42% of patients weaning from prolonged MV have depression, and weaning failure is twice as common in patients with depression, (43, 44) Fatigue, excessive daytime somnolence, and associated depression also delay weaning. (45) Second-generation antipsychotic and stimulants such as donepezil, modafinil and methylphenidate have been used in difficult-to-wean patients depression.(45-49). Whether their effect is through counteracting depression or anxiety, or as a direct respiratory stimulus is unclear.

Up to 80% of patients in ICU have delirium and is associated with delayed weaning and higher 6-month mortality. (13, 50) Prevention strategies include an early and exercise/mobility. Patients exposed to a "ABCDE " bundle spent three more days breathing without assistance and experienced nearly half the delirium, than patients treated with usual care.(22) Haloperidol is most commonly used for ICU delirium although evidence is entirely anecdotal (13) Dexmedetomidine is also recommended(51). Olanzapine, risperidone and quetiapine are also used and may have some advantages in the critically ill. (13)

Consent, Compliance and Comfort

Prolonged MV could produce suffering. While deeply sedated, with adequate analgesia and ventilator support, it is unlikely that a patient are "suffers". However, later as patient "emerges", and weaning begins "suffering" may manifest. Long-term outcomes from prolonged MV are worse than generally expected by relatives and physicians. (52) In a recent systematic review of studies reporting outcomes of patients requiring MV for more than 14 days, only half were successfully weaned, one in five were able to return home and half were dead in one year (53) ARDS is associated with exercise limitation, physical and psychological sequelae, decreased physical quality of life, and increased costs and use of health care services although there is a similar functional recovery in survivors who did and did not develop ARDS (4, 8). Overly optimistic expectations does not encourage meaningful discussion surrounding weaning outcomes or end of life decision making. Initiation of weaning is a timely juncture when the objectives of future treatments are considered.

Adjunctive Care

Physiotherapy and mobilisation

Early mobilization is beneficial, and it should be incorporated into routine daily acitvities. Early combined progressive mobilizations can be safely initiated. (54). Active mobilization may improve muscle strength and the ability to wean by reducing disuse atrophy. (54).

Tracheostomy

In some situations, tracheostomy has reduced the work of breathing, lowered in-hospital mortality and improved weaning in ICU patients.(55, 56) Systemic analysis of randomized controlled trials suggests that although early tracheotomy generally achieved better outcomes, including more ventilator-free days, shorter ICU stays, shorter sedation, and reduced long-term mortality.(57, 58).

Extubation to Non Invasive Ventilation

Non Invasive Ventilation (NIV) has been used both in an attempt to prospectively reduce the time that "invasive ventilation" is delivered through "early extubation" and as a rescue therapy for patients on the threshold of failing an extubation attempt. Early trials of NIV in post-extubation respiratory failure produced conflicting outcomes. Subsequent trials of "prophylactic" use immediate post-extubation in patients who "fail" a SBT was been found to be beneficial. (59-68) Systematic reviews have evaluated this technique and are support its clinical use in appropriate clinical circumstances.(69, 70).

Extrapolating this data needs considerable caution. (71, 72) Firstly, patients studied were predominantly suffering from chronic lung disease (CLD). Noninvasive ventilation has the capacity to reduce intubation rates, lower length of stay and mortality, in patients with CLD when used before invasive MV. With moderate to severe ARDS, NIV had high intubation rates, and a delivered high tidal volumes and had a high mortality with NIV failure. (72, 73)

With NIV, oxygenation is increased by a raised mean alveolar pressure, a reduction in tidal derecruitment of alveoli, and/or provision of high oxygen concentrations through a semiclosed system.(74). After extubation, a less than perfect NIV mask seal may produce air entrainment and airway pressures below airway "closing" pressure more frequently than during invasive ventilation (75) While entrainment can be managed by mask adjustment, or increasing oxygen, the decreased. Airway pressure may result in small airway collapse with derecruitment.

NIV may assist patients suffering from respiratory failure where work of breathing rather than hypoxia predominates. These patients are less sensitive to short periods of mask removal or leaks,. In patient recovering from ARDS although NIV supports of the work of breathing, there is risk of tidal de-recruitment. (74) At lower levels of support requirement high flow nasal cannula is likely to provide better oxygenation than venturi mask and is as least effective as, and better tolerated than, NIV for treatment of post extubation respiratory failure (76, 77). Its role in ARDS is as yet undefined (78). NIV is not recommended in pneumonia, or severe sepsis, and if used for weaning must be used with caution. (71, 73)

Adaptive and Automated Weaning Systems (AWS)

The first adaptive modes with feedback was pressure regulated volume control which titrated pressures to achieve a TV. Subsequent iterations targeted MV. Adaptive support ventilation (ASV) is a partially automated mode available from Hamilton Medical. ASV targets minute ventilation with an algorithm using the "Otis equation", to target the least work of breathing. Similar modes are availble with Bellavita (IMTmedical), with adpation aimed at addressing the overvolume issue. Studies comparing ASV weaning to standard care found ASV could shorten weaning in post cardiac surgery or chronic lung disease patient. When ASV was compared to assist control in patients with ARDS, no differences was found. (79) Of concern is that ASV allows TV of up to 22 ml/kg and in ARDS delivered median tidal volumes greater than the recommended 8 ml/Kg (79-84).

Most recent fully AWS incorporate feedback loops that titrate to ventilation and oxygenation targets and provides interesting opportunities. Two AWS are currently available the SmartCare® from Draeger Medical, and Intellivent from Hamilton Medical. (85, 86)

While they differ slightly, the principles of the AWS, is to establish ventilation through titration of adaptive ventilation, and when stable, the sequential application of a SBT and then, if successful conversion to titrated pressure support weaning. An early study of Smartcare® found that closed-loop weaning resulted in more rapid weaning, whereas a similar study carried out in an extremely well-staffed unit demonstrated no benefit. (86, 87) Differences in the nursing intensity and clinical governance may be explain on this discrepancy.

This development highlights two possibilities: Firstly a more consistent weaning system, that if calibrated correctly, could provide rapid weaning. Compared to non-automated weaning methods, these systems demonstrated positive advantages in weaning time, time to successful extubation, and possibly assisted in reducing ICU length of stay and the number of patients requiring prolonged MV (88, 89) However most patients studied received relatively short term ventilation after surgery, or ventilation for exacerbation of COPD. Clinical evidence from patients who have suffered from ARDS is remains scarce. (90, 91)

Secondly when skilled personnel are scarce, equivalent outcomes may be achieved with less clinician input. Adaptive weaning systems follow a computerized protocol and as such could be viewed as being identical to a "manual" weaning protocols, with more assured compliance. If "weaning protocols" are non-inferior to standard care an automated form of these should also demonstrate at least equivalent outcomes. While the automated weaning systems show promise and some evidence of efficacy, proprietary systems are generally available only on a single manufacturer's ventilator, and for multiple reasons these systems have not been widely adopted. (89)

Summary

Weaning patients with Severe pneumonia and severe sepsis from ventilator support presents a challenge, with patient presenting disease, type of pneumonia , comorbidity and severity of the sepsis, all influencing the success rate. The evidence supporting the use of specific techniques is very slight, and while it continues to grow remains a significant gap in our understanding of this problem.

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