Mise au point

Goal oriented ventilation in acute respiratory distress syndrome: a concept for optimal gas exchange at lung protective ventilation

Ventilation adaptée au cours du Syndrome de détresse respiratoire aiguë : comment combiner échanges gazeux et protection pulmonaire ?

B. Jonson

Department of Clinical Physiology, University Hospital of Lund, S-221 85 Lund, Sweden

Abstract

The strategy goal oriented ventilation means that mechanical ventilation should aim at clearly defined immediate physiological objectives based upon the actual status of the individual patient. The immediate goals, which ultimately should lead to an optimal outcome, comprise normocapnia, oxygenation and lung protection. Obstacles of physiological nature on the way towards the goals are briefly discussed, as are strategies to overcome each of them. The challenge is to optimise all aspects of mechanical ventilation in order to reach all goals. For that purpose a holistic approach must be taken in which comprehensive information about patient status is taken into account. Shortcomings of available monitoring systems are underlined. On the basis of improved monitoring it should be possible to use computer simulation in order to come closer to the goals of mechanical ventilation, than what is possible on the basis of presently practised clinical routines.

© 2006 Société de réanimation de langue française. Published by Elsevier SAS. All rights reserved.

Keywords: Ventilator induced lung injury; Computer simulation; Acute respiratory distress syndrome

E-mail address: bjorn.jonson@med.lu.se (B. Jonson).

Résumé

Une stratégie de ventilation « ajustée » selon les échanges gazeux et la mécanique respiratoire doit tenir compte d’objectifs physiologiques adaptés à chaque malade. Ces objectifs reposent sur un contrôle optimal de la capnie et de l’oxygénation qui doivent être associés à la protection pulmonaire. Les limites et les solutions physiologiques d’une telle stratégie sont discutées. Le « challenge » est de réussir à combiner ces différents objectifs en ajustant individuellement les réglages du ventilateur. Pour se faire, une approche « holistique » fondée sur des informations physiologiques fiables et pertinentes peut être proposée. Les limites liées aux outils de mesures physiologiques disponibles sont exposées. Des mesures physiologiques fiables permettent de simuler et donc de prédire les effets des différents réglages du ventilateur. Cette stratégie de ventilation « ajustée » pourrait permettre de s’approcher d’avantage des objectifs physiologiques de ce qui est actuellement réalisé dans notre pratique clinique.

© 2006 Société de réanimation de langue française. Published by Elsevier SAS. All rights reserved.

Mots clés : Lésions induites par la ventilation ; Syndrome de détresse respiratoire aiguë modélisation

Goal oriented ventilation stands for the approach that mode and setting of a ventilator aims at clearly defined objectives based upon the actual status of the individual patient. Objectives may be immediate or ultimate. The immediate objectives can be described in physiological terms. The secondary or ultimate objectives refer to outcome. In the acute respiratory distress syndrome (ARDS), survival with preserved organ function is the ultimate objective, the achievement of which depends on adequate ventilation that does not cause ventilator induced lung injury (VILI).
Obviously, optimal ventilation is only one of several features of intensive care necessary to save the ARDS patient. In 1967 Ashbaugh et al. [1] stated: ‘The use of positive end-expiratory pressure (PEEP) merely buys time; unless the underlying process can be successfully treated or reversed the prognosis is grave’ [1]. This statement is still valid but may be expanded to other aspects of mechanical ventilation which may ‘buy time’.

An important new and complementary aspect is that VILI may induce multiorgan failure leading to death [2]. This aspect links the immediate and ultimate goals of ventilation.

Already in 1970, the group of Falke (Kumar et al. [3]) verified the usefulness of PEEP. The research groups referred to above, showed an insight into the pathophysiology remarkable for its time, quote from Ashbaugh et al. [1]: ‘If surfactant is diminished, alveoli should collapse on expiration when the end-expiratory pressure is at atmospheric levels.’

The immediate goal of mechanical ventilation is: Adequate gas exchange with respect to CO₂ and O₂ achieved with lung protective ventilation (LPV). In the present review problems to reach this and its partitions will be discussed in relation to the compromised physiology in ARDS.

1. The goal of normocapnia

Apnoeic oxygenation by extracorporeal CO₂ elimination illustrates that ventilation is not essential for blood oxygenation and O₂ exchange [4]. Ventilation is, however, a prerequisite for CO₂ exchange, if this is not achieved with extracorporeal CO₂ elimination. Accordingly, ventilation serves the purpose to control the arterial partial pressure of CO₂, PₐCO₂. Factors determining PₐCO₂ are metabolic CO₂ production, V’CO₂, and alveolar ventilation, V’ₐ:

$$P_{aCO_2} = V'CO_2/V'\times P_{barometric}$$

Accordingly, in order to reach a target PₐCO₂, V’ₐ, must balance V’CO₂.

What the target PₐCO₂ might be has been a matter of intensive debate during the last years. In order to minimize tidal volumes, permissive hypercapnia has been tried. From physiological aspects, acidosis associated with hypercapnia has many potentially dangerous consequences. It offsets efficient enzyme functions, cell membrane functions, sympathetic and other receptor functions. These are just examples of basic physiological pH dependent functions, which may be disturbed at hypercapnia and lead to negative effects on physiology [5,6]. Not surprisingly, some studies permitting hypercapnia do not show improved outcome [7,8]. Notably, up to moderate variation in PₐCO₂ is well tolerated by the organism. It is rather pH that needs to be controlled by maintaining a target value of PₐCO₂. A primary goal suggested is to achieve a PₐCO₂ that does not lead to respiratory acidosis. A matter outside the scope of this review is that metabolic acidosis should also be avoided. Hyperventilation to compensate for metabolic acidosis leads to deleteriously high tidal volumes and other negative consequences. In conclusion, a primary goal of ventilation in ARDS is to maintain normocapnia. The precise definition of normocapnia may still be debated. Most reasonable seems to have a goal in the upper normal range around 6–7 kPa or 45–50 mmHg.

Surprisingly, little emphasis has been laid on V’CO₂. Since more than 20 years V’CO₂ could be monitored with simple technique [9]. In ARDS, often high and sometimes extremely high values of V’CO₂ are observed. Reasons may be anxiety, pain, fever, inflammation and nutritional imbalance leading to a catabolic metabolism. For reasons difficult to accept monitoring of V’CO₂ is rarely available. Therefore, in clinical practise, the incitement to reduce metabolic requirements on ventilation is missing. A goal of fundamental importance for goal oriented ventilation is to reduce metabolism and thereby the demands on alveolar ventilation. This goal merits an increased attention.

Alveolar ventilation must be adapted to the metabolic rate in order to reach the target PₐCO₂ (Eq. (1)). A serious obstacle to maintain normocapnia is in ARDS a high dead space fraction. Beydon et al. [11] reported physiological dead space values up to 65% and Nuckton et al. [10] up to 83%. A simple monitoring technique known for many years is the single breath test for CO₂, SBT-CO₂, also denoted volumetric capnography, Fig. 1 [12]. Again, the problem of high dead space is often overlooked because of deficient monitoring systems.

The physiological background of the high dead space in ARDS is complex. Microvascular pathology, notably thrombosis within small pulmonary arteries, is an important cause of the problem [13]. To address the problem of microthrombosis by any particular pattern of ventilation has not been suggested. However, it is possible that microthrombosis is provoked or aggravated by lung damaging ventilation. If lung protective ventilation might decrease such pathology needs to be studied.

A further reason for high dead space is intrapulmonary shunt that may reach above 50% of the cardiac output. Shunted blood augments PₐCO₂ above alveolar P’CO₂, thereby contributing to dead space. Fig. 2 shows that shunt contributes to alveolar dead space, particularly in the presence of other factors leading to low saturation of venous blood. Such factors are
anaemia, low cardiac output and increased metabolism. To reduce alveolar dead space, shunt should be reduced, anaemia, low cardiac output and increased metabolism should be avoided. In a study of Beydon et al. [11] the benefit in terms of lower alveolar dead space at increased PEEP was balanced by enlarged airway dead space caused by airway distension. In the small material only few patients showed important recruitment at increased PEEP. Further studies are merited.

In ARDS, the single breath test for CO₂ usually shows a highly sloping alveolar plateau, Fig. 1. This indicates the existence of lung regions with very different alveolar PCO₂ which regions empty in a non-synchronous way. If such regions with highly varying ventilation/perfusion ratio can be ventilated more efficiently remains to be studied.

To minimise dead space is anyway an important and realistic goal. The first way that is not always practised is to replace humidifying filters with active humidifiers. A further mean to reduce dead space is expiratory flushing of airways, later denoted tracheal gas injection (TGI) [14]. TGI has several drawbacks. For example, it interferes with regular ventilator function. When used in conjunction with increased respiratory frequencies associated with a significant flow at the end of expiration, TGI can only dilute rather than eliminate CO₂ in the tracheal tube and y-piece. An alternative is then to aspirate dead space from an extra channel close to the tip of the tracheal tube and replace that gas by fresh gas through the ordinary inspiratory ventilator line. This method, aspiration of dead space (ASPIDS), has proven efficient in animals, healthy man and in patients with ARDS [15,16]. ASPIDS is not commercially available. A simple way to reduce dead space is to deliver the tidal volume in a way that prolongs the mean time available for inspired gas for distribution and diffusion in the respiratory zone (MDT) [17]. Preliminary results indicate that this is also practicable in ARDS (Fig. 3). A logarithmic relationship between tidal elimination of CO₂ and MDT implies that MDT may become critically low at high respiratory rates. Further studies are merited.

In ARDS, the single breath test for CO₂ usually shows a highly sloping alveolar plateau, Fig. 1. This indicates the existence of lung regions with very different alveolar PCO₂ which regions empty in a non-synchronous way. If such regions with highly varying ventilation/perfusion ratio can be ventilated more efficiently remains to be studied.

To minimise dead space is anyway an important and realistic goal. The first way that is not always practised is to replace humidifying filters with active humidifiers. A further mean to reduce dead space is expiratory flushing of airways, later denoted tracheal gas injection (TGI) [14]. TGI has several drawbacks. For example, it interferes with regular ventilator function. When used in conjunction with increased respiratory frequencies associated with a significant flow at the end of expiration, TGI can only dilute rather than eliminate CO₂ in the tracheal tube and y-piece. An alternative is then to aspirate dead space from an extra channel close to the tip of the tracheal tube and replace that gas by fresh gas through the ordinary inspiratory ventilator line. This method, aspiration of dead space (ASPIDS), has proven efficient in animals, healthy man and in patients with ARDS [15,16]. ASPIDS is not commercially available. A simple way to reduce dead space is to deliver the tidal volume in a way that prolongs the mean time available for inspired gas for distribution and diffusion in the respiratory zone (MDT) [17]. Preliminary results indicate that this is also practicable in ARDS (Fig. 3). A logarithmic relationship between tidal elimination of CO₂ and MDT implies that MDT may become critically low at high respiratory rates. Then, a longer inspiration time and particularly a long postinspiratory pause time is advantageous. It is time to reconsider routine settings with expiratory time about 66% of the respiratory cycle.

Adequate oxygenation requires that intrapulmonary shunt is reduced by keeping a sufficient part of the lung open for at least a greater part of the respiratory cycle. PEEP is the traditional resort to reduce end-expiratory lung collapse. It is often argued that PEEP is an inefficient means to recruit the lung in ARDS and that specific recruitment manoeuvres should be used. However, ventilation is a dynamic process in which one must observe what happens during the full respiratory cycle and over a prolonged period of time. In this perspective it has been shown that a PEEP some cmH₂O above the lower inflection point of the elastic pressure volume curve combined even with low tidal volumes is an efficient way to achieve lung recruitment [18,19]. In an immediate perspective recruitment manoeuvres may certainly be more effective in some patients, but the effect above that of an adequate PEEP is usually short lasting. Still, there appears to be a room for recruitment manoeuvres, particularly when much of the lung is collapsed in a patient with a short history of ARDS. Overall, adequate oxygenation can usually be adequately achieved in ARDS at modest values of PEEP (i.e. <20 cmH₂O) and by using a fraction of inspired oxygen, FIO₂, well below 100%.

3. The goal of lung protection

The classical form of VILI, barotrauma, was caused by the very high airway pressures applied to compensate for low lung compliance caused by collapse and morphological lung damage. In the past, barotrauma frequently led to air leakage to the pleura, mediastinum and to subcutaneous emphysema. By limiting airway pressure we have learnt to avoid most of these problems. Currently it is recommended that postinspiratory plateau pressure, Pplat, should be limited to about 30 cm H₂O. If the abdominal pressure, and thereby pleural pressure, is high, higher pressures may be needed and tolerated. Barotraumas is now a rare problem, not further discussed.

Surfactant deficiency is the primary pathogenetic factor in the infantile respiratory distress syndrome (IRDS) and a sec-
ondary factor in ARDS. In both these syndromes lung collapse, intrapulmonary shunt, hypoxia and poorly compliant lungs are at least in part caused by surfactant deficiency.

In 1970, Mead et al. stated: ‘At a transpulmonary pressure of 30 cm H₂O the pressure tending to expand an atelektatic region surrounded by a fully expanded lung would be approximately 140 cm H₂O’ [20]. This represents even today a fundament behind the concepts ventilator induced lung injury, VILI, and its antonym lung protective ventilation (LPV). In 1982 I drew the conclusion from available studies: ‘A respiratory pattern should open up closed units and maintain aeration and stability throughout the respiratory cycle.’ [21]. Fig. 4 illustrates how shear forces may rip the epithelial cells from the bronchiolar basal membrane. Leakage of plasma proteins from the denuded surface leads to surfactant inactivation. A vicious circle is accelerated in which collapse and re-expansion of lung compartments lead to damage, accentuated surfactant inactivation and so on. In ARDS repetitive collapse and re-expansion has been verified with computer tomography (CT) [22]. Notably, healthy lungs tolerate thousands of cycles of breath by breath collapse and re-expansion [23], while the opposite is true after even a slight surfactant perturbation [24]. A prerequisite for the vicious circle mentioned above is therefore an already damaged lung.

In a pioneering study Reynolds reasoned that ventilation with pressure-controlled ventilation at inverse inspiratory/expiratory (I/E) ratio would increase P₅O₂ by keeping alveoli open for a longer proportion of each breath [25]. His ideas did not penetrate and it took more than a decade until my group showed that they were valid and allowed protection of the surfactant deficient lung against VILI [26]. In a very large number of studies it has been shown that lung protection is offered by different modes depressing tidal collapse and re-expansion. Examples are high frequency jet ventilation or high frequency oscillation. Neither inverse I/E ratio nor high frequency modes of ventilation have been widely applied. Inverse I/E ratio is difficult to control. When status improves and compliance increases the longer time constant for the lung to empty may lead to sudden and deleteriously high auto-PEEP. High frequency ventilation is hampered by the fact that one must adopt concepts for controlling gas exchange, which differ fundamentally from traditional physiological concepts [27,28]. Nevertheless, high frequency ventilation remains an alternative that merits further investigation, although additional risks motivate that the technique should be preferred only in the most experienced centres [29,30]. For the foreseeable future mechanical ventilation will in most centres rely upon traditional modes characterised by tidal ventilation at frequencies and other characteristics allowing application or classical concepts like minute ventilation, tidal volume, dead space etc. Such ventilation must then be delivered so that repeated lung collapse and re-expansion is avoided as far as possible.

In a classical study by Mead et al. based upon recording of pressure-volume (P/V) loops of collapsed lungs it was observed that re-expansion was irregular while different lung units “popped open” [31]. The large hysteresis of the P/V loop reflected that collapse reoccurred at much lower airway pressures than re-expansion. The physics behind these observations makes it theoretically possible to ventilate the lung at an initial pressure, i.e. PEEP, which is sufficient to keep an adequate part of the lung open, and stop the insufflation at a pressure that is low enough not to cause barotrauma. Lung partitions particularly difficult to recruit might then be left alone in a collapsed state. If the tidal volume is low enough, its delivery could then be achieved by expansion of open units with minimal if any recruitment of closed units. Setting of PEEP level, tidal volume and other parameters which are optimal in the individual patient remains a challenge.

Already in 1972, Falke et al. [32] realised that the point of increasing compliance of the inspiratory P/V curve indicated recruitment of closed lung units in ARDS. This point, later denoted the lower inflexion point (LIP) has been suggested as a guideline in the setting of PEEP in ARDS [33,34]. However, recruitment is a continuous phenomenon affecting the whole P/V curve. In a study based upon a multi-compartment lung model with variable distribution of opening pressures it was shown that the LIP reflects the onset of recruitment rather than its fulfilment. Recruitment continues up to about the upper inflexion point of the P/V curve [35]. In a recent review the limited information obtained in a single inspiratory P/V curve recorded from zero airway pressure was underlined [36]. A family of inspiratory P/V curves provides a much more comprehensive information of the distribution of opening and closing pressures of lung units [16,37,38]. This information also including expiratory P/V curves can be obtained bedside and automatically using a computer controlled ventilator [39]. In theory, setting of PEEP and other parameters may be optimised to minimise tidal collapse and re-expansion of lung units on the basis of multiple pressure volume loops (Fig. 5). However, there may be alternative ways to reach this goal and combine it with the equally important goal, to achieve adequate gas exchange.

Fig. 4. Drawing illustrating events in a zone undergoing re-expansion from a collapsed state. Densely distributed alveolar septa, which are obliquely attached to bronchiolar walls, cause large shear forces.
This high PEEP should offer optimal oxygenation at a properly chosen FIO2. How should the ventilator be set to reach or to come as close as possible to this combination of goals? Considering complex physiology with regards to mechanics and to gas exchange together with the high degree of freedom in the setting of a ventilator, nobody would be able to choose the optimal minute ventilation or \( V_T \), respiratory rate, \( I/E \) ratio, pause time, external PEEP and shape of inspiratory pressure or flow wave form. However, the experienced physician with a deep insight in physiological mechanisms and with an adequate system for monitoring in his hand can sometimes come much closer to the combined goal of normoxia, normocapnia, low tidal volume and low plateau pressure than what is accomplished in routine care. For routine care we need much better tools than those available.

5. Computer simulation, a tool for goal oriented action

Mechanical ventilation in patients with life threatening lung disease can from some aspects be compared to radiation therapy in malignant disease. In both cases efficient treatment is a prerequisite for life while it at the same time is a dangerous procedure. In both cases treatment should be adapted to the exact nature of the disease. Diagnostic procedures need to be taken which provide as much details as possible so that treatment could be tailored to the exact circumstances at the time of the curative procedure. It appears that in the case of mechanical ventilation we have a long way to go before we approach a stage at which radiotherapy is operating.

As concerns diagnostics, one can come very far on the basis of signals available from modern ventilator systems, which are instant values of flow, pressure and \( CO_2 \), (Figs. 1, 5). On the basis of the single breath test for \( CO_2 \), (Fig. 1), one can calculate the volume of \( CO_2 \) eliminated as a function of tidal volume. One should also take into account the effect of MDT at an alternative ventilator setting. From a family of \( P_{el}/V \) curves (Fig. 5), one may evaluate the relationship between pressure and re-expansion and collapse at increasing and decreasing airway pressure, respectively. Such information is still not generally available and cannot be taken into account in tailoring therapy to the status of the patient.

Computer simulation is a universally used tool in engineering, physics and in many other fields when it comes to foresee what a given action would have on a complex system, the properties of which can be described in mathematical terms. A second step is to simulate a large number of possible actions in order to find out which action it would take to reach a certain effect on the complex system. Already Sir Isaac Newton (1642–1727) defined mathematical strategies as to how to find out which action it would take to reach a defined result by using iterative analysis of action and reaction within complex systems. It seems timely to explore such strategies in medicine and particularly in intensive care and mechanical ventilation.

Computer simulation to predict the result of ventilator resetting with respect to mechanics and \( CO_2 \) exchange was recently tried in pigs by Uttman and Jonson [40]. In healthy pigs, the
hypothesis was tested that the effect of ventilator resetting could be predicted by computer simulation based on a physiological profile. The physiological profile comprised compliance, constant inspiratory and volume dependent expiratory resistance. CO₂ elimination per breath was expressed as a function of tidal volume. During simulation pressures and flow within the respiratory system was calculated moment by moment from data describing ventilator action. In the study respiratory rate was changed in five steps between 10 and 30 min⁻¹. At each step minute ventilation was adjusted in an effort to keep CO₂ elimination constant. Computer simulation allowed precise prediction of airway pressures after resetting. At the rate of 30 min⁻¹, errors up to 6% with respect to CO₂ elimination were explained by the fact that the model did not incorporate the feature that a shorter MDT at high rates lessens CO₂ elimination. (Fig. 3) [17]. Future models used in computer simulation should incorporate this mechanism. In patients with acute respiratory failure, the group of Beydon (Utman et al. [41]) showed that computer simulation may precisely predict the effect on airway pressures following PEEP resetting. After large increments of PEEP, CO₂ elimination was lower than predicted by simulation, probably because of hemodynamic effects. Obviously, much work remains to be done before computer simulation is used in clinical practise to guide the physician to achieve the specific goals strived for in the individual patient. However, it is difficult to see alternatives, if one day we will be able to finely tune mechanical ventilation to the actual status and the immediate needs of the critically sick patient.

6. Conclusions

Ventilation is for CO₂ exchange! Oxygenation depends upon an open lung! To ventilate and keep the lung open while ventilator induced lung injury is avoided is a major challenge in ARDS treatment. It is unquestionable that tidal volume should be low to avoid lung injury. The tidal volume remains high in most intensive care units in patients ventilated for ARDS [42]. This indicates the difficulties to make an impact in clinical intensive care routines. Further progress can be foreseen when treatment is finely tuned to the status of the individual patient at all times. To approach this utopia improved monitoring is required. Such monitoring is feasible on the basis of simple techniques going out from the traditional signals representing flow, pressure and CO₂. Optimal ventilator setting should comprise the full spectrum of settings, like respiratory rate, tidal volume or minute ventilation, PEEP, inspiratory and pause time as well as shape of inspiratory flow or pressure wave. An optimal setting tuning the ventilator to the therapeutic goals requires tools based upon computer simulation of alternative ventilator function.

Acknowledgements

Supported by the Swedish Research Council and the Swedish Heart Lung Foundation.

References


