Old and New Strategies on Artificial Ventilation in ARDS Patients

9

Paolo Pelosi, Maria Vargas and Iole Brunetti

American-European Consensus Conference (AECC) made current definition of Acute respiratory distress syndrome (ARDS) in 1994. According to AECC, ARDS was defined by an acute onset of hypoxemia (PaO_2/FiO_2 ratio <200 mm Hg) and diffuse radiologic infiltrates in the absence of left atrial pressure.

During the years, the way to ventilate ARDS patients is deeply changed thanks to an increased knowledge of its pathophysiology. In this chapter, we report the main changes in the field of mechanical ventilation in ARDS patients.

ARDS is not a new disease; it is know since 1821 as "Idiopathic anasarca of the lung" [1]. Ashbough et al., made the first modern description of ARDS in 1967, while AECC made current definition of it in 1994 [1]. According to AECC ARDS was defined by an acute onset of hypoxemia (PaO_2/FiO_2 ratio < 200 mm Hg) and diffuse radiologic infiltrates in the absence of left atrial pressure [1].

During these 40 years the way we treat ARDS has truly changed. At the beginning, this disease was treated using mechanical ventilation obtained from

P. Pelosi (✉) · M. Vargas · I. Brunetti
Department of Surgical Sciences and Integrated Diagnostics, University of Genoa, Largo R. Benzi, Genoa, Italy
e-mail: ppelosi@hotmail.com

M. Vargas
Department of Anesthesia and Intensive Care Medicine, University of Naples, Largo R. Benzi, Genoa, Italy
e-mail: vargas.maria82@gmail.com

I. Brunetti
e-mail: ibrunetti@tin.it

A. Gullo (ed.), *Anaesthesia, Pharmacology, Intensive Care and Emergency A.P.I.C.E.*,
DOI: 10.1007/978-88-470-5516-2_9,

anesthesiological and not from intensive care clinical practice. Actually, ARDS is well-known pathology but still a challenge for the intensive care physician.

As follow we report the main changes in the field of mechanical ventilation in ARDS patients.

9.1 Old Strategies on Artificial Ventilation in ARDS Patients

9.1.1 Tidal Volume

The mechanical ventilation approaches for patients with ARDS over the decades of the 1970s, 1980s, and early 1990s aimed to improve oxygenation and to normalize arterial carbon dioxide levels [2].

In those years, the recommended strategies to achieve these targets included the use of high tidal volume of 10–15 ml/kg actual body weight [2]. These levels of tidal volume seemed to be useful and safe for patients with normal lung parenchyma after major abdominal surgery but not so safe for lung injured patients. Just in that period, the first animal studies about the use of high tidal volume in mechanical ventilation provided an evidence of a severe lung damage produced by this ventilation strategy, probably due to the disruption of pulmonary endothelium and epithelium and the release of inflammatory mediators [3]. Later research demonstrated that the so-called *volotrauma* may worsen the lung damage in ARDS patients as a result of excessive distension or stretch of the aerated lung. In the 1986 Gattinoni et al., evaluated the distribution of lung aerated and non-aerated regions in patients with ARDS [4]. Interesting results of this study demonstrated an inhomogeneous distribution of aerated lung regions with normal compliance and non-aerated lung regions with a significantly reduced compliance [4]. So according to this study, the single areas of the same lung didn't have the same conduct regard lung injury. Gattinoni et al., in further studies also demonstrated that the lung aerated regions in ARDS patient were similar to a lung of a healthy child, so they called this small aerated lung parenchyma as *baby lung* [5].

The concept of baby lung had a key role in the comprehension and treatment of ARDS. In the 1990s years, according to this concept many clinical studies started to use a small tidal volume in mechanical ventilation of ARDS. In this period Hinckling et al., gained favor regards their animal study about small tidal volume versus large tidal volume in ARDS animals [6] and following human studies confirmed this topic. Brochard et al., evaluated the effect of low tidal volume (treatment group) versus high tidal volume (conventional group) in severe ARDS patients [7]. In the treatment group, the tidal volume was maintained between 6 and 10 ml/kg of actual body weight (IBW), while plateau pressure below 25/30 cm H_2O; in conventional group tidal volume was set above 10 ml/kg IBW. In this study, the author failed to find a favorable outcome in any of exanimated variables [7]. Amato et al., evaluated the effect of protective mechanical ventilation on mortality in ARDS patients [8]. In this study, the tidal volume was set on

12 ml/kg IBW in conventional ventilation and 6 ml/kg IBW with a peak airway pressure between 20 and 40 cm H_2O. This author found that a protective approach in mechanical ventilation improved the survival rate at 28 days and the weaning rate but not improved the hospital discharge [8].

Low tidal volume strategy in mechanical ventilation of ARDS patients may result in an increase of arterial carbon dioxide levels, called *permissive hypercapnia.* This event may have potentially harmful consequences as cerebral vasodilation, pulmonary vasoconstriction, and pulmonary hypertension. Experimental data suggested that permissive hypercapnia was not an adverse event but it was safe and potentially beneficial in this disease [9].

9.1.2 Positive End Expiratory Pressure

The use of positive end expiratory pressure (PEEP) during mechanical ventilation may improve oxygenation in ARDS patients. This effect was due to the PEEP prevention of the collapse of alveoli and small airway lacking of surfactant [2]. Further, keeping the alveoli open throughout the respiratory cycle, PEEP may prevent the damage produced by the repetitive opening and closing of the small airway and alveoli. PEEP levels used in clinical practice for ARDS patients were wide. Some studies in the 1990's years sustained that the adequate PEEP level for ARDS patients could be chosen by the analysis of pressure–volume curve [10]. During ARDS the pressure–volume curve assumed a particular sigmoidal shaped with two inflection points. According to the sigmoidal curve, the PEEP level at which recruitment of collapsed alveoli began, could be set between the lower and the upper inflection point [11]. Rupie et al., evaluated the static pressure–volume curve in ARDS patients [11]. They demonstrated in patient with severe ARDS the lower and the upper inflection point of sigmoidal compliance curve occurring at approximately 10 and 30 cm H_2O of inspiratory plateau pressure. At times, the ideal PEEP level to set in mechanical ventilation of ARDS patients could be chosen according to the lower inflection point, in contrast with the previous study of Ashbough et al., in which PEEP levels didn't exceed 5–10 cm H_2O [12].

9.1.3 ARDS Clinical Trials Network

ARDS clinical trial network was established in 1994 with the aim to test treatment strategies to improve the care of patients with ARDS using multi-center clinical trials.

After the study of Amato and Brochard, the first clinical trials of ARDS-network aimed to clarify the role of the low tidal volume on some important clinical outcome in this disease [13]. This multi-center clinical trial recruited 861 patients from 1996 to 1999 in 10 University intensive care department. 429 patients received traditional tidal volume set as 12 ml/kg of predicted body weight.

This volume was subsequently reduced stepwise by 1 ml/kg in order to achieve an inspiration plateau pressure less than 50 cm H_2O. 432 patients received the lower tidal volume set as 6 ml/kg of predicted body weight and subsequently adjusted to maintain the inspiratory plateau pressure less than 30 cm H_2O. The use of the lower tidal volume strategy was found to be efficacious in the reduction of mortality. Mortality was reduced of 22 % and also the number of ventilator free days was greater in lower tidal volume group.

In 2004 the ARDS-network published another clinical trial with the aim to investigate the role of higher PEEP levels on clinical outcome in ARDS patients receiving mechanical ventilation with lower tidal volume [14]. This clinical trial, conducted from 1999 to 2002 in 23 hospitals of the National Heart, Lung and Blood Institute (NHLBI), recruited 549 patients. 273 patients received mechanical with lower PEEP level (8.9 ± 3.5 in day 1, 8.5 ± 3.7 in day 3, 8.4 ± 4.3 in day 7), while 276 patients received the higher PEEP level (14.7 ± 3.5 in day 1, 12.9 ± 4.5 in day 3, 12.9 ± 4.0 in day 7). As results of this study, there were no significant differences in mortality, in ventilator free days or organ failure between lower and higher PEEP groups [14].

Checkley et al., in 2008 evaluated the effects of ARDS-network clinical trial on mechanical ventilation practise in ARDS patients [15]. In ARDSnet hospital tidal volume was 10.3 ml/kg of predicted body weight (PBW) during the lower tidal volume trial, 7.3 ml/kg PBW at the end of this trial and 6.8 ml/kg PBW in 2005. Plateau pressure was 27.7 cm H_2O during lower tidal volume trial and 26.3 cm H_2O in 2005. The use of PEEP changed modestly from 1996 to 2005. PEEP increased from 8 cm H_2O in the lower tidal volume to 10 cm H_2O in 2005. This study demonstrated that in ARDS-network hospital physicians changed the setting of mechanical ventilation in ARDS patients. The changes adopted were most apparent in the management of tidal volume that was set to a lower level, but not in the management of PEEP levels that didn't changed significantly across the years.

9.2 New Strategies on Artificial Ventilation in ARDS Patients

Protective ventilator strategy based on lower tidal volume became the standard of care for ARDS patients in intensive care unit. Nevertheless, tidal volume level of 6 ml/kg seemed to be not appropriate for all ARDS patients [16]. Recently Gattinoni et al., stated that tidal volume adjusted for ideal body weight and airway pressure are surrogate of lung stress and strain and may be misleading in ARDS patients [17]. In fact, the protective mechanical ventilation was found harmful in a prospective randomized clinical study by Fanelli et al. [18]. In this study, the author found that low stretch/lung rest strategy, defined as TV of 6 ml/kg and PEEP of 8–10 cm H_2O, was associated to less apoptosis, which were protective against lung damage, and more ultrastructural evidence of cell damage [18]. In patients suffering from ARDS, mechanical ventilation is the life-treating therapy required to optimize gas exchange, to avoid and reduce work of breathing

preventing respiratory fatigue. For many years the use of controlled mechanical ventilation with protective setting and deep patients sedation and muscle paralysis was able to control lung stress and strain, but it may lead to a diaphragmatic dysfunction [19]. With this purpose in mind, the role of spontaneous breathing in ARDS patients has been more debated in the past years. Gama de Abreu et al., supported the use of spontaneous breathing in ALI/ARDS in a recent paper. In this work, the author used biphasic positive airway pressure with spontaneous breathing which is a combination of time-cycled controlled breaths at two levels of continuous positive airway pressure and non-assisted spontaneous breathing [20]. The author found that this ventilation increased the aeration of dependent zones, decreased tidal reparation and hyperaeration during spontaneous breathing, and produced a better oxygenation. Yoshida et al., evaluated the impact of spontaneous ventilation during airway pressure release ventilation (APRV) and pressure support ventilation (PSV) on distribution of lung aeration in patients with ARDS [21]. Pulmonary oxygenation was better during APRV than during PSV when delivered with the same mean airway pressure. While PSV didn't affect lung aeration, spontaneous breathing with APRV improved lung aeration decreasing the amount of collapsed tissue and improving pulmonary oxygenation. Spontaneous breathing activity during ARDS had potential disadvantages. This ventilation lack of a tidal volume control resulting in excessive lung stress and strain on damaged tissue responsible of an increase in proinflammatory response and than in mortality. The interaction between patient and ventilator may have different degrees of asychronization due to the common causes reported in spontaneous activity.

Recently a different model of spontaneous ventilation, involving a variation of breathing pattern, has been proposed in mechanical ventilation for ARDS patients. The variation of breathing pattern in terms of respiratory rate and tidal volume may improve the function of a damaged lung parenchyma. The concept of breathing pattern variation in ARDS/ALI was built on the observation that protective ventilation strategies had a monotonic pattern without any physiological variation of spontaneous breathing. According to this hypothesis, Spieth et al. evaluated the impact of variable tidal volume at fixed respiratory rate in a surfactant depletion model of lung injury [22]. Variable tidal volume was set in a mechanical ventilation previously established by ARDS-network and compared with this one without variability. The use of random variable tidal volume improved lung function and histological damage during mechanical ventilation without increasing lung inflammation and mechanical stress [22]. Variable tidal volume spontaneous ventilation is now known as noisy pressure support ventilation (noisy PSV). In this ventilation the variation of pressure support may lead to different degrees of variation in tidal volume. Spieth et al., in a recent study evaluated the effect of noisy-PSV on lung function in ALI/ARDS animals [23]. The target of pressure support represented the value needed to obtain a tidal volume of 6 ml/kg and the percentage of variability has been set around this value. Noisy-PSV improved the elastance of respiratory system, peak airway pressure, P/F ratio without increasing $PaCO_2$.

9.2.1 Positive End Expiratory Pressure

ARDS-network failed to show the best degree of PEEP to apply in mechanical ventilation for ARDS patients. General consensus exists about the use of PEEP in ARDS to keep open alveoli and small airway. Different high levels of PEEP have been shown to prevent and/or worsen lung damage in animal study. At the same time, random use of high PEEP levels didn't show a significant improvement of lung function in ARDS large human trials. In this scenario, the strategy of open lung approach was suggested with the aim to open recruitable alveoli and keep it open during respiratory cycles. In open lung PEEP strategy, the recruitment of alveoli is performed using recruitment maneuver with different PEEP level. Once the alveoli are open, they are kept open with a PEEP level that prevents their collapse. Recently, Gernouth et al., reported the use of computer-control open lung strategy on respiratory function and hemodynamic in ARDS patients [24]. The open lung procedure was divided into a lung recruitment phase and open lung PEEP titration. In recruitment phase, PEEP level was set to 20 cm H_2O and the lung was recruited with a stepwise increase of driving pressure up to 30 cm H_2O. Then, the alveoli were kept open using a decremental PEEP level by 2 cm H_2O, keeping driving pressure constant and recording dynamic compliance of respiratory system. This study showed that computer-control open lung strategy with recruitment maneuver followed by decremental PEEP trial, improved respiratory system mechanics and oxygenation in ARDS patients already ventilated with the protective strategy of lower tidal volume and higher PEEP.

Nevertheless, this computerized strategy didn't significantly compromise the hemodynamic in the same group of patients.

9.3 Conclusion

The well-known strategy of lower tidal volume and higher PEEP level, suggested by many trials including ARDS-network, for many years was the best mechanical ventilation to apply in ARDS patients. Actually, the huge technological progress in intensive care medicine allowed us to improve our knowledge in lung injury and offered us new and advanced solution to treat it in the best way possible.

References

1. Phua J, Stewart TE, Ferguson ND (2008) Acute respiratory distress syndrome 40 years later: time to revisit its definition. Crit Care Med 36:2912–2921
2. Bernard GR (2005) Acute respiratory distress syndrome. A historical perspective. Am J Respir Crit Care Med 172:798–806
3. Dreyfuss D, Basset G, Soler P, Saumon G (1985) Intermittent positive pressure hyperventilation with highinflation produces pulmonary microvascular injury in rats. A Rev Respir Dis 132:880–884

4. Gattinoni L, Presenti A, Torresin A et al (1986) Adult respiratory distress syndrome profiles by computed tomography. J Thorax Imaging 1:25–30
5. Gattinoni L, Pesenti A (2005) Il concetto di baby lung. Intensive Care Med 31:776–784
6. Hickling KG, Walsh J, Henderson S, Jackson R (1994) Low mortality rate in adult respiratory distress syndrome using low volume, pressure limited ventilation with permissive hypercapnia: a prospective study. Crit Care Med 22:1568–1578
7. Brochard L, Brochard L, Roudot-Thoraval F, Roupie E et al (1998) Tidal volume reduction for prevention of ventilator-induced lung injury in acute respiratory distress syndrome. Am J Respir Crit Care Med 158:1831–1838
8. Amato MB, Barbas CS, Medeiros DM et al (1998) Effect of protective mechanical ventilation strategy on mortality in the acute respiratory distress syndrome. NEJM 338:347–354
9. Malhotra A (2007) Low tidal volume ventilation in the acute respiratory distress syndrome. NEJM 357:1113–1120
10. Bigatello LM, Zapol WM (1996) New approaches to acute lung injury. Br J Anesth 77:99–109
11. Roupie E, Dambrosio M, Servillo G et al (1994) Tritation of tidal volume and induced hypercapnia in acute respiratory distress syndrome. Am J Respir Crit Care Med 149:533–537
12. Ashbough DG, Boyd Bigelow D, Petty TL, Levine BE (1967) Acute respiratory distress syndrome. Lancet 2:319–323
13. The acute respiratory distress syndrome network (2000) Ventilation with lower tidal volume as compared with traditional tidal volume for acute lung injury and the acute respiratory distress syndrome. NEJM 4:1301–1308
14. The NHLBI institute ARDS clinical trial network (2004) Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. NEJM 351:327–336
15. Checkley W, Brower R, Korpak A et al (2008) Effects of clinical trial on mechanical ventilation practice in patients with acute lung injury. Am J Respir Crit Care Med 177:1215–1222
16. Terragni PP, Del Sorbo L, Mascia L et al (2009) Tidal volume lower than 6 ml/kg enhances lung protection: role of extracorporeal carbon dioxide removal. Anesthesiology 111:826–835
17. Gattinoni L, Carlesso E, Langer T (2012) Towards ultraprotective mechanical ventilation. Curr Opin Anesthesiol 25:141–147
18. Fanelli V, Mascia L, Puntorieri V et al (2009) Pulmonary atelectasis during low stretch ventilation: open lung versus lung rest strategy. Crit Care Med 37:1046–1053
19. Gama de Abreu M, Güldner A, Pelosi P (2012) Spontaneuous breathing activity in acute lung injury and acute respiratory distress syndrome. Curr Opin Anesthesiol 25:148–155
20. Gama de Abreu M, Cuevas M, Spieth PM et al (2010) Regional lung aeration and ventilation during pressure support and byphasic positive airway pressure ventilation in experimental lung injury. Crit Care 14(34):1–12
21. Yoshida T, Rinka H, Kaji A et al (2009) The impact of spontaneous breathing ventilation on distribution of lung aeration in patients with acute respiratory distress syndrome: airway pressure release ventilation versus pressure support ventilation. Anesth Analg 109:1892–1900
22. Spieth PM, Carvalho AR, Pelosi P et al (2009) Variable tidal volumes improve lung protective ventilation strategies in experimental lung injury. Am J Crit Care Med 179:684–693
23. Spieth PM, Carvalho AR, Güldner A et al (2009) Effect of different levels of pressure support variability in experimental lung injury. Anesthesiology 110:342–350
24. Gernoth C, Wagner G, Pelosi P, Luecke T (2009) Respiratory and hemodynamic changes during decremental open lung positive end expiratory pressure tritation in patients with acute respiratory distresss syndrome. Crit Care 13:1-10