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ARTÍCULO DE REVISIÓN

Mechanical ventilation in acute lung injury. Is there anything new?

Ventilación mecánica en trauma pulmonar agudo ¿Hay algo nuevo?

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Resumen
Objetivo: **Revisar los avances recientes de ventilación mecánica y el tratamiento de pacientes con trauma pulmonar agudo (TPA).**
Recolección de la información: **Revisión selecta de la literatura (29 artículos).**
Selección de la información: **Se seleccionaron los artículos más importantes relacionados con ventilación mecánica y trauma pulmonar agudo.**
Resultados: **El trauma pulmonar agudo puede producirse por lesiones directas o indirectas al tejido alveolar. La lesión directa al espacio aéreo es causada primariamente por aspiración de contenido gástrico, que conduce a una respuesta inflamatoria local. Además, las lesiones indirectas pueden ser el resultado de estados inflamatorios sistémicos diseminados como la sepsis y el trauma. El manejo del TPA ha sido un problema difícil para los cirujanos que atienden pacientes con trauma severo. A pesar de los avances en la tecnología y la farmacoterapia, el TPA aún genera estancias prolongadas en la terapia intensiva, ventilación mecánica prolongada, y todo muy frecuentemente lleva a la muerte. La causa más frecuente de muerte en los pacientes con TPA es sepsis y falla orgánica multisistémica (FOMS), no la falla respiratoria. La investigación clínica y de laboratorio ha proporcionado diversas e innovadoras estrategias de tratamiento que representan una promesa importante en el tratamiento de este difícil proceso patológico. El uso de estrategias ventilatorias mejoradas, hipercapnia permisiva, ventilación protectora, ventilación líquida y oxigenación de membrana extracorpórea parecen demostrar efectividad en varias etapas del TPA. Posiblemente, la investigación continua en estas áreas definirá mejor la fisiopatología, las indicaciones, y la efectividad de todas las modalidades de tratamiento y proporcionará una mejor atención a los pacientes de trauma.**

Abstract
Objective: **To review current advances in mechanical ventilation and treatment of patients with Acute Lung Injury (ALI).**
Data collection: **Selective review of the literature (29 articles).**
Data selection: **The most relevant papers dealing with mechanical ventilation and acute lung injury were selected.**
Results: **Acute lung injury can result from direct or indirect insults to the alveolar tissue. Direct injury to the airspace is caused primarily by the aspiration of gastric contents, which results in a local inflammatory response. In addition, indirect insults may result from widespread systemic inflammatory states such as sepsis and trauma. The management of ALI has been a difficult problem for surgeons in the care of the acutely injured trauma patient. Despite technologic advancement and improved pharmacotherapy, ALI still leads to lengthy intensive care stays, prolonged mechanical ventilation, and all too often, death. The most common cause of death in patients with ALI is sepsis and multiple system organ failure (MSOF), not respiratory failure. Laboratory and clinical research has provided several new and innovative treatment strategies that show significant promise in the treatment of this difficult pathologic process. The use of improved ventilatory strategies, permissive hypercapnia, protective ventilation, liquid ventilation, and extracorporeal membrane oxygenation all appear to demonstrate effectiveness at various stages of ALI. Hopefully, continued research in these fields will better define the pathophysiology, indications, and effectiveness of all treatment modalities and provide improved patient care for the trauma patient.**
Conclusion: **Despite the better understanding of the pathologic processes of ALI and the etiologies, our**

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Conclusión: **A pesar del mejor entendimiento de los procesos patológicos del TPA y de las etiologías, nuestra capacidad para tratar pacientes con TPA sigue siendo primariamente de apoyo. La ventilación mecánica es la intervención más importante en el manejo del TPA. El mejor entendimiento de los procesos fisiopatológicos del TPA ha conducido a modificaciones de las prácticas existentes de la ventilación mecánica en esta población difícil de pacientes.**

Palabras clave: Trauma pulmonar agudo, ventilación mecánica.
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ability to treat patients with ALI remains primarily supportive. Mechanical ventilation is the most important intervention in the management of ALI. An improved understanding of the pathophysiologic processes of ALI has to modification of the existing practices of mechanical ventilation in this difficult patient population.

Key words: Acute lung injury, mechanical ventilation, trauma
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Introduction

Acute lung injury (ALI) describes a pathologic injury to the lung resulting in diffuse alveolar damage to both epithelial and endothelial tissue. This breakdown in the oxygenation barrier results in flooding of alveolar spaces with protein-rich edema, causing significant abnormalities in the gas exchange function of the lung. Fibroproliferation with collagen deposition and lung remodeling occur if the process is sustained, further worsening gas exchange. Clinical reflections on the process of acute lung injury provide distinct definition criteria, which are based on the severity of gas exchange abnormalities and radiographic manifestations. The American-European Consensus Conference developed the definition criteria most widely accepted today to identify patients with acute lung injury. The criteria are; 1) an oxygenation abnormality: $PaO_2/FiO_2 < 300$; 2) a chest radiograph criterion: bilateral infiltrates compatible with pulmonary edema. An exclusion factor of a pulmonary artery wedge pressure < 18 mmHg or no clinical evidence of increased left atrial pressure is included to rule out cardiogenic pulmonary edema as a cause of the clinical condition.[1]

Acute lung injury can result from direct or indirect insults to the alveolar tissue. Direct injury to the airspace is caused primarily by the aspiration of gastric contents, which results in a local inflammatory response. In addition, indirect insults may result from widespread systemic inflammatory states such as sepsis and trauma. The diffuse, unregulated systemic inflammation results in local organ injury in the lung. Although sepsis is the most common cause of ALI, severe trauma has also been implied in the development of acute lung injury.[2] Prolonged hospitalizations and significant mortality are attributable to ALI in the setting of trauma. Recent studies have reported an overall mortality rate from 35-50%.[3,4] Multiple factors determine the outcome for patients with ALI including severity of lung injury, predisposing medical conditions, age, comorbidities, and subsequent development of MSOF.[1] The most common cause of death in patients with ALI is sepsis and MSOF, not respiratory failure.[5] Unfortunately, despite the improved understanding of the pathologic processes of ALI and the etiologies, our ability to treat patients with ALI remains primarily supportive. Mechanical ventilation is the most important intervention in the management of ALI. An improved understanding of the pathophysiologic processes of ALI have lead to modification of the existing practices of mechanical ventilation in this difficult patient population. This paper will review the current advances in mechanical ventilation and treatment of patients with ALI.

Mechanical ventilation in ALI

Ventilatory support is often an important aspect in the care of ALI. The major objectives have been determined from multiple clinical research trials, and include the improvement of gas exchange, relief of respiratory distress, improvement of lung mechanics, permitting lung healing, and minimizing complications.[6] The standard approach to ventilator management for patients is variable depending on the extent of disease. In general, several principles have been used in the initial ventilator management: 1) A mode with a preset rate, but may allow assisted ventilation; 2) Adequate inspiratory flow, time, and airway pressure to deliver adequate minute ventilation and correct PCO_2 and pH; 3) Adequate PEEP to recruit collapsed alveoli and maintain patency; 4) Sufficient FiO_2 to maintain sufficient arterial oxygen tension.[7] The newer approaches attempt to avoid ventilator-induced lung injury by a lung-protective strategy of enhanced alveolar recruitment with reduced peak transalveolar pressure and reduced alveolar overdistension.[8] In addition, the acceptance of lower oxygen saturation and permissive hypercapnia has also changed the clinical management of ALI.

The initiation of a patient with acute lung injury on ventilatory support requires an understanding of the existing mechanical properties of the diseased lung tissue. To minimize the harmful effects of barotrauma and ventilator-induced lung injury, several protective strategies can be employed: 1) Use of smaller tidal volumes (5-8 ml/kg) and longer inspiratory times delivered using volume cycled ventilation or pressure-targeted ventilation to avoid peak alveolar pressures > 30-35 cm/H_2O; 2) Upward titration of PEEP to optimize recruitment and eliminate cyclic recruitment –collapse– of dependent alveoli; 3) Acceptance of hypercapnia if necessary to avoid high transpulmonary pressures.[7] The utilization of these principles allows for successful oxygenation without injury to the lung. The estimation of transalveolar pressure, or the pressure necessary for alveolar distension, can be obtained by determining the plateau pressure. This measurement can be obtained from standard ventilators and provides information about the compliance of the lung tissue, and the extent of acute lung injury. Plateau pressures should be maintained below 35 cm/H_2O, and ventilator adjustments in tidal volume, rate, and flow can be manipulated to optimize ventilation. In addition, treatment of decreased thoracoabdominal compliance can improve the success of ventilator treatment. Causes such as burn eschar, tight dressings, pleural fluid collections (blood, air, empyema), ascites are examples of situations in which treatment of a confounding variable may improve the ventilatory status of the patient.

The assessment of static pressure-volume curves also provides useful information in the ventilatory strategy to determine pressure required for alveolar recruitment. In addition, pressures consistent with alveolar overdistension, leading to barotrauma and ventilator induced lung injury, can be identified. This pressure-volume curve is created by a series of increasing tidal volumes, with attention focused on the change in lung pressure correlating with each volume.[9] The point at which the slope increases reflecting a greater change in volume is the lower inflection point, which corresponds to the pressure at which most recruitable alveoli are opened.[10] Maintaining PEEP at levels slightly higher than the lower inflection point is thought to keep the recruitable alveoli open during the entire respiratory cycle; thus improving oxygen exchange and preventing the open and closing of alveoli that causes ventilator induced lung injury.[10] The point on the curve that begins to flatten out is the upper inflection point, where alveolar overdistension can occur. The total plateau pressure should, therefore, be set below the upper inflection point to minimize the risk of lung injury caused by overdistension. Proponents of these techniques argue that this strategy is protective ventilation that minimizes further lung injury, and allows for adequate oxygenation and healing of acute lung injury. However, opponent's point out that many patients do not have a clear Pflex, the technique is difficult, and Pflex is variable and difficult to reproduce by observers.[11]

Determination of transpulmonary pressures and static pressure-volume curves are important in determining the optimum level of PEEP required for a safe and effective ventilation. The application of PEEP prevents the collapse of alveoli during the expiratory phase. Ultimately, this minimizes the number of alveoli undergoing repetitive recruitment and collapse, and improves alveolar ventilation.[7] A considerable number of authors have attempted to identify the appropriate level of PEEP for patients with ALI. The difficulty with ALI is that substantial regional variability exists within alveoli in terms of recruitment and distension at any given pressure. The pressure-volume curves generated only indicate the lung as a whole, and likely oversimplify the pressure-volume relationships that occur at each individual alveolus. Dependant areas of the lung have greater consolidation than non-dependant areas, although the vascular permeability occurs uniformly in all lung regions.[12] Therefore, the effectiveness of PEEP is dependent on the number of recruitable, non-consolidated alveoli within the lung. Maneuvers such as prone positioning, and the application of 30-40 cm/H_2O for 5-40 seconds can be used for alveolar recruitment and to retain alveolar patency.[13,14] Caution should also be given when increasing levels of PEEP are applied due to the adverse effects on cardiac performance, and worsening of lung injury if used incorrectly.[15]

Protective ventilation and permissive hypercapnia

An evolving technique in the management of patients with ALI is the use of permissive hypercapnia and protective ventilation. In theory, this technique suggests that ventilation with high airway pressures and alveolar volumes is more harmful than an elevated pCO_2 and moderate acidosis. This protective approach attempts to prevent alveolar collapse and overdistension, regardless of arterial carbon dioxide levels. Various ventilatory modes including pressure-limited and combined volume-ensured pressure support ventilation are utilized to limit tidal volume and peak inspiratory pressures.[16] Amato *et al* employed a protective strategy using small tidal volumes less than 6 ml/kg, respiratory rates < 30, driving pressure and peak airway pressures < 20 and 40, respectively, PCO_2 levels up to 80 mmHg, and arterial pH of > 7.2. Continuous intravenous infusions of sodium bicarbonate were used for pH levels below 7.2 to prevent the adverse effects of acidosis on cellular metabolism. These authors demonstrated an improved survival (62% *versus* 29%) at 28 days, a higher rate of weaning, and a lower rate of barotrauma in the protective ventilation group compared to the conventional treatment group.[16] Several recent studies have criticized the results of this study because of study design, pointing out the use of unlimited airway pressures in the control group to maintain a specific carbon dioxide level. This may explain the increased number of deaths from respiratory failure in the control group, leading to inaccurate mortality assessment between groups.[11] Stewart *et al* designed a similar study protocol as described by Amato *et al*, with the withdrawal of patients from the study if they had profound hypoxemia, acidosis, or barotrauma unresponsive to the interventions of sodium bicarbonate infusion or recruitment techniques. These authors concluded that protective ventilation with limited tidal volume and peak inspiratory pressures did not improve survival for patients with Acute Respiratory Distress Syndrome (ARDS).[17] These studies on the effectiveness of protective ventilation indicate the need for continued research in ventilatory strategies for patients with ALI and ARDS to identify optimal levels of tidal volume, rate, and PEEP. In addition, these studies indicate that employment of different ventilatory strategies should depend on the severity of lung injury in each individual patient rather than a uniform approach to all patients with ALI. Current recommendations suggest that conventional ventilation with permissive hypercapnia is an acceptable approach to treatment in patients with moderate ALI, while patients with severe ALI/ARDS may benefit from strategies of protective ventilation.[7]

Several studies have attempted to determine if pressure-controlled ventilation (PCV) offers benefit over volume-cycled ventilation (VCV) in the treatment of ALI. Pressure controlled ventilation aids in alveolar recruitment and has been demonstrated to distribute ventilation and pressure more evenly among alveolar lung units.[14] In addition, PCV allows for more precise adjustment of inspiratory time and peak airway pressures. The primary disadvantage is that close monitoring is needed to ensure adequate tidal volume if the lung becomes more non-compliant. Comparisons of PCV with a decelerating flow wave form and VCV with a square flow waveform demonstrated an improvement in arterial oxygenation, lower peak inspiratory pressures in patients with PCV.[18] In addition, Krafft *et al* found a decreased mortality rate in patients ventilated with PCV compared to VCV, 35% *versus* 54% respectively.[3] The difficulty in these comparison studies between the two different ventilation strategies is that, often, different treatment modalities such as permissive hypercapnia are also used in some patients. Therefore, the two individual modalities cannot be justly compared. Investigations for the direct comparison have been suggested, and protocols are being developed for accurate assessment of these two ventilator strategies.

Inverse ratio/ventilation

Another developing technique in the ventilator management of patients with ALI is the use of inverse ratio ventilation (IRV). This technique is often used in PCV, where the inspiratory time is adjusted to a ratio of > 1/2 of the respiratory cycle. Multiple studies have evaluated the beneficial and harmful effects of inverse ratio/ventilation in the treatment of ALI. Theoretically, the prolonged inspiratory phase allows for a reduction of peak airway pressures needed during mechanical ventilation. Therefore, inverse ratio ventilation is able to maintain higher peak airway pressures at lower alveolar pressures and PEEP levels.[19] The sustained alveolar inflation can decrease dead space ventilation and allows for the use of smaller tidal volumes to maintain oxygenation.[20] As is common with all newly evolving treatment regimens, differing opinions exist based on results form studies performed by several authors. Tharratt *et al* compared PCV with inverse ratio ventilation to volume controlled conventional ventilation in 31 patients. These authors concluded that PC-IRV demonstrated an improvement in oxygenation at lower minute volume, peak airway pressure, and PEEP requirements.[21] In opposition, Zavala *et al* compared inverse ration ventilation to conventional ventilation with similar PEEP. These authors concluded that PC-IRV improved carbon dioxide clearance, but the lung became less efficient at oxygen exchange. In addition, the risk of barotrauma was not different between groups.[22] Another criticism of inverse ratio ventilation is that the increased inspiratory time and positive intrathoracic pressure may have detrimental effects on cardiovascular hemodynamics. In general, authors have determined that IRV has little effect on venous return or cardiac index when appropriate levels of PEEP are used.[23] Clearly, much debate surrounds the use of inverse ratio ventilation in the management of ALI, and further evaluation in the effectiveness and timing of implementation of this technique is needed.

Liquid ventilation

Liquid ventilation is an evolving technique that has been studied extensively for nearly 30 years. The technique involves the use of perfluorochemical liquid, which has low surface tension (allowing it to spread evenly throughout the lungs) and a high oxygen carrying capacity. Carbon dioxide is eliminated when the fluid is ventilated, either by gas ventilation (in partial liquid ventilation) or by a bubble oxygenator or membrane exchanger (during total liquid ventilation).[24] The lungs are filled with the perfluorochemical liquid, and the ventilator circulates the liquid and provides oxygen exchange and carbon dioxide removal. In humans, partial liquid ventilation (PLV) is the most studied variant of liquid ventilation. In this method, the lungs are partially filled with a functional residual capacity-equivalent volume and ventilated with a conventional ventilator strategy. Several studies have demonstrated the effectiveness of PLV in neonates with respiratory failure. Hirschl *et al* reported a series of 19 patients utilizing PLV in patients on ECMO support. These authors demonstrated a decrease in the alveolar-arterial oxygen difference, decreased inflation pressures, and an increase in static lung compliance, with a 57% survival rate.[25] In addition, other studies have demonstrated improvement in the recruitment of lung volume and improved lung mechanics with the implementation of PLV.[26,27] The technique of liquid ventilation has been studied most extensively in the neonatal and pediatric patient population for respiratory distress syndrome, pulmonary hypertension, meconium aspiration, and childhood ARDS. Unfortunately, no current literature has evaluated the use of liquid ventilation in the treatment of traumatic pulmonary injury or in trauma patients with local organ injury in response to the systemic inflammatory response syndrome. An important difficulty in treating trauma patients is that focal lung injury (i.e. pulmonary contusion) is a common cause of respiratory failure. The use of liquid ventilation in this setting would be difficult because PLV worsens gas exchange in normally functioning areas of the lung. Clearly, the potential benefits of ongoing research may provide insight into the appropriate timing and use of this technique to improve respiratory care to traumatically injured patients.

Extracorporeal membrane oxygenation

Extracorporeal membrane oxygenation (ECMO) is described as prolonged extracorporeal cardiopulmonary bypass achieved by extrathoracic vascular cannulation utilizing a modified heart-lung machine, a membrane lung to exchange oxygen and carbon dioxide, and a heat exchanger to maintain temperature. Patients must be fully anticoagulated to prevent thrombosis within the circuit. Indications for ECMO include acute reversible respiratory or cardiac failure unresponsive to optimal ventilator and pharmacologic management, but from which recovery can be expected within 10-20 days of extracorporeal support. This technique has been studied extensively for nearly 30 years, with impressive results in the management of difficult respiratory conditions in all age groups. Worldwide, over 170 adult patients have been treated with ECMO for respiratory failure, with a survival rate of 42%.[28] The use of ECMO in the treatment of acute respiratory failure in the trauma patient has been limited, primarily due to the need for systemic anticoagulation and complications of bleeding. The first study to utilize ECMO for the treatment of respiratory failure in the trauma patient was performed by Anderson *et al* in 1994. More recently, Michaels *et al* updated this comprehensive study. A total of 30 patients refractory to conventional mechanical ventilation were treated with extracorporeal life support (ECLS) The authors reported pulmonary recovery sufficient to wean from ECLS of 56%, with a survival to discharge of 50%. The most common complication was bleeding, occurring in 58% of patients, which was not associated with mortality. Age, Injury Severity Score, and PaO_2/FiO_2 ratio were not related to outcome in this study.[29] Early intervention (mechanical intervention < 5 days) was associated with good outcome. The authors concluded that despite the risks of anticoagulation in this population with multiple injuries, extracorporeal life support can be a live-saving treatment in patients with severe respiratory failure refractory to conventional mechanical ventilation. The results of these studies demonstrate tremendous hope regarding the potential treatment options available for the treatment of ALI in trauma patients.

Conclusion

The management of acute lung injury has been a difficult problem for surgeons in the care of the acutely injured trauma patient. Despite technologic advancement and improved pharmocotherapy, acute lung injury still leads to lengthy intensive care stays, prolonged mechanical ventilation, and all too often, death. Laboratory and clinical research has provided several new and innovative treatment strategies that show significant promise in the treatment of this difficult pathologic process. The use of improved ventilatory strategies, permissive hypercapnia, protective ventilation, liquid ventilation, and extracorporeal membrane oxygenation, all appear to demonstrate effectiveness at various stages of ALI. Hopefully, continued research in these fields will better define the pathophysiology, indications, and effectiveness of all treatment modalities and provide improved care for the trauma patient.

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