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Research Article

Results of the Application of an Alveolar Recruitment Maneuver in Ventilated Patients

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Abstract

Objective: To evaluate the effects of an Alveolar Recruitment Maneuver on the reduction of complications, days of ventilation, ICU stay and mortality in ventilated patients.

Design: Trial with controlled background.

Scope: 500-bed University Hospital, 10-bed multipurpose ICU.

Patients: Patients ventilated from January 2010 to December 2012 with protective ventilation without MRA and patients ventilated using the same strategy and MRA from January 2013 to December 2015.

Interventions: Alveolar recruitment maneuver variant characterized by gradual increase of PEEP till doubling the previous value, with duration of two minutes and a frequency of three times a day.

Variables: Complications, days of ventilation, ICU stay and mortality.

Results: We included 97 patients in the control group and 101 in the trial´s group. The average days of ventilation were 6.81 in the control group and 6.79 in the study; the average ICU stay was 8.93 in the control group and 9.44 in the trial´s group. Patients in the trial´s group had fewer complications and mortality was 38.6%, lower than control (52.6%).

Conclusions: The two groups were homogeneous in terms of age, causes of ventilation, APACHE II, LIS index and Berlin classification. Mortality was lower than what predicted by the scales used in the trial´s group. Complications and mortality were significantly lower in the experimental group and there was no difference in relation to days of ventilation and ICU stay.

Introduction

Artificial Mechanical Ventilation (MAV) as a ventilator support is vital in a death risk patient treatment. However, it is currently known that it can initiate or exacerbate lung damage and contribute to the morbidity and mortality of the patients in whom it is used [1].

Since the beginning, during the polio epidemic of 1952 in Copenhagen, it was observed that the MAV could cause structural lung damage. In 1967, the term "respirator lung" was stated to describe diffuse alveolar infiltrates and hyaline membranes found in postmortem examination of patients undergoing this procedure [2].

The scientific evidence accumulated in the last three decades of the last century helped to understand the effects of mechanical ventilation on the healthy and diseased lungs and their possible mechanisms of production, which allowed to express the VILI terms for ventilator-induced injury in Animal models and that of VALI to describe the pulmonary complications associated to the use of ventilation in humans [3].

In the current century, the concepts of barotrauma (damage caused by high airway pressure), volutrauma (damage caused by overdistension), biotrauma (systemic and pulmonary inflammation due to the release of inflammatory mediators), atelectrauma and repeated collapses) and oxygen toxicity (damage caused by elevated oxygen concentrations) were defined [4].

Based on the knowledge of the effects of MAV on the lungs and the high mortality of patients who require it, on all those with ARDS, the Protective Ventilation strategy is currently applied (PV), having a positive impact on mortality, as demonstrated by the works of Amato and the ARDS Network [5,6].

The use of PV reduces the complications derived from elevated airway pressure and volume levels (barotraumas and volutraumas), but it is not enough to maintain a homogeneous distribution of inspired air through the different alveolar units [7], favoring alveolar dysreclusion and cyclic opening and closing of functional respiratory units (biotrauma and atelectrauma) related complications. These contribute to the appearing of ARDS, atelectasis, pneumonia and multiple organ failure, impacting negatively on the high lethality of this group of patients.

To correct the negative effects of PV derived from alveolar dysreclutation and cyclic opening and closure of functional respiratory units, the medical community proposes Alveolar Recruitment Maneuvers (ARMs). These are defined as a ventilatory procedure with which a transient increase in transpulmonary pressure is achieved, aiming at recruiting collapsed alveolar units, increasing lung areas available for gas exchange and improving arterial oxygenation [8].

Studies on ARMs in animals and in humans have been carried out for more than 15 years getting not sufficient elements for validation as a routine strategy for ventilatory use in medical practice. It has been shown to improve oxygenation and ventilatory mechanics, with few side effects, but there are no studies yet to confirm that they have positive influences on the days of ventilation, ICU stay and mortality, as reflected in the conclusions of several Systematic reviews and meta-analysis [9-11].

The pathophysiological basis of ARM is the transient increase in transpulmonary pressure, which reflects alveolar opening pressure and was achieved by different techniques (increasing Tidal Volume (TV), inspiratory pressure or end-expiratory pressure). The impossibility of determining the values of transpulmonary pressure at the head of the patient is the justification for the application of the numerous variants of ARM undergoing clinical trials at present.

Taking into account the critical analysis of the results of a comprehensive review and the experience of the intensive care unit staff at the intensive care unit of the university hospital "Dr. Antonio Luaces Iraola "from Ciego de Ávila, a variant of MRA was designed and applied to all ventilated patients, in the absence of contraindications for its use, with the objective of evaluating its effects in relation to the reduction of complications, the days of Ventilation, ICU stay and mortality.

Patients and Methods

Patients were ventilated in the mode selected by the specialist with the ventilators Sabina and Evita 2 from Draguer, Servo 300 (Siemens-Elema AB, Solna, Sweden) and BIRD 8400 STI. The upper inspiratory pressure limit was set at 50 cm H_2O. Blood pressure was taken before and after each ARM and continuous monitoring of pulse oximetry was maintained.

The maneuver variant consisted of a gradual increase of the PEEP (2 cm H_2O every two respiratory cycles) until obtaining twice the value set for the patient. In those who did not have it, the maneuver was carried out in the same way until reaching a value of 8 cm H_2O. During the maneuver, peak inspiratory pressure was never exceeded above 50 cm H_2O, when this value was reached without reaching the double PEEP level, the performance was stopped. After reaching twice PEEP, it was maintained for two minutes, then returned in an inverse and staggered way to baseline or 4 cm H_2O of PEEP in patients that were not applied at baseline. It was performed with a frequency of three times a day and after each time in which the patient was disengaged from the ventilator by some situation. It was performed during the first 7 days of initiation of ventilation.

The maneuver was applied to all ventilated patients except to:

- Pregnant.
- Patients with hemodynamic instability (sustained hypotension despite resuscitation with fluids and amines) (SAT≤100 mm Hg).
- Patients with severe cardiac arrhythmias and acute coronary syndrome.
- Patients with clinical and / or radiological evidence of volutraumas, barotraumas or high risk of suffering from them.
- Recent lung biopsies or resections
- Evidence of endocranial hypertension.

Patients who died or were withdrawn from invasive mechanical ventilation were excluded from the study within 24 hours.

An experimental study was carried out, with a historical control group composed by all patients ventilated from January 2010 to December 2012, who met the same criteria, who did not perform MRA and an experimental group that included patients with invasive ventilation in the period from January 2013 to December 2015, during his stay in the ICU of the University Hospital "Dr. Antonio Luaces Iraola ", of Ciego de Ávila. The universe of study was made up of 97 patients in the historical series and 101 in the study group.

The main variables studied were complications of MAV, days of ventilation, ICU stay and mortality. Mortality was compared by group and predicted by APACHE II, Berlin conference and Murray's Lung Injury Score (LIS).

This study was approved by the Ethics Committee of the Hospital "Dr. Antonio Luaces Iraola ", of Ciego de Ávila and took into account the informed consent requested to the relatives of the patients.

Statistic Analysis

Statistical analysis was performed using SPSS version 20. The results were expressed as average, percent, and standard deviation. It was applied parametric tests such as the student test for variables with normal distribution and nonparametric variables such as Mann-Whitney U and Chi-Square in the absence of normal distribution. A value of $P < 0.05$ was considered statistically significant in all cases.

Results

Table 1 shows the behavior of the variables used to homogenize the groups under study. The average age for the historical series was 53.48 and for the study group of 58.40, whiles the average for the APACHE II score and the mortality predicted and adjusted for this scale was similar in both.

Figure 1 shows the causes by which patients from both groups were ventilated, with no significant differences (U Mann-Whitney Test p =, 937). The most frequent cause was ARDS, without significant differences in relation to the type of ARDS. It was also observed that ARMs were applied to patients with healthy lungs requiring VMA, such as those with postoperative status and neuromuscular diseases.

Table 1: Distribution of average age. APACHE II score and predicted mortality and adjusted by this scale in the groups.

Variables	Groups	№	Mean	Standard deviation	Valor de p
Age	Without MRA	97	53.48	20.16	.058
	With MRA	101	**58.40**	15.60	
Apache II Score	Without MRA	97	18.66	7.51	.172
	With MRA	101	21.54	11.12	
Predicted Mortality	Without MRA	97	36.98	23.14	.603
	With MRA	101	37.48	21.23	
Adjusted Mortality	Without MRA	97	38.02	20.94	.902
	With MRA	101	38.09	19.01	

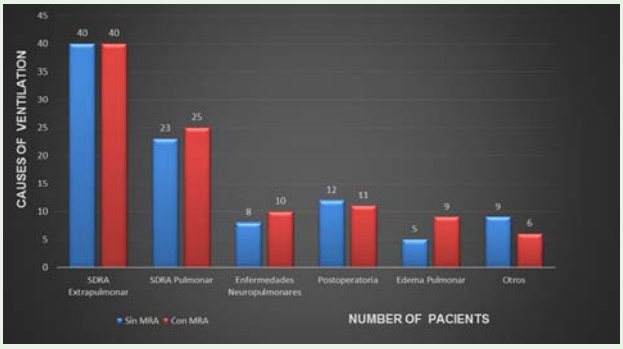

Figure 1: Causes of ventilation by groups.

Table 2 shows the distribution of patients according to the LIS [12] indexes, used to predict survival in ventilated patients. The two groups are similar, although the number of patients in the group that received ARMs in the last interval almost doubles that of the historical series.

Table 2: Distribution of patients according to LIS by groups.

Lung Injury Score	Groups				Total
	Without MRA		With MRA		
	№	%	№	%	
Less than 1.1	27	27.8	27	26.7	54
Between 1.1 and 2.4	57	58.8	51	50.5	108
Between 2.5 and 3.5	13	13.4	**23**	22.8	36
Total	97	100	101	100	198

Mann-Whitney U-test 4520.500 p = 0.298.

Table 3 shows the distribution of patients according to the Berlin definition [13], validated as a scale for predicting mortality in patients with ARDS. The number of patients with ARDS was similar in both groups (63 in the control and 65 in the experimental group) and their distribution according to severity levels did not have a significant difference, which means that they had similar prognoses.

Table 4 shows the behavior of predicted mortality in the different ranges of the APACHE II score. The non-ARM group had a higher than predicted mortality at all intervals on the scale, while in the ARM group, mortality was reduced in relation to prognosis in the range of 20 to 24 and in that of more than 34 points.

Table 3: Distribution of patients according to the Berlin classification by groups.

Classification of Berlin	Groups				Total
	Without MRA		With MRA		
	№	%	№	%	
Light	12	12.4	14	13.9	26
Moderate	39	40.2	40	39.6	79
Severe	12	12.4	11	10.9	23
Sin ARDS	34	35.0	36	35.6	70
Total	97	100	101	100	198

Mann-Whitney U-test = 4851.000 p = 0.901.

Table 4: Mortality prediction according to the APACHE II ranges in both groups.

APACHE II intervals and % of mortality	Groups					
	Without MRA			With MRA		
	№	Deceased	%	№	Deceased	%
Between 5-9 (8%)	8	2	25.0	7	1	14.3
Between 10-14 (12%)	31	7	22.6	13	3	23.1
Between 15-19 (25%)	16	10	62.5	25	10	40.0
Between 20-24 (40%)	25	16	64.0	10	2	20.0
Between 25-29 (50%)	7	6	85.7	12	7	58.3
Between 30-34 (70%)	6	6	100	1	1	100
More of 34 (88%)	4	4	100	33	15	45.4
Total	97	51	52.5	101	39	38.6

Table 5 compares the survival achieved in both groups with that predicted by LIS [12]. In the group with ARM, it was higher than that predicted in the ranges of less than 1.1 and 2.5 to 3.5.Whereas, in the group without ARM the survival was higher than predicted only in the first and very high range. Below for the rest.

Table 5: Survival prediction according to LIS in both groups.

LIS ranks and predicted survival	Groups					
	Without MRA			With MRA		
	№	Live	%	№	Live	%
Less than 1.1 (Greater than 66%)	27	21	77.7	27	24	**88.8**
Between 1.1 and 2.4 (Survival of 59%)	57	23	40.3	51	29	56.8
Between 2.5 and 3.5 (Survival of 30%)	13	2	15.3	23	9	**39.1**
Total	97	46	47.4	101	62	61.4

Table 6 shows the mortality in both groups in relation to that predicted by the Berlin settlement [13] In the historical series, mortality was higher than predicted in all ranges, while in the study group, in the worse prognosis range, mortality was 36.4%, lower than the prognosis.

Table 7 shows that the average number of MAV days for patients in the historical series was 6.81 and for the study group was 6.79, while the mean ICU days were 8.92 for the control and 9.43 for the ICU. Which received the ARM, and there were no significant differences.

Figure 2 shows the mortality in both groups, which was significantly lower in the ARM group (38.6%) than in the control group, which was 52.6%.

Table 6: Prognosis of mortality as defined by Berlin in both groups.

Mortality as defined by Berlin	Groups					
	Without MRA			With MRA		
	№	Deceased	%	№	Deceased	%
Light (24-30%)	12	7	58.3	14	6	42.8
Moderate (33-36%)	39	28	71.8	40	19	47.5
Severe (40-49%)	12	9	75.0	11	4	**36.4**
Total	63	44	69.8	65	29	44.6

Table 7: Ventilatory and ICU stay in the study groups.

Ventilatory and ICU stay	Groups	Mean	Valor de p
Days with VMA	GC	6.81	p = 0.981
	GE	6.79	
Stay in UCI	GC	8.93	p = 0.667
	GE	9.44	

Figure 2: Mortality by groups p = 0,049.

The number of patients without complications was higher in the group that received ARM (70.3%) compared to the historical series (53.6%). The most frequent complication in both groups was NAV, followed by atelectasis, but both were less frequent in patients with ARM than in the historical series as reflected in Table 8.

Table 8: Distribution of patients according to the complications of MAV in the study groups.

Complications Of the MAV	Without MRA		With MRA		Total
	№	%	№	%	
Without complications	60	61.8	83	82.2	123
NAV	21	21.6	10	9.9	56
NAV + Atelectasis	9	9.3	4	3.9	13
Atelectasis	5	5.2	1	1.0	13
Other	2	2.1	3	3.0	6
Total	97	100	101	100	198

Mann-Whitney U-test = 4075.500 p = 0.017.

In this study, 72 patients (71.29%) had no complications attributable to ARM. Among the complications described, the most frequent was transient hypotension in 25 patients (20.79%), followed by episodes of desaturation in 6 (5.94%) (Figure 3). Only one pneumothorax was present in a patient with pneumonia of possible staphylococcal etiology.

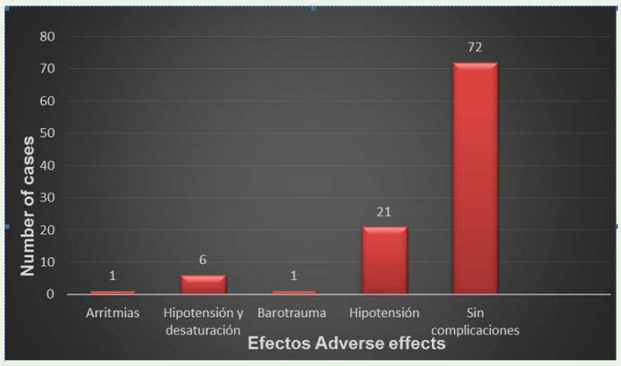

Figure 3: Adverse effects attributable to ARM.

Discussion

Age was considered as a poor prognostic factor in ventilated patients, [14-18] in the study group the average ages was higher relative to the historical series, but without significance according to the T test for the equality of averages (p .058), something similar occurred with the individual APACHE II score, which implies a higher mortality in this group. Mortality predicted and adjusted for APACHE II, which are used as prognostic indices in critical patients [19], was similar in both groups. These data confirm that according to the age and prognosis of mortality by APACHE II the groups are homogeneous.

Patients from both groups were similarly ventilated and there were no significant differences (p. 937, U Mann-Whitney Test). The most frequent cause for both groups was ARDS, with no significant difference in relation to type Of ARDS, which is important, as it is known that extrapulmonary ARDSs have a higher recruitment potential than pulmonary ones, where condensed areas are more difficult to expand with ARM.

In epidemiological studies, it was demonstrated that after nosocomial infections and the administration of hemotherapy and fluid therapy, MAV is the main cause of ARDS in the in-hospital setting and is avoided with the use of a ventilatory strategy to keep the lung open [20] . The ARMs were used in patients with healthy lungs who required MAV, such as: postoperative patients with neuromuscular diseases, in whom, as in patients receiving general anesthesia, the reflex of the sigh is lost with Decreased compliance and the appearing of atelectasis, effects that can be reversed with the use of ARM [21-24].

Pulmonary edema and end-expiratory alveolar collapse characterize the main causes of respiratory failure in patients receiving MAV in this study (ARDS and PAD); in these situations the PV strategy was associated with ARM and the use of adequate PEEP values with the aim of improving oxygenation and reducing lung injury associated with the respiratory failure.

A total of 11 patients hospitalized in the ICU ventilated after major surgeries received MRA, which is beneficial according to some authors [22,25,26].

According to the LIS values [12], both groups are similar, but the number of patients in the range of higher severity is higher in the study group, so, the expected survival for this group would be lower.

In the range of more than 3.5, with the worst prognosis of survival, no patient of both groups appears, this is because the parameters for this scale were taken at the beginning of the ventilation and therefore it is not excluded the possibility that at a certain point in their evolution they will reach it.

The greater survival rate achieved in patients in the 2.5 to 3.5 range of the ISL scale in the group that received the ARMs suggests that they contribute to the improvement of this indicator.

Mortality was higher than predicted for all intervals of the APACHE II scale in the non-ARM group, while in the receiving group, mortality was reduced in relation to prognosis at several intervals. In the range of 20 to 24 points where the expected mortality is 40%, it was halved by 20%. In patients with scores above 34, where the largest number of patients is included and the expected mortality exceeds 88%, the actual mortality was 45.4%. These results confirm that for these ranges of APACHE II there was dependence between the application of the maneuver and the reduction of mortality.

The definition of ARDS proposed by the Berlin conference established a mortality forecast depending on the classification of severity [13]. When the mortality of the studied groups is compared to the one predicted by this scale, it can be seen that the mortality of the group without ARM was higher than the one predicted in the three grades of the same, whereas in the group with ARM was inferior to the one predicted in the severe degree, that is the one of worse prognosis. The increase in mortality in the remaining intervals in the ARM group could be related to the differences in the inclusion criteria, since it is known that for the definition of Berlin a large number of patients (4188) were considered 518 in which PEEP was not used, but not in the current study, where both groups included patients without PEEP because of hemodynamic disorders.

In a large international, multicenter observational study carried out for 4 weeks in a row, in the winter of 2014, in a sample of 459 ICUs from 50 countries on 5 continents, hospital mortality was found to be 46.1% for severe ARDS [27] according to the Berlin conference, which is in the range of predicted, But higher than what obtained in the group that received ARM from this study (36.4%).

There are numerous proposed uses for prognostic assessment systems in critical patients, one of which is to homogenize the severity of the disease in groups of patients undergoing clinical investigations and another is to evaluate the effects of a new procedure. This study used a widely used scale for critical patients such as APACHE II and two more specific prognostic indices for patients with MAV (LIS and Berlin definition). In relation to the first utility, the values obtained for the APACHE II score, the LIS index and the Berlin definition for ARDS cases confirm that the control group and the study are homogeneous. Regarding the second use, depending on the accuracy of the model (expressed in terms of calibration and discrimination), the reliability and validity of the system used, mortality and survival of the patients in the MRA group was better to that predicted by the scales applied.

The MAV days and the stay are two parameters that evaluate the effectiveness of any procedure in the patients that are treated in ICU, both variables were similar in the studied groups, which coincides with the results of the systematic review and meta-analysis published by Suzumura EA, et al. [28].

The analysis of the behavior of the average of ventilation days and the ICU stay in the deceased and alive in each group showed that, without significant differences, the patients who survived the averages were inferior in the study group in relation to the control group , Whereas in the deceased the opposite happened. These results are explained by the positive effects of ARMs on oxygenation parameters, ventilatory mechanics and decreased MAV complications. The author considers it advisable to carry out studies with a greater number of cases and to perform subgroup analyzes, separating living and deceased patients to have a better evaluation of these two variables. Mortality in the study groups was significantly lower than that of the historical series and lower than that reported by Caballero in the two national surveys on mechanical ventilation in Cuba, the first with 52.5% in 2005 and the second with 51.7% in 2010 [29]; It is also smaller than reported by a study conducted in the province of Mayabeque in Cuba, which was 58% [30].

Three meta-analyzes published on the effects of ARMs concluded that most studies evaluated oxygenation rates, respiratory mechanics and side effects, but very few analyzed mortality and assessed ones, no differences were reported Significant at 28 days, [9-11] which differs from the results found in this study, where with ARM mortality was reduced by 14% (52.6 control group to 38.6 study group).

The few studies evaluating mortality with the use of ARM in ARDS patients report very varied rates; this may be related to the fact that the maneuver variants used are also very different. The analysis of mortality in patients with ARDS from the study groups showed a decrease of 25.2% (69.8% historical series to 44.6% study group, see table 6 total), reduction is above 6% reported by a systematic review published in 2014 [28]. The mortality rate of patients in this study is within the range reported by recent studies for patients with ARDS ranging from 33 to 52% [31-33].

Gómez Cortés LA, et al. point out that mortality in ventilated patients is closed to 50% around 50 years and greater than 80% after 80 years, then the decrease in mortality to 38.6% in the group is significant in the group receiving ARMs, where the average age was 58.4 [16].

Mols G, et al. report that the indicators for assessing alveolar recruitment are grouped into four categories: pulmonary function, which evaluates gas exchange; pulmonary mechanics; lung volumes and imaging techniques [34]. Most MRA studies are focused on the evaluation of these indicators, which are not sufficient to validate their daily use in medical practice, whereas days of ventilation, ICU stay and more sensitive mortality are less evaluated. This study, which has as limitation the size of the sample, which was performed in a single hospital at secondary level and that the control group consisted of a historical series showed a significant decrease in mortality.

PEEP is used in all patients with pulmonary edema because of its oxygenation benefits. Adequate selection of its value allows the avoidance of alveolar disrelation and serves as a starting point for the selection of the PEEP levels to be used in the realization of some variants of ARM, with which it is possible to individualize the values of this for each patient and avoid the negative consequences derived from rigid protocols. The average PEEP value used in this study was 13.5 cm H_2O. With a minimum of 8 and maximum of 28 cm H_2O. The average number of maneuvers performed by patients was 13, with a minimum of 2 and a maximum of 32.

Ventilation with positive pressure generates tension in the boundaries between the aerated and non-aerated lung areas, which characterize the diseased lungs, which, together with cyclic opening and closure during inspiration and expiration, produce epithelial and endothelial damage, cellular inflammation and release of cytokines that cause more injures to the lung, this is avoided if alveolar opening is achieved with ARMs and maintained with adequate PEEP. The ventilatory strategy applied to the patients included in this study was designed with this objective, which was achieved, since the decrease in complications in the experimental group was significant. The most frequent complication in both groups was PAV, but in the group with ARM its incidence was lower than that reported by other authors [35,15].

Barotraumas, hemodynamic disorders, episodes of desaturation, bacterial translocation and increased intracranial pressure are adverse effects caused by ARM [36]. In this study, 72 patients had no complications attributable to this procedure. Transient hypotension was the most frequent, followed by the episodes of desaturation. These two complications appeared in patients with hypovolemia who presented hemodynamic disorders at some point in their evolution; in all cases their recovery was immediate after suspending or concluding the maneuver.

The low incidence of barotrauma is related to the fact that levels of transpulmonary pressure, peak inspiratory pressure and PEEP used were not as high as in other studies [37,38].

The maneuver performed corresponds to the current trend of the experimental work that is to perform the MRA in a slower and more progressive way, raising the pressure through several steps or in the form of a ramp until reaching the objective, which offers better results and Lower hemodynamic involvement [39].

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