0021-7557/00/76-05/349
Jornal de Pediatria

ORIGINAL ARTICLE

High frequency oscillation ventilation compared to conventional mechanical ventilation plus exogenous surfactant replacement in rabbits

Jefferson Piva[1], Phornlert Chatrkaw[2], Karen Choong[3], Helena Frndova[4], Peter Cox[5]

Abstract

Objectives: (a) to evaluate the effect on oxygenation and ventilation of rabbits with induced surfactant depletion when they are submitted to a conventional mechanical ventilation, plus a small dose of exogenous surfactant; (b) to compare this group with another group submitted to a High Frequency Oscillation (HFO) without exogenous surfactant administration.

Methods: twenty New Zealand White rabbits weighing (± 3 kg) were anaesthetized and artificially induced to a endogenous surfactant depletion by successively lung lavage with normal saline (aliquots of 25 ml/kg) until to reach a persistent PaO_2 less than 100 mmHg when submitted to a mechanical ventilation in a pressure control mode with a target tidal volume of 10ml/kg, PEEP of 5cm H_2O, FiO_2 1.0, respiratory rate 30/min, and inspiratory time of 0.65 s. Then the rabbits were divided in (a) CMV+S group, submitted to a conventional mechanical ventilation plus exogenous surfactant replacement; (b) HFO group, submitted to a High Frequency Oscillation Ventilation. Arterial blood gases were measured at control period, post lung lavage, 15, 16 and 120 minutes after treatment started. The groups were compared using Student t test.

Results: the post lung lavage PaO_2 in both groups was lower than 50mmHg (p=0.154), increasing after 15 min of treatment to 254 mmHg (CMV+S) and 288 mmHg (HFO, p=0.626). The PaO_2 at 60 and 120 minutes were higher (p=0.001) in the HFO group (431 e 431 mmHg) when compared with the CMV+S group, which showed a progressive fall (148 e 126 mmHg). At 60 minutes of treatment, the $PaCO_2$ was lower (p=0.008) in the CMV+S group (29 versus 41 mmHg).

Conclusions: in ARDS animal model a protect mechanical ventilation strategy as HFO by itself promotes a fast and persistent increase in the oxygenation, with superior levels than those observed in animals treated with conventional mechanical ventilation plus exogenous surfactant replacement.

J Pediatr (Rio J) 2000; 76(5): 349-56: surface-active agents, artificial respiration, hypoxemia, respiratory insufficiency.

Introduction

In acute respiratory distress syndrome (ARDS) pulmonary involvement is not homogeneous; in some areas, compliance is reduced, whereas in others it is nnearly normal.[1,2] As a consequence, there is a progressive decrease in pulmonary volume, which causes lungs with ARDS to be frequently described as "small," an expression that replaces the older expression "stiff lungs".[3] Although mechanical ventilation is necessary to maintain life in patients with ARDS, the specific method or the ideal ventilation pattern have yet to be defined. Depending on the adopted ventilation pattern, it may lead to progressive pulmonary lesions. The technique used to ventilate "low compliance" areas may not be adequate to ventilate "normal compliance" areas, possibly causing ventilator-induced lung injury (VILI).[2-6]

1. Professor
2. Graduate student, Medical Research.
3. Graduate Student, Clinical Practice.
4. Biomedical engineer.
5. Clinical Director, Department of Critical Care Medicine (Pediatric Intensive Care), Hospital for Sick Children and School of Medicine of The University of Toronto.

Ventilator-induced lung injury in ARDS has been associated with: a) *barotrauma*, when the excessive pressure used during mechanical ventilation causes air leaks (pneumothorax, interstitial emphysema, pneumomediastinum, ...); b) *volutrauma*, when the tidal volume administered preferably distends areas of normal or increased compliance, occasioning stretching and tissue rupture, followed by capillary overflowing, alveolar edema, abnormalities in the production and distribution of surfactant; c) *atelectrauma*, a lesion related to the opening and closing (collapse and distension) of the alveolar units. In this case, lungs are ventilated by using low tidal volumes, inferior to the inflexion point of the volume pressure curve, and/or the final pressure of expiration is not able to maintain terminal airways and alveoli open, leading to progressive pulmonary collapse; to reopen these units a higher pressure will be necessary; d) *biotrauma*, when mechanical ventilation causes collapse, stretching, or pulmonary tissue rupture leading to cellular injury with increase of local inflammatory mediators (cytokines, oxygen free radicals, etc.).[2,4-7]

During the past three years, several studies showed the importance of using of mechanical ventilation protectiVE techniques in patients with ARDS, reducing the incidence of VILI and influencing survival.[8,9]

In addition, in patients with ARDS surfactant dysfunction promotes instability of alveolar units, favoring repetivie colapse and reexpansion.[3,5,6,10] Protective ventilation in this situation is based on increasing pulmonary expiratory volume (for example, increasing positive-end expiratory pressure, PEEP) in order to prevent alveolar collapse, as well as on using low tidal volumes to prevent alveolar hyperinsufflaction (distension). Strategies involving recruiting maneuvers, maintaining pulmonary volume by using PEEP, surfactant-associated use, liquid ventilation, or ventilation by oscillation with an airway pressure superior to that used in conventional ventilation may reduce VILI, promote a more physiological alveolar insufflaction, and reduce pulmonary infflamation.[2,5,7-9,11-15]

High frequency oscillation (HFO) ventilation was developed about 50 years ago and is based on the use of tiny tidal volumes with constant mean airway pressure, and thus avoiding extreme pulmonary volumes (both low and elevated).[13,16-18] Several investigators were able to demonstrate in different animal models that HFO may protect lungs from induced lesion when compared to conventional ventilation.[11,17,19,20] Although clinical studies with humans are still controversial, HFO is being recognized as an efficient alternative for children and newborns with respiratory insufficiency. Clinical studies have suggested that HFO could be associated with a smaller incidence of conventional VILI.[5,13,16,18,21]

In animals with ARDS, VILI was avoided when exogenous surfactant associated with a PEEP of 4 cmH_2O was administered.[11,14,15,22,23] However, the use of exogenous surfactant in clinical series of patients with ARDS presented controversial results.[18,24,25] This may be attributed to the following factors: a) type and origin of the surfactant used; b) method of surfactant administration; c) dose and stage of disease in which the surfactant was administered; d) presence of inhibitor proteins on the terminal airway; and d) ventilator strategy used concomitantly with surfactant administration.[14,15,24,26]

Alveolar surfactant is found in two different structural forms: a) large aggregates (active); and b) small aggregates (inactive).[14,15,24,27] Exogenous surfactant consists basically of large aggregates. Once deposited in the lung, the exogenous surfactant may be converted into its active form. Studies demonstrate that using small tidal volumes during mechanical ventilation is one of the best ways to preserve endogenous surfactant.[12,14,15,17] On the other hand, the use of large tidal volumes was associated with a higher rate of conversion from the large aggregates form (active) into the small aggregates form (inactive).[14,15,24,27]

Our objective in this study was: a) to evaluate oxygenation and ventilation in rabbits in a situation of artificial surfactant depletion when submitted to conventional mechanical ventilation, using a tidal volume of 10 ml/kg and PEEP of 5 cmH_2O associated with partial exogenous surfactant replacement; b) to compare the evolution of this group with that of another group submitted to HFO ventilation without surfactant replacement.

Methods

The present study followed the guidelines of the National Institute of Health for use of experimental animals (Canada). The study was approved by the Institutional Animal Care and Use Committee (Canada).

Twenty New Zealand white rabbits, weighing approximately 3 kg each were pre-medicated with acepromazine (0.5mg/kg, intramuscular) and anaesthetized with sodium pentobarbital (10-20mg/kg, intravenous). A peripheral venous access was created for fluid infusion and an arterial line was inserted in the auricular artery for continuous hemodynamic monitoring (Hewlett-Packard pressure transducer model 1280). It also allowed seriate blood collections for arterial gasometry (Radiometer ABL 3300). An endotracheal tube with a diameter of 3.5 mm or 4,0 mm was inserted through a tracheostomy. Anesthesia and muscular paralysis were achieved through continuous infusion with pentobarbital (6mg/kg/h) and pancuronium (0.2mg/kg/h). Hydric maintenance was 7 ml/kg/hour, with a saline solution (NaCl at 0.9%) to which glucose at 5% was added. Hemoglobin saturation was continuouslly monitored (Nellcor) and body temperature was monitored and kept constant (between 38 and 39 degrees Celsius) with the use of a heat irradiating source and thermal blankets. Tidal volume was controlled through a monitor (thermistor

pneumotachograph - BEAR NVM-1, BEAR medical Systems, Riverside, CA) with reduced dead space (1.3 ml), inserted between the tracheal tube and the respirator circuit.

Intervention: Immediately after tracheostomy the animals were ventilated in the controlled pressure mode so as to achieve a tidal volume of 10ml/kg, with PEEP of 0cm H_2O, 100% of FiO_2, respiratory frequency of 30 ventilations a minute, and inspiratory time of 0.65 seconds. (Humming V, Senko Medical Instruments, Tokyo, Japan). The animals were kept in this regimen for a period of 30 minutes (control). Later, endogenous surfactant depletion was artificially induced by successive lung lavages (aliquots of 25 ml/kg) with heated saline solution, administered through the tracheal tube. Concomitantly, the animals' thorax was gently massaged for a better distribution of the fluid inside the lungs. As soon as a marked fall was observed in arterial pressure, cardiac frequency, or hemoglobin saturation, the liquid infused in the lungs was aspirated. The maneuver was repeated (usually from 4 to 6 times) until reaching a hemoglobin saturation inferior to 90% and a PaO_2 smaller than 100 mmHg with a FiO_2 of 100%, PEEP of 5 cmH_2O; respiratory frequency of 30 mpm, inspiratory time of 0.65 seconds and peak of inspiratory pressure (PIP) required to reach a tidal volume of 10 ml/kg.

Depending on the ventilation strategy to be adopted, the animals were divided in two main groups: A) Conventional ventilation associated with partial exogenous surfactant replacement (CMV+S); B) HFO ventilation. In each group, some animals received slightly different treatments, related to other associated experiments. Consequently, there were four different subgroups:

A) Conventional ventilation associated with partial exogenous surfactant replacement (CMV+S): eight rabbits were submitted to conventional mechanical ventilation with the following parameters: FiO_2 of 1.0; PEEP of 5 cmH_2O; respiratory frequency of 30 mpm; inspiratory time of 0.65 seconds and PIP needed to obtain a tidal volume of 10 ml/kg. These parameters were set before the administration of exogenous surfactant and remained unchanged during the entire period of study. According to the surfactant regimen used, the rabbits were placed in one of two groups:

A1) CMV+Sa: conventional ventilation associated with partial exogenous surfactant replacement. Four rabbits (mean weight: 2.99±0.10 kg) received bovine surfactant extract (27 mg/ml) in a dose of 1 ml/kg immediately after ventilation parameters were reached and set.

A2) CMV+Sd: conventional ventilation associated with partial exogenous surfactant replacement and with Dextran. Four rabbits (mean weight: 3.00±0.14 kg) received bovine surfactant extract (27 mg/ml) in a dose of 1 ml/kg associated with 2 ml of Dextran (molecule weight: 70,000) at a concentration of 50mg/ml. Dextran was associated in order to investigate the possibility of increase in surfactant activity, as demonstrated in some *in vitro* studies.[28,29] Bovine surfactant extract and dextram were administered only after conventional mechanical ventilation parameters were reached and set.

B) HFO ventilation without exogenous surfactant administration. Depending on the respiratory frequency used, the 12 rabbits in this group were divided into two subgroups:

B1) HFO_{15} - oscillation ventilation with 15 Hz frequency, used in six rabbits (mean weight: 3.03±015 Kg), with mean airways pressure (MAP) of 15 cmH_2O, inspiratory time of 33%, 100% FiO_2. Amplitude and power were adjusted so that pCO_2 was kept around 40 mmHg.

B2) HFO_5 - oscillation ventilation with 5 Hz of frequency, used in six rabbits (mean weight of 2.93 +0.22 kg), with mean airway pressure (MAP) of 15 cmH_2O, inspiratory time of 33%, 100% FiO_2. Amplitude and power were adjusted so that pCO_2 was kept around 40 mmHg.

Evaluations: arterial gasometries were collected at five distinct moments: prior to lung lavage (control), after lung lavage, 15, 60, and 120 minutes after the treatment was initiated. The two main groups (CMV+S versus HFO) and the four subgroups (CMV+Sa, CMV+Sd, HFO_{15}, HFO_5) were evaluated and compared, based on their differences concerning paO_2, pH, PCO_2, oxygenation rate [(FiO_2 x MAP / PaO_2) x 100], and mean arterial pressure in these five observation moments.

Continuous data were expressed as means and standard deviation (SD). The means of the two main groups (HFO vs. CMV+S) were compared by using Student's t test, while the one way ANOVA was used to compare the means of each variable in the four subgroups (CMV+Sa, CMV+Sd, HFO_{15}, and HFO_5). A P value of less than 0.05 was considered as significant.

Results

During the control period (pre-lavage), the four subgroups did not present any difference concerning mean weight of the rabbits or number of lung lavages. Mean PaO_2, $PaCO_2$, and pH in the four subgroups were also similar (one way ANOVA) before the lung lavage. Similar results were also observed during the other four evaluations (post-lung lavage, 15, 60, and 120 minutes post-treatment) when we compared the four subgroups (CMV+Sa, CMV+Sd, HFO_{15}, and HFO_5) using one way ANOVA, and when the two main groups were compared (HFO and CMV+S, Student's t test). Thus, for practical reasons, the results of this study will be presented (Table 1) for the two main groups: HFO (HFO_{15} plus HFO_5) and CMV+S (CMV+Sa plus CMV+Sd).

After lung lavage, mean PaO_2, in the group submitted to conventional ventilation associated with surfactant replacement (CMV+S), was 43.6±9.9 mmHg. This was not statistically different (P=0.154) from the result obtained in rabbits submitted HFO ventilation (50.7±10.9 mmHg). After 15 minutes of treatment, we observed an important increase in mean PaO_2 in both groups. Mean PaO_2 at 15 minutes in rabbits in the CMV+S froup increased to 254.2±107.7 mmHg, while in the HFO group, it reached 288.5±173.6 mmHg, without statistical difference (P=0.626). However, after 1 and 2 hours of treatment (Figure 1, Table 1), the HFO group presented rather elevated PaO_2 values (431.8±65.4 mmHg and 431.4±72.4 mmHg, respectively) when compared to the CMV+S group (148.8±101.6 mmHg and 126.1±88.1 mmHg, respectively) (P<0.001).

We did not observe any difference in oxygenation rates between the two groups after lung lavage (P=0.166) and after 15 minutes (P=0.187). However, after 60 and 120 minutes (Figure 2, Table 1), the oxygenation rate in the group submitted to HFO ventilation was smaller (3.6±0.6 and 3.4±0.8; respectively) when compared (P<0.001) to the rabbits receiving CMV+S (10.3±6.1; 12.3±3.4; respectively).

After lung lavage, mean airway pressure (MAP) was similar in both groups (P=0.980). However, at 15, 60, and 120 minutes after being allocated for HFO or CMV+S, we observed that the CMV+S group presented a significantly smaller MAP (P<0.001) than the HFO group (Table 1 and Figure 3).

In the post-lung lavage period, we did not observe any differences between the two groups in $PaCO_2$ levels (P=0.508). However, after 1 hour (Table 1, Figure 4) the groups submitted to CMS+S presented a significantly smaller (P=0.008) mean $PaCO_2$ (29.0±5.4 mmHg) than the rabbits submitted to HFO (41.5±12.6 mmHg).

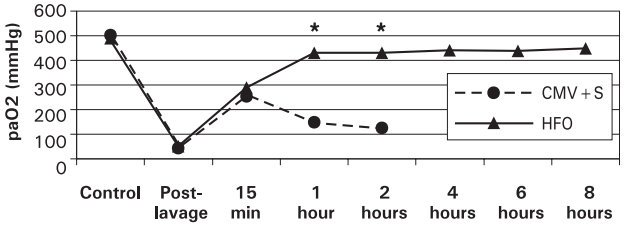

Figure 1 - PaO_2 evolution in the first five moments of the study: (1) control (pre-lavage); (2) post-lav (post-lung lavage); (3) 15 min, (4) 1 hr, (5) 2 hr of having been allocated to one of the two main groups (CMV+S: conventional mechanical ventilation plus partial surfactant replacement or HFO: high frequency oscillation ventilation); * P<0.001

Table 1 - Evolution of PaO_2, $PaCO_2$, oxygenation rate, mean airway pressure, mean arterial pressure, and pH during at four moments in two groups of rabbits: CMV+S (conventional mechanical ventilation associated with partial bovine surfactant replacement) and HFO (5 and 15 Hz high frequency oscillation ventilation)

	CMV+S (n=8)	HFO (n=12)	P
PaO_2 (mmHg)			
Pós lavagem pulmonar	43,6 ±9,9	50,7 ±11,0	0,154
15 min	254,2 ±107,7	288,5 ±173,6	0,626
60 min	148,8 ±101,6	431,8 ±65,4	<0,001
120 min	126,1 ±88,1	431,4 ±72,4	<0,001
PaO_2 (mmHg)			
Post-lung lavage	43.6±9.9	50.7±11.0	0.154
15 min	254.2±107.7	288.5±173.6	0.626
60 min	148.8±101.6	431.8±65.4	<0.001
120 min	126.1±88.1	431.4±72.4	<0.001
$PaCO_2$ (mmHg)			
Post-lung lavage	35.6±5.9	37.5±6.3	0.508
15 min	28.3±7.5	40.7±19.1	0.101
60 min	29.0±5.4	41.5±12.6	0.008
120 min	36.9±14.0	37.4±6.0	0.925
Oxygenation rate			
Post-lung lavage	26.8±6.9	22.9±6.9	0.166
15 min	5.0±2.7	8.3±6.4	0.187
60 min	10.3±6.1	3.6±0.6	0.001
120 min	12.3±3.4	3.4±0.8	<0.001
Mean airways pressure (cmH_2O)			
Post-lung lavage	11.1±0.4	11.1±0.9	0.980
15 min	10.4±0.7	15.00±0.0	<0.001
60 min	10.3±0.9	15.4±1.2	<0.001
120 min	10.4±0.9	15.0±0.1	<0.001
Mean Arterial Pressure (mmHg)			
Post-lung lavage	70.4±18.5	74.6±13.5	0.615
15 min	67.0±19.6	73.5±16.8	0.477
60 min	55.6±11.1	71.8±18. 5	0.026
120 min	56.4±14.8	67.4±19.8	0.172
pH			
Post-lung lavage	7.37±0.06	7.40±0.05	0.303
15 min	7.46±0.04	7.43±0.16	0.672
60 min	7.41±0.03	7.38±0.09	0.325
120 min	7.36±0.09	7.39±0.06	0.420

Student's t test.

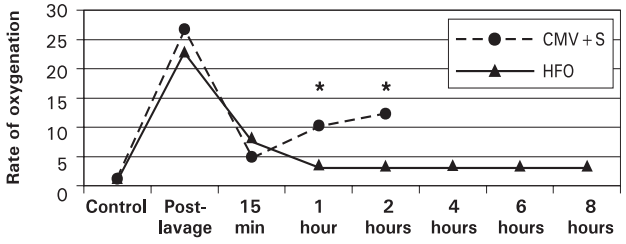

Figure 2 - Evolution of the oxygenation rate in the five moments of the study: (1) control (pre-lavage); (2) post-lav (post-lung lavage); (3) 15 min, (4) 1 hr, (5) 2 hrs of having been allocated to one of the two main groups (CMV+S: conventional mechanical ventilation plus partial surfactant replacement or HFO: high frequency oscillation ventilation); * P<0.001

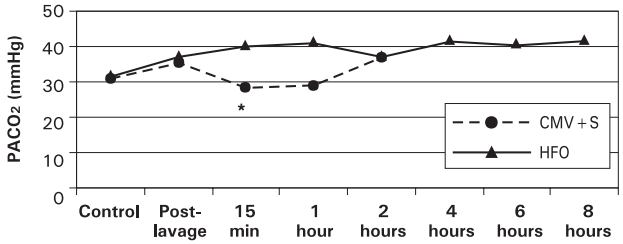

Figure 4 - Evolution of $PaCO_2$ in the five moments study: (1) control (pre-lavage); (2) post-lav (post-lung lavage); (3) 15 min, (4) 1 hr, (5) 2 hrs of having been allocated to one of the two main groups (CMV+S: conventional mechanical ventilation plus partial surfactant replacement or HFO: high frequency oscillation ventilation); * P<0.01

After 1 hour of treatment, the rabbits in the CMV+S group presented mean blood pressures of 55.6±11.1mmHg, which were significantly smaller (P=0.026) than the blood pressure levels presented by the HFO group (71.8±18.5mmHg). During the other observation periods we did not find any statistical differences between the groups concerning this parameter (Table 1, Figure 5).

During the five observation moments, we did not observe any differences when the blood pH in the two groups were compared (Table 1).

Discussion

In this study, involving rabbits who suffered induced surfactant depletion and were later submitted to two different treatment strategies, it was possible to demonstrate: (a) that the use of a non-protective ventilation strategy associated with surfactant replacement promoted an immediate increase (15 min) in oxygenation. This effect, however, was quickly and progressively dissipated during the next 120 minutes; (b) that the use of a protective ventilation strategy (HFO), even if not associated with surfactant replacement, promoted

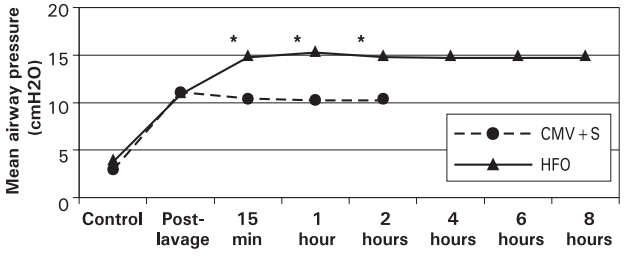

Figure 3 - Evolution of MAP - Mean Airway Pressure in the five moments of study: (1) control (pre-lavage); (2) post-lav (post-lung lavage); (3) 15 min, (4) 1 hr, (5) 2 hrs of having been allocated to one of the two main groups (CMV+S: conventional mechanical ventilation plus partial surfactant replacement or HFO: high frequency oscillation ventilation); * P<0.001

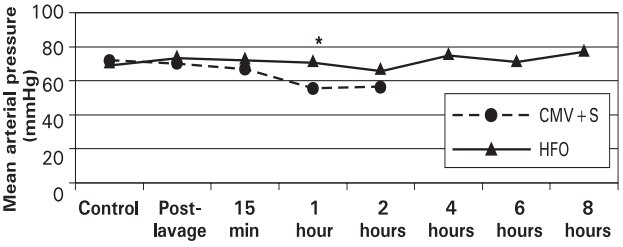

Figure 5 - Evolution of Mean Arterial Pressure in the five moments study: (1) control (pre-lavage); (2) post-lav (post-lung lavage); (3) 15 min, (4) 1 hr, (5) 2 hrs of having been allocated to one of the two main groups (CMV+S: conventional mechanical ventilation plus partial surfactant replacement or HFO: high frequency oscillation ventilation); * p<0,03

a quick (15min) and persistent (60 and 120 minutes) increase in oxygenation, at superior levels than those obtained in animals submitted to conventional mechanical ventilation (non-protective) associated with surfactant replacement during the two-hour observation.

Before discussing these results, some details of this experiment must be considered.

Definition of surfactant dose used: the estimated dose to replace the entire surfactant store in the lung is around 100 mg/kg.[24,27] Similar studies with animals employed a dose ranging from 50 to 100 mg/kg .[14,15-26] In good conditions the half-life of exogenous surfactant is estimated to be 5 hours.[24,27] However, depending on the preparation used, administration method, disease course, presence of inhibitors, and on the ventilation strategy used, the half-life of exogenous surfactant may be significantly reduced.[3,10,12,14,15,23] Thus, we opted to use what is considered to be the smallest effective dose of surfactant (27 mg/kg), obtained through previous studies in our laboratory. When analyzing our data, it is possible to observe that 15 minutes after surfactant administration there was a significant increase in PaO_2 (from 43.6 to 254.2 mmHg). There was also an increase in the oxygenation rate (from 26.8 to 4.96), demonstrating that the dose administered, although small, was effective. In addition, the choice of a minimal effective dose makes more evident the effect of conventional ventilation on the activity of the exogenous surfactant administered. If this form of ventilation is protective, or if it acts in synergy with the surfactant, its effect on oxygenation could be maintained for a long period. On the other hand, if the ventilation acts as inhibitor, the effect on oxygenation would be quickly lost.

Why did a subgroup receive Dextram associated with surfactant? There are in vitro studies demonstrating that dextram, in addition to presenting a protective effect, could optimize surfactant action.[28,29] Some of the animals in our experiment also belonged to this parallel study whose aim was to evaluate this possibility in vivo. However, since both subgroups (isolated surfactant and surfactant associated with dextram) in this study presented the same behavior, we decided to consider them as a single group.

Why was a more elevated PEEP not used? Previous results with the same animal model showed that applying a PEEP above 9 cmH_2O resulted in ta 100% mortality rate 1.5 h after the surfactant was administered. On the other hand, the use of a PEEP around 5 cmH_2O proved effective, safe, and produced a longer effect on oxygenation.[10,12,23,30]

At 15 minutes, oxygenation was similar in both the group of rabbits submitted to conventional ventilation (non-protective) associated with surfactant administration, and the rabbits submitted to HFO ventilation. Parallel to this effect, it is important to stress the marked fall in $PaCO_2$ (increase in the minute volume) in the group receiving surfactant. Since the respirator parameters were set (respiratory frequency and inspiratory pressure), we imagine that after surfactant administration, previously collapsed areas were ventilated again, contributing to the increase verified in minute volume. However, at 60 and 120 minutes, when respirator parameters had not yet been modified, there was an increase in $PaCO_2$ in the group receiving surfactant in association with a progressive diminution of PaO_2. Following this reasoning, it is possible to speculate that at this point a progressive decrease in exchage surface area occurred, probably due to a progressive collapse of alveolar units.

In ARDS, the progressive pulmonary collapse during mechanical ventilation has been associated with a) the use of insufficient PEEP, allowing a reduction of alveolar volume at the end of expiration (*atelectrauma*); b) the use of high tidal volumes leading to alveolar hyperdistension (*volutrauma*), distension of the alveolar tissue with local inflammatory process (*biotrauma*), and surfactant progressive inactivation.[2-6,10,23]

Since we opted to use PEEP levels that are considered to be adequate and protective in this animal model,[10,12,23,30] we believe that the progressive pulmonary collapse is mainly a consequence of *volutrauma* and *biotrauma*.[2-4] In these two types of mechanical ventilation induced lesion, the elevated tidal volume (in this case 10 ml/kg), is the main causative agent.[2-4,10] The iatrogenic power of elevated tidal volume as inductor of pulmonary lesions was so marked and fast in our study, that it neutralized the benefits obtained with surfactant replacement within less than 60 minutes.

On the other hand, the use of a non-conventional ventilation technique (HFO), based on extremely low tidal volumes administered at high respiratory frequencies (5 and 15 Hz), allowed immediate elevation in oxygenation, which was maintained throughout the 2-hour experiment. In this experiment with rabbits surfactant-depleted rabbist, it should be stressed that already in the 1st hour, HFO ventilation proved to be more efficient to improve oxygenation than the use of surfactant associated with conventional ventilation. Although it is not part of our objectives, it is interesting to note that the improvement in oxygenation remained unaltered until the 6th hour of observation (Figure 1), when the evaluation was interrupted (data from another experiment not shown here).

HFO ventilation has yielded consistent results in laboratory animals with induced ARDS.[11,17,20,31] HFO benefits in ARDS could be attributed to two factors: the maintenance of a constant airway pressure and the use of very small tidal volumes.[11,17,20,31] The main advantage of these two factors is that they prevent progressive pulmonary collapse (since alveolar stability is maintained) and great oscillations in alveolar volume (collapse and reexpansion), saving surfactant and diminishing local inflammation.[2,5,6,11,13,18,20,21,31]

Differently from hyaline membrane disease, ARDS is a multifactorial disease in which surfactant deficiency is only one among multiple aspects.[1,2,24,25] Therefore, the best treatment plan must be based on a set of actions that take advantage of the benefic possibilities of each of individual action. It has been extensively demonstrated that the use of protective mechanical ventilation in patients with ARDS reduces the incidence of pulmonary injury induced by mechanical ventilation, and significantly increases survival.[8,9] From this perspective, HFO ventilation seems to adequately fulfill the required safety and effectiveness criteria, and to be an excellent treatment alternative.

References

1. Piva JP, Garcia PC, Carvalho PR, Luchese S. Síndrome do desconforto (angústia) respiratório agudo (SDRA/SARA). In: Piva J, Carvalho P, Garcia PC, eds. Terapia Intensiva em Pediatria. 4th ed. Rio de Janeiro: Medsi; 1997. p.176-96.
2. Slutzky AS. Lung injury caused by mechanical ventilation. Chest 1999; 116:9S-15S.
3. Hudson LD. Progress in understanding ventilator-induced lung injury. JAMA 1999;282:77-8.
4. Ranieri VM, Slutzky AS. Respiratory physiology and acute lung injury: the miracle of lazarus. Intesive Care Medicine 1999; 25: 1040-3.
5. Clark RH, Slutsky AS, Gerstmann DR. Lung protective strategies of ventilation in the neonate: what are they? Pediatrics 2000; 105:112-4.
6. Dreyfuss D, Saumon G. Ventilator-induced lung injury. Am J Respir Crit Care Med 1998; 157:294-323.
7. Creamer KM, McCloud LL, Fisher LE, Ehrhart I. Closing pressure rather than opening pressure determines optimal positive end expiratory pressure and avoids overdistention. Chest 1999; 116:26s-27s.
8. Amato MB, Barbas CS, Medeiros DM. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 1998; 338:347-54.
9. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000;342:1301-8.
10. Taskar V, John J, Evander E, Robertson B, Jonson B. Surfactant dysfunction makes lungs vulnerable to repetitive collapse and reexpansion. Am J Respir Crit Care Med 1997; 155:313-20.
11. Kolton M, Cattran CB, Kent G, Volgyesi G, Froese AB, Bryan AC. Oxygenation during high-frequency ventilation compared with conventional mechanical ventilation in two models of lung injury. Anesth Analg 1982; 61:323-32.
12. Froese AB, McCulloch PR, Sugiura M, Vaclavik S, Possmayer F, Moller F. Optimizing alveolar expansion prolongs the effectiveness of exogenous surfactant therapy in the adult rabbit Am Rev Respir Dis 1993;148:569-77.
13. Doctor A, Arnold J. Mechanical support of acute lung injury: options for strategic ventilation. New Horizons 1999; 7:359-73.
14. Ito Y, Manwell SEE, Kerr CL, Veldhuizen RAW, Yao LJ, Bjarneson D, et al. Effects of ventilation strategies on efficacy of exogenous surfactante therapy in a rabbit model lung injury. Am J Respir Crit Care Med 1997; 157:149-55.
15. Ito Y, Veldhuizen RAW, Yao LJ, McCaig A, Barttlett AJ, Lewis JF, et al. Ventilation strategies affect surfactant aggregate conversion in acute lung injury. Am J Respir Crit Care Med 1997; 155:493-9.
16. Hatcher D. Watanabe H, Ashbury T, Vincent S, Fisher J, Froese A. Mechanical performance of clinically available neonatal, high-frequency, oscilatory-type ventilators. Crit Care Med 1998; 26:1081-88.
17. McCulloch PR, Forkert PG, Froese AB. Lung volume maintenance prevents lung injury during high frequency oscillation in surfactant deficient rabbits. Am Rev Respir Dis 1988; 137: 1185-92.
18. Thome U, Töpfer A, Achaller P, Pohlandt F. Effect of mean airway pressure on lung volume during high-frequency oscillatory ventilation of preterm infants. Am J Respir Crit Care Med 1998; 157:1213-18.
19. Meredith KS, de Lemos RA, Coalson JJ. Role of lung injury in pathogenesis of hyaline membrane disease in premature baboons. J Appl Physiol 1989; 66:2150-8.
20. Hamilton, PP, Onayemi A, Smyth JA, Gillan JE, Cutz E, Froese AB, et al. Comparison of conventional and high-frequency ventilation: oxygenation and lung pathology. J Appl Physiol 1983; 55:131-8.
21. Takata M, Abe J, Tanaka H, Kitano Y, Doi Z, Koshaka T, et al. Intra-alveolar expression of tumor necrosis factor gene during conventional and high frequency ventilation. Am J Respir Crit Care Med 1997; 156:272-9.
22. Cochrane CG, Revak SD. Surfactant lavage treatment in a model of respiratory distress syndrome. Chest 1999; 116:85s-87s.
23. Kerr CL, Ito Y, Manwell SEE, Veldhuizen RAW, Yao LJ, McCaig LA, Lewis JF. Effects of surfactant distribution and ventilation strategies on efficacy of exogenous surfactant. J Appl Physiol 1998; 85:676-84.
24. Bauman LA, Willson DF. Surfactant in pediatric respiratory failure. New Horizons 1999; 7:399-413.
25. Gregory TJ, Steinberg KP, Spragg R. Bovine surfactant therapy for patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 1997; 155:1309-15.
26. Kruse MF, Schült-Mönting J, Hoehn T. Rate of surfactant administration influences lung function and gas exchange in a surfactant-deficient rabbit model. Pediatr Pulmonol 1998; 25: 196-204.
27. Hills BA. An alternative view of the role of surfactant and the alveolar model. J Appl Physiol 1999; 87:1567-83.
28. Kobayashi T, Ohta K, Tashiro K, Nishizuka K, Chen W, Ohmura S, et al. Dextran restores albumin-inhibited surface activity of pulmonary surfactant extract. J Appl Physiol 1999; 86:1778-84.
29. Tauesch HW, Lu KW, Goerke J, Clements JA. Nonionic polymers reverse inactivation of surfactant by meconium and other substances. Am J Respir Crit Care Med 1999; 159:1391-5.

30. Sohma, A, Brampton, WJ, Dunnill, MS. Effect of ventilation with positive end-expiratory pressure on the development of lung damage in experimental acid aspiration pneumonia in the rabbit. Intensive Care Med 1992; 18,112-7.
31. Chang HK. Mechanisms of gas transport during ventilation by high frequency oscillation. J Appl Physiol 1984: 56:553-63.

Correspondence:
Dr. Jefferson P. Piva
Hospital Sao Lucas da PUCRS - UTI
Avenida Ipiranga, 6690 - 5º andar
CEP 91610-000 – Porto Alegre, RS, Brazil
Phone/Fax: + 55 51 3315.2400
E-mail: jpiva@pucrs.br