Partial liquid ventilation combined with kinetic therapy in acute respiratory failure in piglets

Abstract  Objective: To investigate the effect of the combination of kinetic therapy (KT) with partial liquid ventilation (PLV) on gas exchange, lung mechanics and hemodynamics in acute lung injury (ALI).

Design: Prospective, randomized, controlled pilot study.

Setting: University research laboratory.

Subjects: Eleven piglets weighing 8.3 ± 0.9 kg.

Intervention: ALI was induced by the infusion of oleic acid (0.08 ml/kg) and repeated lung lavages with 0.9% NaCl (20 ml/kg). Thereafter the animals were randomly assigned either for PLV or a combination of PLV with KT (PLV/KT). The dose of perfluorocarbon administered was 30 ml/kg, evaporative losses were substituted with 5 ml/kg per h.

Measurements and main results: Airway pressures, tidal volumes, dynamic compliance (Cdyn), expiratory airway resistance and arterial blood gases were measured. Hemodynamic monitoring included right atrial, mean pulmonary artery, pulmonary capillary wedge and mean systemic arterial pressures, and continuous flow recording of the pulmonary artery. In both groups the induction of ALI significantly reduced PaO2/FIO2, Cdyn and cardiac output, and significantly increased pulmonary artery pressure. After the initiation of PLV there was a significant increase of PaO2/FIO2 and Cdyn, and a significant decrease of pulmonary artery pressure in both groups. Except the PaCO2, which showed significantly lower values in the PLV/KT group, no variables showed any differences between the two groups.

Conclusion: The additional use of KT did not show beneficial effects on oxygenation and lung mechanics during PLV. However, at constant minute ventilation PaCO2 levels were significantly lower during PLV/KT, indicating some positive influence on the ventilation/perfusion distribution within the lung. Extreme body positions during PLV/KT did not show any significant hemodynamic side effects.

Key words  Acute lung injury · Partial liquid ventilation · Kinetic therapy · Lung function · Hemodynamic monitoring
proved to be effective in reducing alveolar collapse and ventilation/perfusion mismatch. Furthermore, KT significantly reduced the incidence of atelectasis and pneumonia in critically ill, immobilized patients [4, 5].

In recent years increasing interest has been shown in liquid ventilation with perfluorocarbon (PFC) to improve pulmonary gas exchange in experimental models of ALI [6–9]. PFC liquids are biologically inert, non-biotransformable and immiscible in both aqueous and lipid media. PFC liquids are absorbed minimally into the systemic circulation via the respiratory epithelium, and are eliminated by evaporation through the lungs. In contrast to total liquid ventilation (TLV), in 1991 Fuhrman et al. reported on the use of a combined technique of liquid ventilation and tidal gas volume ventilation in 13 piglets with normal lungs [10], which was later called partial liquid ventilation (PLV) or perfluorocarbon-associated gas exchange (PAG). The lungs were filled with a volume of 30 ml kg⁻¹ PFC liquid according to the normal functional residual capacity (FRC) followed by tidal gas ventilation using conventional ventilator settings. Several animal studies using this technique showed an enhanced gas exchange, improved pulmonary mechanics and improved survival in models of ALI.

Whereas the liquid distribution within the lung is quite homogenous during TLV [11], there is inhomogeneous liquid distribution during PLV [12]. With a patient in the supine position the distribution of the liquid is typically gravity-dependent, preferentially distending the dependent alveoli most. An animal experimental study by Curtis et al. [13] showed that, despite the presence of a fluid level in the endotracheal tube, radiography, taken at end-expiration with no PEEP applied, revealed some gas trapped throughout the lung. Furthermore Curtis et al. [13] also showed that, compared to conventional gas ventilation, during KT a beneficial effect of PLV on oxygenation was only achieved with an FRC dose of liquid. We hypothesized that the combination of KT with PLV may be able to optimize liquid and gas distribution within the lung, associated with an improved ventilation/perfusion relationship. The aim of this study was to investigate the effects of PLV combined with KT on lung mechanics, gas exchange and hemodynamics.

### Methods

The protocol was approved by the Institutional Animal Research Committee and the care of the animals was in accordance with guidelines for ethical animal research.

#### Animal preparation

In 11 piglets of either sex, weighing 8.3 ± 0.9 kg and premedicated with azaperone (8 mg kg⁻¹) and atropine (0.02 mg kg⁻¹), anesthesia was induced with ketamine (10 mg kg⁻¹) and thereafter maintained by a continuous infusion of fentanyl (0.15 μg/kg⁻¹ per min⁻¹), pentobarbital sodium (4 mg/kg⁻¹ per h⁻¹) and pancuronium (0.3 mg/kg⁻¹ per h⁻¹). All animals were placed in the supine position. After placing a 5.5 mm-ID Hi-Lo cuffed tube (Hi-Lo jet tube, National Catheter Corp., Malinekrodt, Glen Falls, N. Y.) via tracheostomy, controlled mechanical ventilation was established using a volume-controlled, time-cycled ventilator (Evita 4, Dräger Company, Lübeck, FRG). The tidal volume was set at 10–12 ml/kg⁻¹ with a decelerating inspiratory flow profile, respiratory rate at 24 min⁻¹, I/E ratio at 1:2, PEEP at 0.4 kPa, and FIO₂ at 0.21. Initially a 4 Fr double-lumen catheter (Duocath, Peter von Berg Medizintechnik, Kirchseeon, FRG) was inserted into the right subclavian vein for nutrition and anesthesia. After induction of anesthesia a Ringer solution was infused initially at a rate of 20 ml/kg⁻¹ per 30 min, followed by a continuous infusion of 5 ml/kg⁻¹ per h⁻¹. A 5.5 Fr thermodilution O₂-saturation fiber-optic pulmonary artery catheter (Edwards Swan-Ganz Oximetry TD catheter, Edwards Critical Care Division, Irvine, Calif., USA) was placed into the pulmonary artery by peripheral cutdown of the right external jugular vein. A 4 Fr O₂-saturation catheter (Edslab double-lumen O₂ Sat II catheter, Edwards Critical Care Division) was inserted via the right common carotid artery and placed into the thoracic aorta for continuous arterial oximetry measurement. A short 16 gauge catheter (Abbocath, Abbott Ireland LTD, Sligo, Republic of Ireland) was placed into the femoral artery for continuous pressure recording. A second 4 Fr double-lumen catheter (Duocath, Peter von Berg Medizintechnik, Kirchseeon, FRG) was placed via the left external jugular vein.

#### Protocol

After a median, longitudinal sternotomy, an ultrasonic flowprobe (T208 Dual Channel Flowmeter, Transonic Systems Inc., Ithaca, N.Y., USA) was placed around the pulmonary artery. Then two thorax drains were inserted and the thorax was closed again. After instrumentation the animals were allowed to rest for 30 min before control measurements were performed. Before the induction of ALI the O₂ of the ventilator was increased to 1.0 and the PEEP level to 1.0 kPa [14]. Acute respiratory failure (PaO₂/FIO₂ < 100 mm Hg; < 13.3 kPa) was induced initially by a 30-min infusion of oleic acid (0.08 ml/kg) into the right atrium followed by 3–5 lung lavages using 0.9% saline (20 ml/kg per lavage). After the last lung lavage the animals were randomly assigned either for PLV or PLV in combination with kinetic therapy (PLV/KT). After 60, 120, 180, and 240 min all hemodynamic and respiratory data were registered in the piglets in the supine position, and in both extreme body positions in the PLV/KT group. One animal died after the oleic acid infusion during the first lung lavage and was excluded from the study. All the other animals tolerated the experimental protocol. After the end of the trial the animals were killed with an overdose of potassium chloride.

#### Partial liquid ventilation (PLV)

After induction of ALI, PLV was started using the Rimar 101 PFC liquid (Rimar 101, Miteni Corp., Milan, Italy). The PFC liquid was oxygenated at an FIO₂ of 1.0 and warmed to 38°C. Thereafter the oxygenated PFC liquid (30 ml/kg⁻¹) was instilled into the trachea over 5 min via the distal port of the endotracheal tube. PLV was continued for 4 h without changing the ventilator settings. Evaporative losses of the liquid were compensated by adding 5 ml/kg⁻¹ per h⁻¹ of the oxygenated perfluorocarbon liquid. Rimar 101 has a specific gravity of 1.77 g ml⁻¹ at 25°C, a surface tension of...