EXPERIMENTAL

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Tracheal double-lumen ventilation attenuates hypercapnia and respiratory acidosis in lung injured pigs

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Abstract *Objective:* Evaluation of ventilatory and circulatory effects with coaxial double-lumen tube ventilation for dead-space reduction as compared with standard endotracheal tube ventilation. *Design:* Experimental study in a pig model of lung lavage induced acute lung injury. *Setting:* University research laboratory. *Measurements and results:* Tidal volumes of 6, 8 and 10 ml/kg body weight with a set respiratory rate of 20 breaths per minute were used in a random order with both double-lumen ventilation and standard endotracheal tube ventilation. Measurements of ventilatory and circulatory parameters were obtained after steady state at each experimental stage. With a tidal volume of 6 ml/kg, $PaCO_2$ was reduced from 10.9 kPa (95% CI 9.0–12.9) with a standard endotracheal tube to 8.2 kPa (95% CI 7.0–9.4) with double-lumen ventilation. This corresponds to a reduction in carbon dioxide levels by 25%. At 6 ml/kg, pH increased from 7.17 (95% CI 7.09–7.24) with a standard endotracheal tube to 7.27 (95% CI 7.21–7.32) with double-lumen ventilation. Tracheal pressure was monitored continuously and no difference between single- or double-lumen ventilation was noted at corresponding levels of ventilation. There was no formation of auto-PEEP. Partial tube obstruction due to secretions was not observed during the experiments. *Conclusions:* Coaxial double-lumen tube ventilation is an effective adjunct to reduce technical dead space. It attenuates hypercapnia and respiratory acidosis in a lung injury pig model.

Keywords Dead space · Tracheal pressure · Carbon dioxide · Hypercapnia · Acute respiratory distress syndrome · Double-lumen tube

Introduction

One of the most important developments related to mechanical ventilation is the recognition that mechanical ventilation can induce lung injury [1] and that protective ventilation, i.e. small tidal volumes (6 ml/kg) with rapid ventilatory rates [2], reduce mortality in acute respiratory distress syndrome (ARDS) patients [3, 4]. The drawback with tidal volume restriction is hypercapnia and respiratory acidosis, since a further increase in respiratory rate is difficult, due to auto-PEEP formation. Permissive hypercapnia is tolerated in many patients [5] and respiratory acidosis per se may provide part of the lung protective effect [6, 7]. Hypercapnia is, however, less well tolerated in patients with head trauma, sepsis and cardiac dysfunction especially in combination with renal failure [8, 9].

Tracheal gas insufflation (TGI), i.e. insufflation of a secondary gas flow at the tip of the endotracheal tube (ETT), has been advocated as a solution to remove CO_2 from the technical dead space of the ETT and the ventilator circuit. The TGI method was proposed as an adjunct to mechanical ventilation 30 years ago. In spite of extensive research, the method has not been implemented as standard care for severe ARDS patients mostly due to
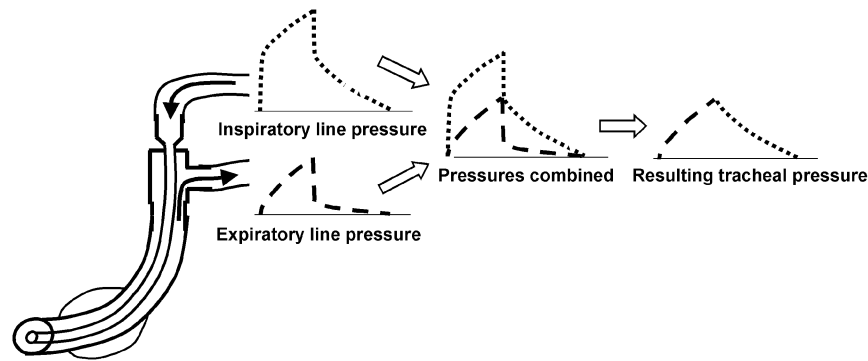
Fig. 1 Inserting a 5-mm-outer-diameter Teflon tube fixed to an adapter, into the suction outlet of a standard swivel on a standard 8-mm ID ETT creates the coaxial double-lumen tube. Inspiration is through the inner Teflon tube and expiration around the inner tube via the ETT. The expiratory limb sensor correctly measures tracheal pressure during inspiration due to static (no flow) conditions in the expiratory limb during inspiration. During expiration, tracheal pressure is measured in the inspiratory limb due to static (no flow) conditions in the inspiratory limb. By combining the pressure measurements, tracheal pressure can be monitored continuously throughout the ventilatory cycle

safety and monitoring issues [10, 11]. Elimination of technical dead space can also be obtained by excluding the Y-piece and thereby let gas mixing take place in the trachea.

We have developed a coaxial double lumen tube ventilation system by simply inserting a 5-mm-outer-diameter Teflon tube into a standard 8-mm-inner-diameter ETT (Fig. 1). Inspiration is through the inner Teflon tube and expiration between the outer surface of the inner tube and the ETT. By measuring the pressure in the two limbs above the tube, tracheal pressure can be measured throughout the ventilatory cycle. The coaxial double lumen tube has been evaluated in an artificial lung model study and found to be as effective as TGI in dead-space reduction. The tendency for auto-PEEP formation and the precision of tracheal pressure measurements has also been studied [12].

We conducted this study for evaluation of the coaxial double-lumen tube on ventilatory and circulatory effects in a lung-lavage-induced acute lung injury pig model. This study also serves as a preclinical safety evaluation.

Materials and methods

The Committee for Ethical Review of Animal Experiments of Gothenburg University approved the experimental protocol. The animal study was conducted in accordance with the National Institutes of Health guidelines for the use of laboratory animals. Eight landrace pigs 31±2 kg body weight, of either gender, were used for the study.

Anaesthesia

Anaesthesia was induced with an intramuscular bolus of ketamine (30 mg kg^{-1}; Ketalar Park-Davis, Solna, Sweden), intravenous α–chloralose (100 mg kg^{-1}; Merck, Darmstadt, Germany), and intravenous fentanyl (3 μg kg^{-1}; Leptanal, Janssen-Cilag, Sollen-tuna, Sweden). Anaesthesia was maintained by continuous intravenous infusion of α–chloralose (25 mg kg^{-1} h^{-1}) and fentanyl (1 μg kg^{-1} h^{-1}). The animals were orally intubated with a cuffed 8-mm-inner-diameter ETT (SIMS Portex, Kent, UK) and mechanically ventilated with a Servo 900C ventilator (Engström, Solna, Sweden) with a F_IO_2 of 0.35–1.0. Normovolaemia, expressed as central venous pressure between 7 and 10 mmHg, was maintained by intravenous infusion of Ringer's solution with 2.5% glucose during surgery at 20 ml kg^{-1} h^{-1} and reduced to 10 ml kg^{-1} h^{-1} thereafter to the completion of the study. Body temperature was maintained at 38–39°C with heating blankets.

Surgical preparation

Intravascular catheters were placed in the superior vena cava for pressure monitoring and vascular access. A 7-F Swan-Ganz thermodilution catheter (Baxter Healthcare, Irvine, Calif.) was inserted in the pulmonary artery.

Lung lavage

Bilateral lung lavage was performed with isotonic saline (13±1 l) with aliquots of approximately 1 l warmed to 39°C. During the procedure the animals were allowed to stabilise for approximately 2–5 min between lavages. Lung lavage was continued until the pigs desaturated below 85% at F_IO_2 1.0 with zero PEEP and returning lavage fluid was clear from surfactant.

The double-lumen tube

A Teflon tube (5/4 mm outer/inner diameter) was fixed to an aluminium adapter. By introducing the Teflon tube into the suction outlet of the swivel connected to a standard 8 mm ID ETT, a coaxial double lumen tube (DLT) was created. The inspiratory tubing was connected directly to the inner Teflon tube and the expiratory tubing of the breathing circuit was connected to the swivel, collecting the expiratory gas from outside the inner tube via the endotracheal tube (Fig. 1). To end double-lumen ventilation, the Teflon tube was withdrawn and the suction outlet closed. The cross-section area of the inspiratory lumen was 13 mm^2 and the expiratory lumen was 31 mm^2. The total dead space eliminated by

the DLT was 45 ml, compared with the standard endotracheal tube with Y-piece and a small humidifier.

Measurements

During single-lumen ventilation, tracheal airway pressure was measured through a low compliant pressure line (outer diameter 2 mm) introduced through the ETT, its end positioned 2 cm below the tube tip. The pressure line was connected to a pressure transducer (DPT 6003, PvB Medizintechnik, Eglharting, Germany), using the AS/3 monitoring system (Datex-Ohmeda, Helsinki, Finland). During double-lumen ventilation, pressure transducers were connected to each limb of the breathing circuit. Tracheal pressure was sampled from the AS/3 analogue output via an DI220 A/D converter (Metrabyte, Keithly, USA) and analysed in a TestPoint application (Capital Equipment, Massachusetts, USA) on a standard PC. End tidal CO_2 concentration was measured using infrared absorption technology using the AS/3 monitoring system. Mixed expired CO_2 concentration was determined in a mixing chamber connected to the expiratory outlet of the ventilator where CO_2 was measured using infrared absorption technology using a Normocap CO_2 analyser (Datex-Ohmeda, Helsinki, Finland). The AS/3 and the Normocap measuring systems were calibrated with reference gas mixture and the entire breathing system was pressurised before experiments to detect any leaks. Intravascular pressures were measured continuously, by using calibrated pressure transducers (DPT 6003, PvB Medizintechnik, Eglharting, Germany) positioned at one-third of the distance from the back to the top of the thorax with the animal in supine position. Cardiac output was recorded as the mean of triplicate determinations by thermodilution injecting 10 ml of 4°C saline measured by the AS/3 cardiac output module.

Experimental procedure

All animals were allowed to stabilise for 1 h after the surgical procedure and lung lavage, before the experimental protocol was started. Ventilator mode was set to volume control, respiratory rate to 20/min and PEEP 10 cmH2O. Tidal volumes of 6, 8 and 10 ml/kg body weight were used in a random order with both single- and double-lumen tube. To resemble the clinical situation, when ventilating with the standard ETT a standard Y-piece and a small passive humidifier was included in the ventilatory circuit. Each ventilation period was maintained for at least 30 min and steady state was verified with end-tidal capnography. After reaching steady state, simultaneous registrations were made of tracheal peak inspiratory pressure (Pinsp), tracheal positive end-expiratory pressure (PEEP), inspiratory oxygen fraction (F_IO_2), end-tidal carbon dioxide concentration ($F_{ET}CO_2$), mixed expired carbon dioxide concentration ($F_{EM}CO_2$), mean arterial pressure (MAP), central venous pressure (CVP), mean pulmonary artery pressure (MPAP), pulmonary capillary wedge pressure (PCWP), heart rate (HR) and cardiac output (CO). Arterial and mixed venous blood samples were also obtained for blood-gas measurements. Tracheal pressure was sampled continuously and analysed for intrinsic PEEP (PEEPi) and peak tracheal pressure.

Calculations

Standard hemodynamic formulas were used to calculate systemic vascular resistance (SVR), pulmonary vascular resistance (PVR) and shunt fraction. To calculate carbon dioxide production (VCO_2) and dead space/tidal volume ratio (V_D/V_T) measurements from expired CO_2 concentration ($F_{EM}CO_2$) were used. The CO_2 production was calculated as: VCO_2 in BTPS=$F_{EM}CO_2 \times V_E$, where V_E=

minute ventilation. Alveolar ventilation (V_A) was calculated as: V_A in BTPS=$(V_E \times F_{EM}CO_2)/(PaCO_2/P_B)$, where P_B is barometric pressure. Dead space/tidal volume ratio was calculated as: $V_D/V_T=(V_E-V_A)/V_E$.

Data analysis

Data are expressed as mean±SD unless otherwise stated. For means 95% confidence interval is given. Control conditions (standard ETT) and the experimental conditions (DLT) were compared using a one-way analysis of variance (ANOVA). Student's paired t-test was used for post hoc analysis. A p value <0.05 was considered statistically significant.

Results

Gas exchange

Arterial carbon dioxide tension increased progressively when tidal volume was reduced from 10 to 8 and 6 ml/kg, at a fixed respiratory rate of 20 breaths per minute, due to decreased ventilation as well as increased dead-space ventilation (Fig. 2). When using the double-lumen tube at a tidal volume of 6 ml/kg, $PaCO_2$ was reduced from 10.6 kPa (95% CI 8.9–12.4) to 7.6 kPa (95% CI 6.6–8.7). The difference by introducing double-lumen tube ventilation was 3.0 kPa (95% CI 2.2–3.7; $p<0.001$), which corresponds to a 25% reduction in carbon dioxide level. At a tidal volume of 8 ml/kg, the difference with the double lumen tube was 1.3 kPa (95% CI 0.7–1.9; $p<0.001$) and at 10 ml/kg the difference was 0.8 kPa (95% CI 0.6–1.0; $p<0.001$).

The reduced respiratory acidosis, with double-lumen tube ventilation, was markedly greater at lower tidal volumes (Fig. 3). When inserting the double-lumen tube at a tidal volume of 6 ml/kg, pH increased from 7.17 (95% CI 7.09–7.24) to 7.27 (95% CI 7.21–7.32). The difference in pH by introducing double-lumen tube ventilation was 0.10 ($p=0.012$) as compared with the
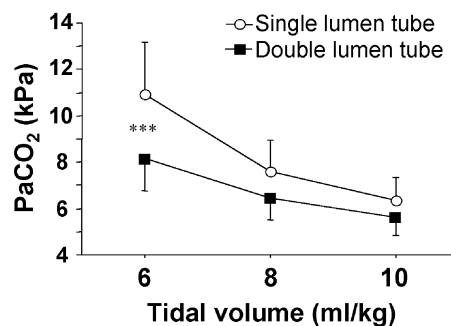

Fig. 2 Arterial CO_2 (expressed in kPa), at steady-state ventilation, with a tidal volume of 6, 8 and 10 ml/kg and a set frequency of 20/min with either a standard single-lumen endotracheal tube or with the double-lumen tube. *Error bars*=±1 SD. ***$p<0.001$

Fig. 3 The pH, at steady-state ventilation with a tidal volume of 6, 8 and 10 ml/kg and a set frequency of 20/min with either a standard single-lumen endotracheal tube or with the double-lumen tube. *Error bars*=±1 SD. *$p<0.05$, **$p<0.01$
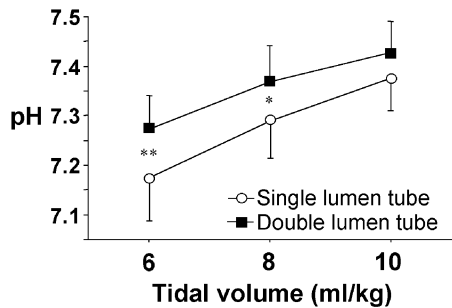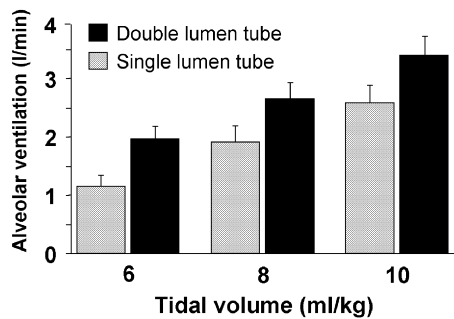

Fig. 4 Alveolar ventilation (in litres per minute), at steady-state ventilation with a tidal volume of 6, 8 and 10 ml/kg and a set frequency of 20/min with either a standard single-lumen endotracheal tube or with the double-lumen tube. *Error bars*=±1 SD

standard endotracheal tube. At a tidal volume of 8 ml/kg, the difference with double lumen ventilation was 0.08 ($p=0.011$) and at 10 ml/kg the difference was 0.05 ($p=0.011$).

Elimination of technical dead space resulted in an increase in alveolar ventilation described as a reduction of the V_D/V_T ratio. At 6 ml/kg the V_D/V_T ratio was 0.69 (95% CI 0.62–075) with the SLT and 0.47 (95% CI 0.41–0.53) with the DLT.

With double-lumen ventilation the effective alveolar ventilation increased. This increase in effective alveolar ventilation was similar to that obtained by increasing tidal volume by 2 ml/kg in single lumen tube ventilation (Fig. 4). The venous admixture increased from 1.8% (95% CI 0.6–2.9) at 10 ml/kg to 6.9% (95% CI 2.7–11.0) at 6 ml/kg with standard ETT ventilation. There was no significant difference in venous admixture between single- or double-lumen tube ventilation.

Airway pressures

There was no statistically significant difference in peak tracheal inspiratory pressure between single- or double-lumen tube ventilation. There was also no difference in PEEP level measured in the trachea, i.e. there was no formation of auto-PEEP during double lumen ventilation (Table 1). We could not detect any tendency of partial tube obstruction due to secretions throughout the experiments.

Hemodynamics

Central venous pressure and mean arterial pressure were stable during the experiments. There were no statistically significant differences in the hemodynamic parameters between single- or double-lumen tube ventilation (Table 2).

Discussion

We recently described a new coaxial ventilating system, the coaxial double-lumen tube, eliminating all technical dead space and some anatomic dead space, by separating inspiration and expiration to the level of the tip of the endotracheal tube [12]. Since there are separate limbs for inspiration and expiration of the ventilator circuit extending into the trachea, inspiratory and expiratory pressures and volumes can be monitored throughout the ventilatory

Table 1 Ventilatory parameters. *SLT* single lumen tube, *DLT* double lumen tube, *PEEP* positive end-expiratory pressure, V_A alveolar ventilation, V_D/V_T deadspace/tidal volume ratio

Tidal volume	6 ml/kg		8 ml/kg		10 ml/kg	
	SLT	DLT	SLT	DLT	SLT	DLT
Tracheal peak (cmH_2O)	20±2.4	21±2.7	24±2.1	24±1.9	28±3.0	28±2.7
PEEPe (cmH_2O)	10	10	10	10	10	10
PEEPi (cmH_2O)	−0.4±0.2	−0.3±0.3	0.0±0.3	0.1±0.1	0.0±0.1	0.1±0.4
V_A, l	1.2±0.3[a]	2.0±0.3[a]	2.0±0.4[a]	2.7±0.4[a]	2.6±0.4[a]	3.4±0.5[a]
V_D/V_T	0.69±0.07[a]	0.47±0.08[a]	0.62±0.06[a]	0.46±0.07[a]	0.58±0.06[a]	0.45±0.07[a]
PaO_2/FIO_2 (kPa)	35±10	35±14	44±8	47±11	51±8	55±10
Shunt (%)	6.9±5.0	5.6±5.2	3.2±2.2	2.6±2.5	1.8±1.4	1.8±1.3

[a] Statistical significance between SLT and DLT ventilation ($p<0.05$)

Table 2 Hemodynamic parameters. *MAP* mean arterial pressure, *CVP* central venous pressure, *MPAP* mean pulmonary artery pressure, *PCWP* pulmonary capillary wedge pressure, *SVR* systemic vascular resistance, *PVR* systemic vascular resistance

Tidal volume	6 ml/kg		8 ml/kg		10 ml/kg	
	SLT	DLT	SLT	DLT	SLT	DLT
MAP (mmHg)	92±18	94±18	92±11	94±5	101±8	102±11
CO (l/min)	3.2±1.1	3.1±1.1	2.8±0.8	2.8±0.4	2.7±0.7	2.7±0.5
MPAP (mmHg)	31±5.1	28±2.9	26±4.4	25±3.3	25±4.4	23±3.2
PCWP (mmHg)	11±3.6	10±2.2	10±1.4	11±2.9	11±3.2	10±2.7
CVP (mmHg)	8±1.5	8±1.2	8±2.1	8±1.6	8±1.6	8±1.7
SVR (dyne·s·cm^{-5})	2205±605	2372±674	2513±484	2514±331	2811±476	2772±461
PVR (dyne·s·cm^{-5})	574±128	490±118	458±142	412±109	429±119	389±112

cycle. The main findings in this study are that at protective levels of ventilation (tidal volumes of 6 ml/kg), coaxial double-lumen tube ventilation reduced the $PaCO_2$ by 25% without any change in tracheal pressure as compared with a standard endotracheal tube. Tracheal pressure including peak tracheal pressure and intrinsic PEEP could also be monitored continuously [12].

Airway pressure effects and monitoring

Tracheal gas insufflation (TGI), i.e. insufflation of a secondary gas flow at the tip of the tube, removes CO_2 from the technical dead space of the endotracheal tube and the ventilator circuit [13]. Unfortunately, TGI is not as simple as inserting a small catheter into the endotracheal tube and insufflating gas. Continuous TGI increases the tidal volume delivered and increases peak alveolar pressure during volume control ventilation. The use of pressure control ventilation minimizes this problem, but if the ventilator flow decreases to zero before the end of inspiration, tidal volumes and pressures do increase. The TGI limited to the expiratory phase has minimal effects on tidal volumes and alveolar pressures, but it is worth emphasising that a high respiratory rate, the possibility of termination of expiratory TGI flow slightly after the start of inspiration [2] and the increase in expiratory resistance due to mucus in the endotracheal tube can also contribute to the risk of development of unobserved PEEPi. Occlusion or partial occlusion of the endotracheal tube around the TGI catheter results in a marked increase in distal lung pressure and may result in lung damage.

In contrast, the DLT technique offers a possibility of monitoring tracheal pressure, including PEEPi, over the whole ventilatory cycle, without interrupting ventilation. The expiratory limb pressure sensor correctly measures tracheal pressure during inspiration, as there is no flow in that limb during inspiration; thus, peak tracheal pressure can be measured without any end-inspiratory pause or interruption of ventilation. During expiration the tracheal pressure is simply measured in the inspiratory limb, as there is no flow in the inspiratory limb during expiration. Inspiratory and expiratory pressures and volumes can be appropriately monitored and all of the alarms and monitors of the ventilator function uninterruptedly, providing the same level of safety as standard ventilation [11].

Effects on gas exchange

The lung-lavage-induced lung injury model showed a marked increase in dead space with V_D/V_T ratio ranging from 0.58 to 0.69. This corresponds well with previous studies of an animal model of acute lung injury [14, 15, 16, 17]. At low-minute ventilation, the effect of the double-lumen tube was more pronounced. This is explained by the fact that technical dead space represents an increasing proportion of the tidal volume as the tidal volume is decreased. In a lung model, we have previously shown that the DLT ventilation is as effective in reducing CO_2 tension as tracheal gas insufflation irrespective of mode [12]. Our results, from this animal study, confirm that coaxial DLT ventilation is efficient in attenuating hypercapnia and respiratory acidosis, with a reduction in arterial CO_2 tension ranging from 11–25%. This corresponds well to values obtained in studies performed in animal lung injury models and in man for evaluation of tracheal gas insufflation [14, 15, 16, 17, 18]. The differences in CO_2 reduction between the studies can be related to different metabolism due to different level of sedation and that TGI systems often influences the minute volume delivered and thus peak alveolar pressure. We observed a moderately decreased PaO_2/F_IO_2 ratio and a slightly increased venous admixture with reduction of tidal volume. Our interpretation is that in spite of a relatively high PEEP level, this can be attributed to derecruitment.

Safety issues

Further careful evaluation of safety issues should be undertaken before this method is introduced in the ICU. It is advisable that at the initiation of coaxial double-lumen tube ventilation tidal volume be set to low levels and gradually increased while observing peak tracheal pressure and intrinsic PEEP. The coaxial double-lumen tube ventilating system should only be used in volume control

ventilation at protective levels in accordance with the protocol of ARDSnet [4]. There are two reasons why pressure control ventilation should not be used. With pressure control ventilation at an increased respiratory rate, resonance of the inspiratory pressure is seen and may cause the ventilator to stop. The second, main reason is that in case of tube obstruction, when removing the inner tube it is of paramount importance that no non-physiological pressures be set in the ventilator. With volume control ventilation, the inner tube can safely be removed, since the ventilator will automatically reduce the inspiratory pressure when the inspiratory resistance is reduced.

To prevent excessive airway pressures reaching the patient, the inspiratory pressure limit should be set slightly above peak inspiratory pressure. In case of partial tube obstruction, the delivered volumes will decrease and the alarm will be activated. A build-up of PEEPi will lead to a concomitant increase in peak tracheal pressure and inspiratory ventilator pressure. We advocate that when using the coaxial DLT, one pressure sensor in each limb be used, giving a direct visualisation of peak tracheal pressure and intrinsic PEEP. One alternative is that only the inspiratory limb pressure be monitored. The inspiratory pressure will indicate a partial inspiratory tube occlusion and also a partial expiratory lumen occlusion with intrinsic PEEP formation. It would still be possible to measure plateau pressure and thereby follow peak tracheal pressure. In the future, we hope that a ventilator manufacturer will provide a new DLT mode with tracheal pressure displayed on the ventilator including alarms set on the tracheal pressure.

In this study we could not detect any intrinsic PEEP formation, largely because the pigs' weight was only 31 kg on average, which corresponds to tidal volumes of only 175–340 ml.

Clinical implications and limitations

The first-line intervention to improve CO_2 washout is a reduction of instrumental dead space (by using an active humidifier and smaller dimensions of the Y-piece) and an increase in breathing frequency [2]. A further reduction of instrumental dead space (the ETT and the Y-piece) can be obtained by TGI or double-lumen ventilation. Compared with TGI, double-lumen ventilation has some advantages. Online tracheal pressure measurements can be used to optimise ventilatory settings. Intrinsic PEEP is monitored continuously and in case of tube blockage there is no risk of barotrauma. Introduction or termination of coaxial double-lumen ventilation is a simple and straightforward procedure. Although the number of suitable patients are limited, they are often young, have a high mortality, high morbidity and consume large ICU resources. With the knowledge of the technical and safety aspects of coaxial double-lumen tube ventilation gathered from our lung model study and animal study, we now feel it is safe to conduct a limited safety and efficacy evaluation of the coaxial DLT ventilation system in patients with acute lung injury.

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