

# Volume-controlled ventilation with superimposed high frequency ventilation during expiration in healthy and surfactant-depleted pig lungs

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In the healthy and surfactant-depleted lungs of five pigs the influence of different forms of high frequency ventilation superimposed on conventional mechanical ventilation during the expiratory phase of the ventilatory cycle (SHFVE) on gas exchange and cardiocirculatory parameters was investigated. Subsequently the effects of end-expiratory flushing (EF), i.e. cleaning the large airways and connecting tubes from the ventilator free from end-expiratory CO<sub>2</sub>, with a volume greater than the dead space of the large airways and connecting tubes was investigated. SHFVE and EF resulted in a significant improvement in CO<sub>2</sub> elimination in both healthy and surfactant-depleted lungs. Furthermore, in stiff lungs, at a certain level of oxygenation and CO<sub>2</sub> elimination, SHFVE produced the lowest peak and mean airway pressure without any additional depression of cardiocirculatory parameters.

*Key words:* Airway pressure; ARDS; cardiocirculatory parameters; end-expiratory flushing; gas exchange; pig; superimposed high frequency ventilation.

The aim of ventilatory therapy is to maintain adequate gas exchange with minimal cardiocirculatory depression and barotrauma of the lung.

The side effects of artificial ventilation are related to the intrapulmonary airway pressure, especially when there is unequal distribution of ventilation (1). To minimise changes in airway pressure, one should investigate methods of decreasing dead space. If one flushes CO<sub>2</sub> out of the large airways and connecting tubes from the ventilator during the expiratory phase, it should be possible to reduce tidal volume during volume-controlled ventilation and so to lower peak airway pressure. Two possible methods of achieving this are: (1) the superimposition of high frequency ventilation during the expiratory phase of the ventilatory cycle (SHFVE) or (2) an end-expiratory flush (EF) (2, 3). During EF the large airways, and the connecting tubes from the ventilator, are flushed with a volume of fresh gas larger than the dead space of the large airways and connecting tubes. The flushing volume has to be delivered to the carina via a special tube and has to start when the expiratory flow is zero.

The aim of this study was to investigate in pigs the influence of different frequencies combined with different pulse volumes during SHFVE and of varying flush volumes during EF in healthy and surfactant-depleted lungs on blood gases, intrapulmonary airway pressure and cardiocirculatory parameters.

## MATERIAL AND METHODS

Five pigs (weighing 20–25 kg) were anesthetized with pentobarbital (600 mg), intubated with a 35 Fr. Mallinckrodt Hi-Lo Jet™ tube, paralysed with pancuronium bromide (0.08 mg/kg/h) and ventilated with a Siemens Servo Ventilator 900C (Siemens-Elema, Sweden) with a frequency of 12 breaths/min and F<sub>IO<sub>2</sub></sub> = 1.

The minute volume was set to maintain the arterial CO<sub>2</sub> tension between 35–40 mmHg during preparation. The I:E ratio was set to 25% inspiratory time and 10% pause time.

Catheters were placed in the femoral artery and vein and a Swan-Ganz catheter was placed in the pulmonary artery via the femoral vein. Cardiovascular monitoring was done by means of a Marquette monitor system 7000™ (Marquette Electronics Inv. Milwaukee, Ws, USA) and printed directly with a Marquette monitor printer 7100. Blood gases and pH were measured with the blood gas analyser (ABL 330, Radiometer, Copenhagen). Intrapulmonary airway pressure was measured with a tip catheter pressure transducer (PPG Hellige, The Netherlands) connected to the Marquette monitor. Superimposed high frequency ventilation during expiration (SHFVE) was performed with a High Frequency Unit 970 (Siemens-Elema, Solna, Sweden) connected to and triggered by a Servo Ventilator 900C (Siemens-Elema, Solna, Sweden) and applied through the high frequency channel of the Hi-Lo Jet™ tube.

In healthy animals the following ventilator settings were used: during conventional mechanical ventilation (CMV) with the Servo Ventilator 900C, the tidal volume was set to 18 ml/kg BW and the frequency was set to 12 and 5 breaths/min. The slow ventilatory rate was used to induce hypercapnia between 60 and 70 mmHg. During expiration frequencies of 2.5, 5 and 15 Hz with corresponding pulse volumes of 32, 16 and 6 ml were superimposed. At these settings the duty cycle was set to 20%. In addition, the influence of the pulse duration of 80% was tested at frequencies of 5 and 15 Hz and a

Table 1

Arterial  $P_{CO_2}$  and  $P_{O_2}$ , cardiac output (CO), peak airway pressure (Paw peak), mean arterial pressure (P art), mean pulmonary pressure (P pulm) and dynamic PEEP in healthy animals during conventional mechanical ventilation (CMV) (F=12) with end-expiratory flush and with superimposed high frequency ventilation at different frequencies (Hz) and pulse volumes (P.V.). Figures are given as means  $\pm$  SD. Statistical analysis was performed with the Wilcoxon's signed ranking test.

	CMV F=12	Flush 100 ml	Flush 200 ml	2.5 Hz P.V. 32 ml	5 Hz P.V. 16 ml	15 Hz P.V. 6 ml
Paco <sub>2</sub> (mmHg)	41 $\pm$ 4	34 $\pm$ 5*	36 $\pm$ 4	36 $\pm$ 5	35 $\pm$ 5	30 $\pm$ 4*
Pao <sub>2</sub> (mmHg)	448 $\pm$ 53	472 $\pm$ 34	502 $\pm$ 38	493 $\pm$ 23	512 $\pm$ 17	481 $\pm$ 31
CO (l/min)	4.0 $\pm$ 0.6	3.8 $\pm$ 0.7	3.1 $\pm$ 0.6	4.2 $\pm$ 0.8	4.4 $\pm$ 0.9	4.9 $\pm$ 0.7
Paw peak (cm H <sub>2</sub> O)	17.5 $\pm$ 2	20 $\pm$ 2	23 $\pm$ 2*	21 $\pm$ 2	20 $\pm$ 3	19 $\pm$ 2
P art. (mmHg)	106 $\pm$ 12	102 $\pm$ 16	97 $\pm$ 19	102 $\pm$ 14	101 $\pm$ 15	107 $\pm$ 18
P pulm. (mmHg)	11 $\pm$ 3	13 $\pm$ 3	15 $\pm$ 4	13 $\pm$ 4	12 $\pm$ 4	12 $\pm$ 3
Dynamic PEEP (cm H <sub>2</sub> O)	0	2 $\pm$ 1*	4.4 $\pm$ 2*	2 $\pm$ 1*	3 $\pm$ 2*	3 $\pm$ 2*

\* = significant differences ( $p < 0.05$ ) to CMV.

Table 2

Arterial  $P_{CO_2}$  and  $P_{O_2}$ , cardiac output (CO), peak airway pressure (Paw peak), mean arterial pressure (P art), mean pulmonary pressure (P pulm) and dynamic PEEP in healthy animals during conventional mechanical ventilation (CMV) (F=5) endexpiratory flush (Flush) and superimposed with high frequency ventilation at different frequencies (Hz) and pulse volumes (P.V.). Figures are given as means  $\pm$  SD. Statistical analysis was performed with the Wilcoxon's signed ranking test.

	CMV F=5	Flush 100 ml	Flush 200 ml	2.5 Hz P.V. 32 ml	5 Hz P.V. 16 ml	15 Hz P.V. 6 ml
Paco <sub>2</sub> (mmHg)	66 $\pm$ 8	52 $\pm$ 8	56 $\pm$ 9	51 $\pm$ 9	47 $\pm$ 8*	42 $\pm$ 6*
Pao <sub>2</sub> (mmHg)	324 $\pm$ 78	355 $\pm$ 48	347 $\pm$ 37	338 $\pm$ 73	409 $\pm$ 53	446 $\pm$ 42
CO (l/min)	3.4 $\pm$ 1.2	3.6 $\pm$ 0.9	3.0 $\pm$ 1.1	3.9 $\pm$ 1.3	4.2 $\pm$ 1.0	4.8 $\pm$ 0.8
Paw peak (cm H <sub>2</sub> O)	19.3 $\pm$ 2	22 $\pm$ 2	25 $\pm$ 3*	23 $\pm$ 3	22 $\pm$ 2	21 $\pm$ 2
P art. (mmHg)	95 $\pm$ 14	92 $\pm$ 11	88 $\pm$ 12	94 $\pm$ 17	96 $\pm$ 16	97 $\pm$ 19
P pulm. (mmHg)	14 $\pm$ 3	15 $\pm$ 4	16 $\pm$ 3	14 $\pm$ 3	14 $\pm$ 3	12 $\pm$ 4
Dynamic PEEP (cm H <sub>2</sub> O)	0	2 $\pm$ 1*	5 $\pm$ 2*	1 $\pm$ 1*	1 $\pm$ 1*	2 $\pm$ 1*

\* = significant differences ( $p < 0.05$ ) to CMV.

frequency of 12 during CMV. Finally, the effects of an end-expiratory flush with volumes of 100 and 200 ml were tested.

These different ventilation settings were applied in a randomized order to each animal and repeated three times. Then the animals' lungs were lavaged with warm saline (1, 4, 5) to produce severe respiratory insufficiency resulting in an arterial  $P_{O_2}$  between 50 and

70 mmHg at ventilator settings of: frequency 12;  $V_t = 35$  ml/kg; I:E ratio of 1:2; static PEEP of 4 cm H<sub>2</sub>O.

After surfactant depletion we applied to the animals SHFVE (15 Hz, duty cycle 20%, pulse volume 6 ml) and EF of 100 and 200 ml and static PEEP was set to 8 cm H<sub>2</sub>O to prevent severe hypoxemia.

## RESULTS

SHFVE at 15 Hz and EF (100 ml) improved CO<sub>2</sub> elimination during conventional mechanical ventilation in animals with healthy lungs without significantly influencing the cardiocirculatory parameters (Tables 1 and 2). CO<sub>2</sub> elimination was also increased by SHFVE at 5 and 15 Hz when the initial  $P_{CO_2}$  was above 60 mmHg. The duration of the duty cycle did not affect CO<sub>2</sub> elimination or oxygenation at 5 or 15 Hz (Table 3).

In animals with surfactant-depleted stiff lungs SHFVE and EF also significantly improved CO<sub>2</sub> elimination without additional depression of cardiocirculatory parameters (Table 4).

## DISCUSSION

Superimposed HFV is reported to improve gas exchange under special circumstances (e.g. ARDS) in

Table 3

Arterial  $P_{CO_2}$  and  $P_{O_2}$ , cardiac output (CO), peak airway pressure (Paw peak), mean arterial pressure (P art), mean pulmonary pressure (P pulm) and dynamic PEEP in healthy animals during conventional mechanical ventilation (CMV) (F=12) superimposed high frequency ventilation at different frequencies (5 and 15 Hz) and duty cycles of 20% and 80%. Figures are given as means  $\pm$  SD. Statistical analysis was performed with the Wilcoxon's signed ranking test.

	5 Hz 20%	5 Hz 80%	15 Hz 20%	15 Hz 80%
Paco <sub>2</sub> (mmHg)	35 $\pm$ 5	35 $\pm$ 4	30 $\pm$ 4	33 $\pm$ 3
Pao <sub>2</sub> (mmHg)	512 $\pm$ 17	480 $\pm$ 28	480 $\pm$ 31	480 $\pm$ 46
CO (l/min)	4.4 $\pm$ 0.9	4.7 $\pm$ 0.8	4.9 $\pm$ 0.7	4.5 $\pm$ 1.1
Paw peak (cm H <sub>2</sub> O)	20 $\pm$ 3	22 $\pm$ 2	19 $\pm$ 2	20 $\pm$ 2
P art. (mmHg)	101 $\pm$ 15	90 $\pm$ 19	107 $\pm$ 18	106 $\pm$ 19
P pulm. (mmHg)	12 $\pm$ 4	13 $\pm$ 3	12 $\pm$ 3	12 $\pm$ 2
Dynamic PEEP (cm H <sub>2</sub> O)	3 $\pm$ 2	2 $\pm$ 1	3 $\pm$ 2	2 $\pm$ 1

Table 4

Arterial  $P_{CO_2}$  and  $P_{O_2}$ , cardiac output (CO), peak airway pressure (Paw peak), mean arterial pressure (P art), mean pulmonary pressure (P pulm) and dynamic PEEP in surfactant depleted animals during conventional mechanical ventilation (CMV) with a PEEP of 4 and 8 cm  $H_2O$  and CMV with a PEEP of 8 cm  $H_2O$  with endexpiratory flush (Flush) and with superimposed high frequency ventilation at a frequency of 15 Hz, pulse volume (P.V.) of 6 ml. Figures are given as means  $\pm$  SD. Statistical analysis was performed with the Wilcoxon's signed ranking test.

	CMV PEEP=4	CMV PEEP=8	Flush 100 ml	Flush 200 ml	15 Hz 6 ml
$P_{aCO_2}$ (mmHg)	47 $\pm$ 6	43 $\pm$ 4	38 $\pm$ 5	35 $\pm$ 4*	35 $\pm$ 4*
$P_{aO_2}$ (mmHg)	64 $\pm$ 12	248 $\pm$ 72*	310 $\pm$ 48*	328 $\pm$ 32*	322 $\pm$ 34*
CO (l/min)	4.3 $\pm$ 0.7	3.6 $\pm$ 0.9	2.7 $\pm$ 0.6*	2.4 $\pm$ 0.5*	2.8 $\pm$ 0.6*
Paw peak (cm $H_2O$ )	29 $\pm$ 3	34 $\pm$ 2*	37 $\pm$ 4*	41 $\pm$ 4*	30 $\pm$ 2
P art. (mmHg)	102 $\pm$ 9	97 $\pm$ 11	101 $\pm$ 8	96 $\pm$ 12	98 $\pm$ 9
P pulm. (mmHg)	19 $\pm$ 4	22 $\pm$ 3	15 $\pm$ 4	17 $\pm$ 4	16 $\pm$ 3
Dynamic PEEP (cm $H_2O$ )	-	-	11 $\pm$ 2	15 $\pm$ 2	10 $\pm$ 2

\* = significant differences ( $p < 0.05$ ) to CMV.

human beings (this volume). But from experimental results in pigs with acute respiratory failure we know that the reason for these findings may be the increased peak and mean airway pressures during SHFV. When the tidal volume and/or PEEP was increased during conventional volume-controlled ventilation to produce the same peak- or mean airway pressures as with superimposed HFV we failed to find any additional improvement in gas exchange with SHFV (unpublished observation). Thus the application of SHFV will not avoid the side effects of conventional volume controlled ventilation.

On the other hand, it appears that SHFVE and EF

may help to remove  $CO_2$  from the large airways and the tube up to the Y-piece, thus decreasing the volume of  $CO_2$  reinspired during the next inspiratory cycle. This may also explain why SHFVE and EF appear to be more effective when the initial arterial  $P_{CO_2}$  is high. The better results with higher frequencies may also imply that there are some additional effects on  $CO_2$  elimination during HFV.

Although a given arterial  $CO_2$  tension may be maintained with a smaller tidal volume and peak pressure using either SHFVE or EF when they are added to conventional mechanical ventilation, these techniques proved inferior to pressure-controlled ventilation with a prolonged inspiratory cycle up to 80% (unpublished observation).

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