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Impact of Different Inspiratory Flow Patterns on Arterial CO_2-tension

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ABSTRACT

Ventilation with decelerating inspiratory flow is known to reduce the dead space fraction and to decrease $PaCO_2$. Constant inspiratory flow with an end-inspiratory pause (EIP) is also known to increase the removal of CO_2.

The aim of the study was to elucidate the effect of the pause/no-flow period while both the pattern and rate of inspiratory flow was unchanged, and when the lung was ventilated with sufficient PEEP to prevent end-expiratory collapse.

Surfactant depleted piglets were assigned to decelerating or constant inspiratory flow with 24 breaths per minute (bpm) or 12 bpm, or to constant flow, without and with an end-inspiratory pause of 25%. By adding an EIP the total time without active inspiratory flow of the respiratory cycle was kept unchanged. Gas exchange, airway pressures, functional residual capacity (using sulfurhexafluoride) and haemodynamics (thermo-dye indicator dilution technique) were measured.

Irrespective of ventilatory frequency, $PaCO_2$ was lower and serial dead space reduced with decelerating flow, compared with constant inspiratory flow. With an end-inspiratory pause added to constant inspiratory flow, serial dead space was reduced but did not decrease $PaCO_2$.

The results of this study corroborate the assumption that total time without active inspiratory flow is important for arterial CO_2-tension.

INTRODUCTION

Examples of newer means of mechanical ventilation are modified forms of pressure-controlled ventilation (PCV), High Frequency Positive Pressure Ventilation (HFPPV), Pressure Support Ventilation (PSV), and Airway Pressure Release Ventilation (APRV), (6,10,21,27). Under these modes a square wave of pressure is intermittently applied to the airway opening, and alveolar pressures and volumes are established during inspiration. Opinions differ as to whether improvements in gas exchange and lung mechanics can be specifically attributed to particular types

of inspiratory flow pattern (1,3,5,28). In patients, the pathophysiology of acute respiratory failure is complex, having many causes and effects. This diversity is an important consideration when applying mechanical ventilation. Physiological and theoretical arguments favour strategies that avoid tidal alveolar collapse (12,26) and maintain transalveolar pressure within normal limits.

Compared with constant flow inspiration, ventilation with decelerating inspiratory flow is known to reduce the dead-space fraction due to improved distribution of inspired gas (7,9). As the rapid gas inflation gives inspired gas a longer residence time, it presumably enhances intrapulmonary gas mixing (20) and improves CO_2 exchange (11). Volume-controlled ventilation guarantees minute ventilation but allows airway pressure to increase as impedance increases. An end-inspiratory pause (EIP) is known to improve ventilation and is commonly used during volume-controlled ventilation (VC-EIP) (8,9,17). Several studies have shown improved gas distribution and increased removal of CO_2 when using an end-inspiratory pause, but most studies have failed to show improved arterial oxygenation (28,11,17,). Modell and co-workers (20) claim that gas exchange impairment must exist before significant response to flow pattern can be detected. In this study the PEEP level was set sufficient high to prevent end-expiratory collapse, thereby no improvement in oxygenation was expected.

The aim of the study was to elucidate the effect of the pause/no-flow period while both the pattern and rate of inspiratory flow were kept unchanged. In order to arrange similar conditions during the active inspiration we added an EIP to the constant inspiratory flow. The respiratory cycle is then divided into 2.5 seconds (s) active inspiration both with and without addition of an EIP. By choosing 12 breaths per minute (bpm), the period of no-flow with decelerating inspiratory flow corresponded to a pause of 25% with constant inspiratory flow.

MATERIAL AND METHODS

Twelve Swedish Landrace piglets, with a mean body mass of 28 kg (± 4), were subjected to lavage. Surfactant was removed (15,22). Anaesthesia (18,29) was induced with tiletamine 3 mg x kg^{-1}+ zolazepam 3 mg x kg^{-1} and xylazine 2.2 mg x kg^{-1} and atropine 0.04 mg x kg^{-1} given intramuscularly, followed 5 min later by a ketamine infusion at 20 mg x kg^{-1} x h^{-1}. In addition, 20 mg of morphine was given iv. before the initial tracheotomy, preparation and introduction of intravascular catheters. Pancuronium bromide was given as relaxant as a continuous infusion at 0.26 mg x kg^{-1} x h^{-1}. The animals´ lungs were ventilated through an 8 mm diameter

Mallinckrodt endotracheal tube (Mallinckrodt Inc, Glens Falls, N.Y., USA) with a Servo 300 (Servo Ventilator 300, Siemens-Elema AB, Solna, Sweden). To maintain the animals body temperature at 38.0 C (±0.6) a thermostatically controlled heating pad was used. The animals were given 0.45% NaCl with 2.5% glucose (Rehydrex, Pharmacia Infusion AB, Uppsala, Sweden) at 20 ml x kg^{-1} x h^{-1} and a bolus of 15 ml x kg^{-1} of dextran-70 (Macrodex 70, Pharmacia Infusion AB) to ensure normovolaemia. The investigations were performed at the Experimental Laboratories of the Department of Anaesthesiology and Intensive Care at University Hospital, Uppsala. The local medical ethics committee for animal experimentation reviewed and approved the protocol.

Monitoring

Intravascular catheters were surgically placed for the measurement of central venous, pulmonary arterial (via the external jugular vein) and aortic (via the carotid artery) pressures. The position of each catheter was confirmed by pressure tracing on a bedside monitor (Siemens Sirecust) and recorded with reference to the mid-thorax and at end-expiration level. Arterial and venous blood gases were measured (ABL 300/OSM III, Radiometer A/S Denmark). Cardiac output (14,16,23) and extravascular lung water (ETV), were estimated using a COLD System (Pulsion Medizintecknik KG, Germany). Airway pressures were obtained from the digital displays of the ventilator. Every morning a pre-use functional check was performed according to the schedule set out in the operating manual for the ventilator and the ventilator's pressure and flow transducers had been calibrated with independent devices.

The static chest-lung compliance (CLT) was calculated according to the formula CLT = Tidal volume x (end-inspiratory pressure – expiratory pressure)$^{-1}$, but with appropriate modifications to make allowance for the compressible volume (24,25). When the end-inspiratory occlusion pressure and the total end-expiratory pressure (PEEP) were measured, the ventilator's hold function was used for 5 s before the equilibrium values were noted. To measure functional residual capacity (FRC), serial dead space (SDS), the SF_6 tracer gas wash-in/wash-out method was used (13). FRC was calculated as the total volume of SF_6 washed-out divided by the alveolar concentration at the end of wash-in. SDS was obtained from the first few expirations during wash-out, and was defined as the volume expired when the SF6 concentration reached 50% of the alveolar concentration in that breath. In our laboratory the coefficient of variation for three sequential measurements in 9 animals for FRC, under a broad range of tidal volumes and different flow conditions, was 1 ± 0.08%.

Recruitment

Immediately after lavage, the surfactant depleted lungs were recruited with I:E 1:1 and the external PEEP was set to 25 cmH_2O and with a tidal volume to produce a peak inspiratory pressure (PIP) of 50 cmH_2O during cyclic ventilation for 5 min.

Ventilatory settings

A Servo Ventilator 300 (Siemens-Elema AB, Solna, Sweden) provides both Volume Controlled ventilation (VC; constant inspiratory flow) and Pressure-Regulated Volume Controlled ventilation (PRVC; decelerating inspiratory flow).

Experimental procedure

Following anaesthesia and preparation, the animals were placed in prone position. Bronchoalveolar lavage was performed as described previously (16, 22). After lavage, a recruitment procedure was performed. Ventilation during the study was with inspiration-expiration ratio of 1:1, FIO_2 0.3, and constant tidal volume. PEEP was set to 13 cm H_2O. In this animal lung model several studies have proven that PEEP of 13 cm H_2O is sufficient to prevent alveolar collapse. This PEEP level was maintained during the whole study. At 24 bpm the animals were normocapnic but hypercapnic at 12 bpm. To study how different inspiratory flow patterns utilized inspiration time, we used recordings from the inspiratory-expiratory flow (see Fig 1). The animals were then assigned to either decelerating or constant inspiratory flow without EIP at 24 or 12 bpm, or to constant inspiratory flow at 12 bpm with an EIP of 25% added . The respiratory cycle with 12 bpm was divided into 2.5 s active inspiration both with and without EIP. By adding the pause of 1.25 s (25%) the total inspiration time was 3.75 s, resulting in an I:E ratio of 3:1. Each setting was applied for 15 min before measurements.

Calculations and statistics

All ventilatory volumes and derived parameters have been converted to BTPS conditions. Indexed values are related either to body mass, or to body surface area (BSA). Differences were evaluated with a non-parametric analysis of variance (Friedman test). If significant differences were detected, these differences were evaluated using the paired sign *t* test. A standard statistics package was used (StatView, Abacus Concepts, Berkeley, CA). Statistical significance was accepted at $*p \leq 0.05$.

RESULTS

The results are presented in Tables 1 and 2 and in Figures 1 and 2. With all modes under study the tidal volumes remained constant, which produced normocapnia at 24 bpm, though at 12 bpm the animals were hypercapnic. Table 1 presents the results for decelerating versus constant inspiratory flow at 24 bpm and normocapnia. In Table 2 the results for decelerating versus constant inspiratory flow without and with 25% EIP and hypercapnia are presented. During a short period, postlavage with zero PEEP ventilation and FIO_2 1.0, PaO_2 was reduced from 98 ±4 to 9 ±2 kPa, while venous admixture (Qva/Qt) increased from 7 to 32.5%. During the postlavage studies with a PEEP level of 13 cmH_2O and FIO_2 of 0.3, the (Qva/Qt) ranged between 6% and 14%.

Airway pressure

With 24 bpm and decelerating flow, peak inspiratory pressure (PIP) was 25 ±3 cmH_2O and with constant inspiratory flow PIP was 28 ±3 cmH_2O. At 12 bpm and decelerating flow, PIP was 24±2 cmH_2O, with constant inspiratory flow 25 ±3 cmH_2O, increasing to 27±3 cmH_2O with an EIP.

$PaCO_2$, serial dead space, functional residual capacity

Decelerating flow at 24 bpm yielded a $PaCO_2$ of 6.3 ±2 kPa, and with constant inspiratory flow, 6.9 ±1 kPa. At 24 bpm and decelerating flow, serial dead space was 146 ±13 ml, and for constant flow inspiration, 156 ±14 ml.

At 12 bpm and decelerating flow, $PaCO_2$ was 8.4 ±1 kPa, with constant inspiratory flow, 9.1±1 kPa, and 8.9 ±1 kPa with an EIP. Serial dead space (SDS) was 141±8 ml for the decelerating flow and it was reduced to the same extent (141 ±12) for constant inspiratory flow with EIP.

For significances see Tables 1 and 2.

DISCUSSION

In a previous study (19) we found that $PaCO_2$ was lower with the decelerating inspiratory flow than with constant inspiratory flow. We assumed that this could be related to how the flow patterns distribute and redistribute the gas. The aim of the present study was to elucidate the effect of the pause/no-flow period while both the pattern and rate of inspiratory flow was unchanged, and when the lung was ventilated with a PEEP level set to prevent end-expiratory collapse. We found that arterial carbon dioxide tension ($PaCO_2$) was lower and serial dead space reduced with decelerating flow, compared with constant inspiratory flow, irrespective of ventilatory frequency. With an end-

Postlavage	PC_{24}	*≤0.05	VC_{24}
Total PEEP [cmH_2O]	13 ±1		13 ±1
PIP [cmH_2O]	25 ±3	*VC24	28 ±3
Mean airway pressure	19±2	*VC24	17±2
Tidal volume [$ml*kg^{-1}$]	12 ±2		12 ±1
End-inspiratory hold pressure [cmH_2O]	24 ±3		24 ±3
Compliance [$ml*cmH_20^{-1}$]	33 ±4		35 ±6
Functional residual capacity [ml]	1063±216		1075 ±204
PaO_2 [kPa]	16 ±4		18 ±2
$PaCO_2$ [kPa]	6.3 ±2	*VC24	6.9 ±1
SDS [ml]	146 ±13	*VC24	156 ±14
SvO_2 [%]	55 ±11		61 ±12
ITBV [$ml*kg^{-1}$]	19 ±3		21 ±3
CI [$l*min^{-1}*(m^2)^{-1}$]	6.0 ±0.8		6.0 ±0.8
Qva/Qt [%]	9 ±9		6 ±4
DO_2I [$ml*min^{-1}*(m^2)]^{-1}$	557 ±156		591 ±148

Table 1. Results for decelerating versus constant inspiratory flow at 24 bpm under normocapnia
Values are means ±1 SD. In the paired t-test on mean difference of a given value "PC_{24}" (decelerating flow at 24 bpm) denotes a significant difference vs "VC_{24}" (constant inspiratory flow at 24 bpm). All ventilatory volumes and derived parameters have been converted to BTPS conditions. Indexed values are either vs body mass, or vs body surface area (BSA). Statistical significance was accepted at: *p≤ 0.05.

inspiratory pause (EIP) added to constant flow, serial dead space was reduced but no significant difference in $PaCO_2$ was seen. After comments on the inspiratory–expiratory flow recordings and the rationale behind the EIP, these findings will be discussed in the following paragraphs.

Inspiratory–expiratory flow recordings

These pressure/flow recordings (Figure 1) illustrate that, with decelerating flow, the pre-set inspiratory pressure remains constant throughout inspiration. At 24 bpm the no-flow period is 0.3 s and at 12 bpm it is 1.25 s. During constant inspiratory flow there is a linear increase in pressure while the tidal volume is delivered. With constant inspiratory flow and an EIP, there is also a linear increase in airway pressure which decreases during the pause i.e. no-flow period. The respiratory

Postlavage	PC_{12}	*≤0.05	VC_{12}	$VC_{12}EIP$	*≤0.05
Total PEEP [cmH_2O]	13±1		13±1	13±1	
PIP [cmH_2O]	24 ±2	*VC12 *VC_{12} EIP	25 ±3	27 ±3	
Mean airway pressure	18±2	*VC12	16±2	19±2	*VC12,PC12
Tidal volume [ml*kg^{-1}]	13 ±1		13 ±1	13 ±1	
End-inspiratory hold pressure [cmH_2O]	23 ±3		23 ±3	24 ±3	*VC12
Compliance [ml*cmH_20^{-1}]	38±8		42±11	36±7	
Functional residual capacity [ml]	1057 ±210		1033±177	1128 ±200	*PC12 *VC12
PaO_2 [kPa]	14 ±1		13 ±2	14 ±1	
$PaCO_2$ [kPa]	8.4 ±1	*VC12	9.1 ±1	8.9 ±1	
SDS [ml]	141 ±8	*VC12	154±13	141 ±12	*VC12
SvO_2 [%]	53 ±12		53 ±10	55 ±9	
ITBV [mL*kg^{-1}]	21 ±4		21 ±3	20 ±3	
CI [l*min^{-1}*$(m^2)^{-1}$]	6 ±0.8		6.0 ±0.8	6.0 ±0.8	
Qva/Qt [%]	12 ±7		14 ±6	11 ±4	
DO_2I [ml*min^{-1}*$(m^2)^{-1}$]	563 ±121		569±140	571 ±117	

Table 2. Results for decelerating versus constant inspiratory flow at 12 bpm without and with EIP under hypercapnia. Values are means ±1 SD. In the paired t-test on mean difference of a given value, "PC_{12}" (decelerating flow at 12 bpm), denotes significant difference vs "VC_{12}" (constant inspiratory flow at 12 bpm), and vs "$VC_{12}EIP$" (constant flow at 12 bpm with end-inspiratory pause of 25%). All ventilatory volumes and derived parameters have been converted to BTPS conditions. Indexed values are either vs body mass, or vs body surface area (BSA). Statistical significance was accepted at three levels: *p≤ 0.05.

cycle at 12 bpm is divided into 2.5 s active inspiration both with and without EIP. By adding the pause of 1.25 s (25%) the total inspiration time will be 3.75 s, resulting in an I:E ratio of 3:1. Notably: From the figure it is obvious that there was an ongoing flow at expiration i.e. there was an intrinsic PEEP when an EIP was added.

Rationale for adding the end-inspiratory pause

We wanted to elucidate the effect of the pause/no-flow period. For constant inspiratory flow this was only possible if the pause was added to an otherwise unchanged inspiratory phase. To obtain similar pause/no-flow periods, we chose 12 bpm. With this frequency the no-flow period with decelerating inspiratory flow was 1.25 s, corresponding to an EIP of 25% with the constant

inspiratory flow. By adding the 1.25 s pause after the active inspiration in the constant inspiratory mode, the active inspiration time of 2.5 s was unchanged, but the added pause time of 1.25 s increases the total inspiratory time to 3.75 s, reducing expiratory time. Consequently, the inspiration/expiration (I:E ratio) increases to 3:1, and also produces an intrinsic PEEP which increased FRC (see Table 2). That was why 12 bpm was chosen, as adding a 24 bpm pause had resulted in an unacceptably intrinsic PEEP.

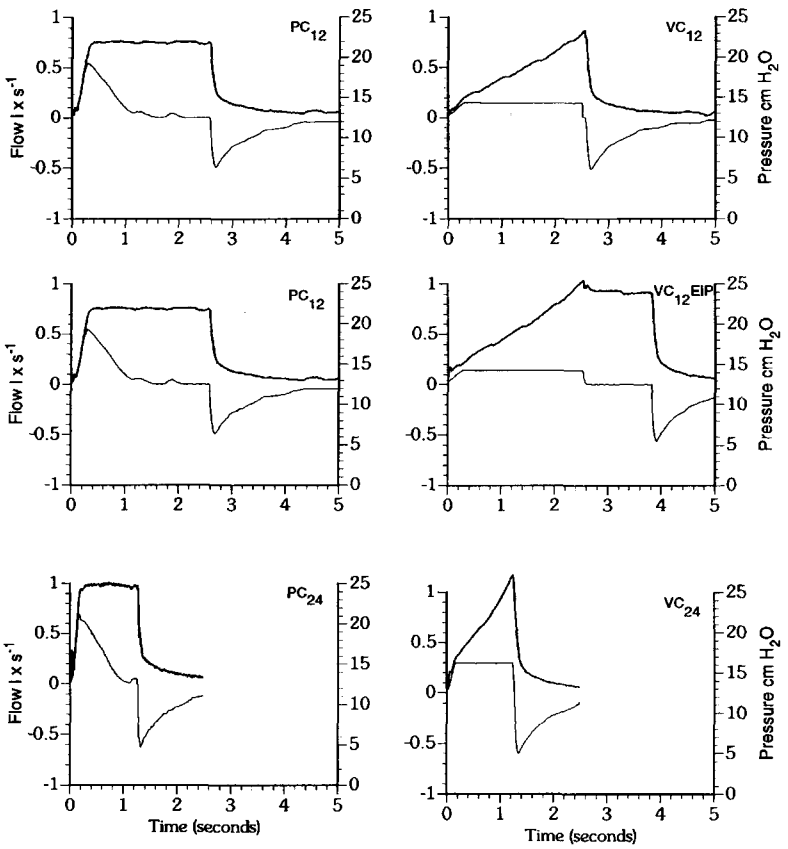

Figure 1

Recordings of ventilatory cycles in one of the piglets with a PEEP level of 13 cmH_2O and tidal volume kept constant. *Top*; decelerating inspiratory flow at 12 bpm (PC_{12}) and constant flow at 12 bpm without EIP (VC_{12}). *Centre;* PC_{12} and VC_{12} with end-inspiratory pause (VC_{12}+EIP). *Bottom:* PC_{24} and VC_{24}. These pressure/flow conditions illustrate that, with decelerating flow, the pre-set inspiratory pressure is constant throughout inspiration. With PC_{12}, the no-flow period is 1.25 s and with PC_{24}, 0.3 s. During constant inspiratory flow there is a linear increase in pressure while the tidal volume is delivered. With constant inspiratory flow and an EIP, there is also a linear increase in airway pressure which decreases during the pause/no-flow period. The respiratory cycle at 12 bpm is divided into 2.5s active inspiration, both with and without EIP. By adding the pause of 1.25 s (25%) total inspiration time will be 3.75 s, resulting in an I:E ratio of 3:1.

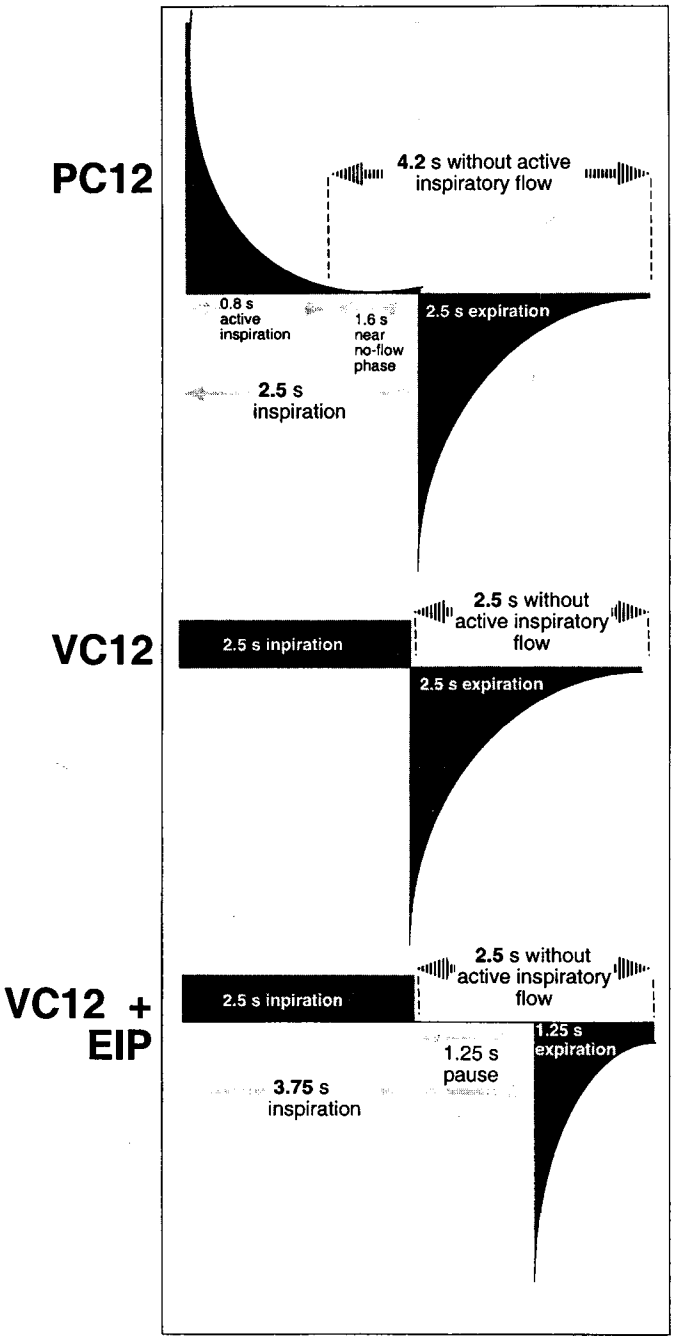

Figure 2.

Schematic drawing of inspiratory and expiratory flow curves with PC_{12} (top), VC_{12} (centre) and VC 12+EIP (bottom). Left side of the panel: inspiratory flow. Right side: expiratory flow. The time (in seconds) during which flow is active, near no-flow as well as pause time are indicated. The total inspiratory time, and the time during which neither active inspiratory flow nor an inspiratory near no-flow (PC_{12}) nor an inspiratory pause (VC_{12}+EIP) exists are also given and labelled as: "without active inspiratory flow".

Mean airway pressure

Mean airway pressure is closely related to certain ventilation settings, and influences haemodynamic function and ventilator-induced barotrauma. Ventilation with decelerating inspiratory flow has always a higher mean airway pressure, since a greater proportion of volume and flow is delivered earlier during the inspiration period than with constant inspiratory flow. Baker et al (2) hypothesised that the combination of increased mean airway pressure, better intrapulmonary gas distribution, and longer diffusion time all accounted for the improved gas exchange with decelerating inspiratory flow.

Constant inspiratory flow with an EIP will also maintain the lung volume and alveolar pressures. The pause adds directly to the mean airway pressure and this will be further accentuated if the pause also causes intrinsic PEEP by shortening expiratory time. This study shows that the mean airway pressure is even higher for the constant flow with EIP.

Constant inspiratory flow with and without an EIP

Irrespective of ventilatory frequency, with decelerating flow $PaCO_2$ was lower and serial dead space reduced, compared with constant inspiratory flow. This could be due either to early delivery of tidal volume, or to the period of no-flow, or to both. Adding an EIP to the constant inspiratory flow precluded assessment of the impact of the early delivery of tidal volume with the decelerating inspiratory flow. Instead, the intention was to obtain similar active inspiration conditions for both inspiratory patterns.

Using constant inspiratory flow with EIP, serial dead space (SDS) was reduced but no statistically significant decrease in $PaCO_2$ could be demonstrated, compared with constant flow without a pause. This finding was unexpected. One reason for the absence of decreased $PaCO_2$ when EIP was added could be related to the fact that the "total time without active inspiratory flow" remains the same as for constant flow without a pause, as illustrated in Fig. 2. With decelerating inspiratory flow, flow takes place mainly during the first 0.8 s, thereafter followed by a no-flow period of 1.7 s before expiration for 2.5 s. The "total time without inspiratory flow" was 4.2 s, which was 2.5 s expiration +1.7 s no-flow period. For constant flow without a pause inspiratory flow was ongoing during 2.5 s , followed by a 2.5 s expiration, yielding a "total time without inspiratory flow" of 2.5 s (expiration). When an EIP was added to the constant flow, the total inspiratory time was prolonged resulting in an I:E 3:1, but the inspiratory flow continues for 2.5 s followed by a pause of 1.25 s during which flow ceases and time of expiration will be only 1.25 s.

Note that, "total time without inspiratory flow" was exactly the same as for constant flow without a pause, viz. 2.5 s expiration 1.25 s + 1.25 s pause.

The above is related to what happens when gas is inspired into the lungs; part of it mixes with the resident gas, while some remains unmixed in the conducting airways (4). This unmixed portion con-stitutes the serial dead space (SDS) because it is in series with the mixed gas in the alveolar region and is only partly determined by anatomical factors. The interface of the distal boundary of the dead space moves up the airway during breathholding and down if flow is increased. The SDS is reduced when the flow rate at changeover from inspiration to expiration slows down and especially if the expiration phase is allowed to start slowly. Time is then allowed for mixing to occur and the interface of gas mixing is allowed to move up the airways.

With decelerating inspiratory flow, initial flow is high and diminishes rapidly, the major part of the tidal volume being delivered after only 0.8 s. During the remaining 1.7 s of inspiratory time, convective flow ceases and hence the distal boundary at which convective flow equals diffusion moves up the airway, resulting in increased $PaCO_2$ elimination. This is in contrast to constant flow both with and without EIP, where flow is ongoing and tidal volume is not delivered until the end of 2.5 s.

In summary, the results of this study corroborate the assumption that total time without active in-spiratory flow is important for arterial CO_2- tension .

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