Intensive Care Med (2002) 28:1742–1749
DOI 10.1007/s00134-002-1522-0

ORIGINAL

Peter Neumann
Wolfgang Golisch
Antje Strohmeyer
Hergen Buscher
Hilmar Burchardi
Michael Sydow

Influence of different release times on spontaneous breathing pattern during airway pressure release ventilation

Received: 26 June 2001
Accepted: 10 September 2002
Published online: 10 October 2002

This study was supported by a grant of the Deutsche Forschungsgemeinschaft (SFB 330; Teilprojekt B17)

P. Neumann (✉) · W. Golisch
A. Strohmeyer · H. Buscher · H. Burchardi
M. Sydow
Department of Anaesthesiology,
Emergency and Intensive Care Medicine,
Georg-August-Universität Göttingen,
Robert Koch Strasse 40,
37075 Göttingen, Germany
e-mail: pneuman@gwdg.de
Tel.: +49-551-398863
Fax: +49-551-398725

Abstract *Objective:* Airway pressure release ventilation (APRV) is a ventilatory mode with a time cycled change between an upper (P_{high}) and lower (P_{low}) airway pressure level. APRV is unique because it allows unrestricted spontaneous breathing throughout the ventilatory cycle. We studied the influence of different release times (time of P_{low}) on breathing pattern and gas exchange in patients during partial mechanical ventilation. *Setting:* Mixed intensive care unit in a university hospital. *Patients:* Twenty-eight patients were included in the study. Nine patients suffering from acute lung injury (ALI), 7 patients with a history of chronic obstructive pulmonary disease (COPD) and 12 patients with nearly normal lung function, ventilated for non-respiratory reasons (postoperatively), were studied prior to extubation. *Interventions:* At constant pressure levels and a pre-set airway pressure release rate of 12/min, P_{low} was diminished and P_{high} was prolonged in four steps of 0.5 s. Each respiratory setting was studied for 20 min after a steady state period had been achieved. *Measurements and main results:* We measured gas exchange and respiratory mechanics. The different time intervals of P_{high} and P_{low} had only minor effects on the actual spontaneous inspiration and expiration times, but the proportion of spontaneous breathing on total ventilation increased when the duration of P_{low} was decreased. Gas exchange was almost unaffected by the interventions despite a significant increase in mean airway pressure. However, when P_{low} was set to only 0.5 s an increase in $PaCO_2$ occurred in patients with COPD and ALI, probably due to a decrease in mechanical ventilatory support. *Conclusions:* Airway pressure release ventilation is an open system which allows patients to maintain the "time control" over the respiratory cycle independent of the chosen duration for P_{high} and P_{low}.

Keywords Airway pressure release ventilation · Unrestricted spontaneous breathing · Partial mechanical ventilation · Different time intervals · Breathing pattern · Gas exchange

Introduction

Airway pressure release ventilation (APRV) is a pressure-regulated ventilatory mode which was recently introduced by Downs and Stock for ventilatory support of patients with acute respiratory failure (ARF) [1, 2]. APRV is unique because unrestricted spontaneous breathing is possible throughout the whole ventilatory cycle, while mechanical ventilatory support is provided by a time-cycled release of airway pressure (Paw) from an upper (P_{high}) to a lower Paw level (P_{low}). Compared to controlled mechanical ventilation, APRV has been shown to improve gas exchange in acute lung injury (ALI) in clinical [3, 4, 5] and experimental [6, 7, 8]

Table 1 Patient characteristics (*ALI* acute lung injury, *COPD* chronic obstructive pulmonary disease, *NSP* non-specific pathology)

Group	Number of patients	Female/male	Age (years)	Days on ventilation	FIO_2	PaO_2/FIO_2 (mmHg)
All patients	28	4/24	47±19	9.3±7.6	0.37±0.06	296±95
ALI	9	2/7	34±14	8.3±3.7	0.39±0.06	251±67
COPD	7	0/7	66±12	7.3±6.4	0.39±0.06	255±70
NSP	12	2/10	44±17	11.6±10.3	0.35±0.05	359±97

studies. However, the release of Paw from P_{high} to P_{low} may provoke lung collapse in regions with short time constants, since atelectasis can develop rapidly within seconds when Paw decreases below a critical value [9, 10]. Consequently, the shortest possible expiratory time interval which ensures a sufficient gas exchange and an adequate mechanical ventilatory support should be used during APRV in order to avoid cyclic alveolar closing and reopening in patients suffering from acute respiratory disease syndrome (ARDS) or ALI [11]. So far only little is known about how a progressive decrease of the release time affects the breathing pattern and subsequently the gas exchange in spontaneously breathing patients. Thus, in the present study we investigated the influence of various release times in mechanically ventilated patients with ARF due to different causes or patients with a normal lung function ventilated postoperatively.

Methods

Patients

After approval by the local ethics committee, informed consent to participate in the study was obtained from 28 patients or their nearest relatives. At the time of the study all patients required partial mechanical ventilatory support for different reasons: nine patients suffered from ALI as defined by the American-European Consensus Conference [11]. Seven patients had a history of chronic obstructive pulmonary disease (COPD) and were ventilated after major surgical procedures or because of respiratory failure due to bronchopulmonary infection. These patients received a standard bronchodilation therapy with inhalation of beta-adrenergic substances and an intravenous infusion of theophylline. At the time of the study none of these patients had clinical signs of bronchospasm. All of these patients were in states of weaning from mechanical ventilation. The remaining 12 patients with normal lung function or minor "non-specific pathology" (NSP), e.g. small atelectasis or pleural effusion, were ventilated for non-respiratory reasons (e.g. postoperatively) and studied prior to extubation (see Table 1 for patients characteristics).

All patients were studied in a semi-recumbent position of approximately 45°. Prior to the study, inspiratory pressure support or APRV, adjusted to individual needs by the attending physician, were used for ventilatory support. As part of their standard monitoring, all patients had an arterial line which was used for arterial blood gas sampling. A nasogastric balloon catheter (Mallinckrodt, Argyle, N.Y., USA) was inserted to measure oesophageal pressure (Peso) as an equivalent for pleural pressure. The position of the catheter was verified by an occlusion test [12]. Study exclusion criteria were age under 18 years, inability to breath spontaneously, bronchopulmonary leakage, cardiocirculatory instability and elevated intracranial pressure higher than 15 mmHg.

Interventions

Airway pressure release ventilation was performed with the EVITA 1 ventilator with a demand-valve trigger system (Dräger, Lübeck, Germany) in the BIPAP mode. The specific APRV settings were adjusted individually for each patient in the following way: the lower airway pressure (P_{low}) was always set at 5 cmH_2O, and if necessary the FIO_2 was increased so that the displayed arterial oxygen saturation remained above 90%. Thereafter the FIO_2 was kept constant throughout the study. The duration of the ventilator cycle, referred to as T_{high} for the upper airway pressure (P_{high}) and T_{low} for P_{low}, was set at 2.5 s, corresponding to a cycle rate given by the ventilator of 12 min^{-1}. Then P_{high} was stepwise increased until the patient stopped breathing spontaneously, indicated by the absence of major negative pressure swings in the oesophageal pressure curve in combination with a typical flow curve of pressure-controlled ventilation. Thereafter, P_{high} was reduced by 25% in order to provide less mechanical ventilatory support and, thereby, to induce spontaneous breathing. The ventilator setting obtained in this way was the first to be measured and the resulting individual pressure difference (P_{high}–P_{low}) as well as the pressure release rate of 12/min remained unchanged during the entire study period.

After this first measurement, T_{low} was diminished in steps of 0.5 s and T_{high} was simultaneously prolonged in steps of 0.5 s. Thus, five different settings of T_{high} and T_{low} were studied:

1. T_{high} 2.5 s/ T_{low} 2.5 s,
2. T_{high} 3.0 s/ T_{low} 2.0 s,
3. T_{high} 3.5 s/ T_{low} 1.5 s,
4. T_{high} 4.0 s/ T_{low} 1.0 s,
5. T_{high} 4.5 s/ T_{low} 0.5 s.

Since the EVITA 1 ventilator allows the patient to trigger the change of airway pressure during the last 25% of the pre-set time interval, the actual time intervals T_{high} and T_{low} may vary slightly according to the respiratory drive of the patient.

Respiratory parameters

Respiratory flow was measured with a heated pneumotachograph (Fleisch No. 2, Lausanne, Switzerland) at the proximal end of the endotracheal tube. The calibration procedure was described in detail elsewhere [3]. Paw was measured at the same position. All pressure lines were connected to the same type of differential pressure transducers (Huba Control, Würenlos, Switzerland). Data were sampled via an analogue-digital converter (DT 2801-a, Data Translation, Marlboro, Mass., USA) at a rate of 20 Hz, processed and stored on an IBM compatible PC for off-line analysis. The software for data acquisition and evaluation was programmed using a commercially available software tool (ASYST 4.0, Asyst software technologies, Rochester, N.Y., USA). Tidal volume (V_t), minute volume (V_e) and mean airway pressure (Paw_{mean}) were calculated by integration of the respective signals.

Variables such as minimal and maximal airway pressures were obtained from the pressure signal over a period of 5 min. Transpulmonary pressure (P_{tp}) was calculated as the difference between Peso and Paw. Since Peso is not equivalent to absolute values of

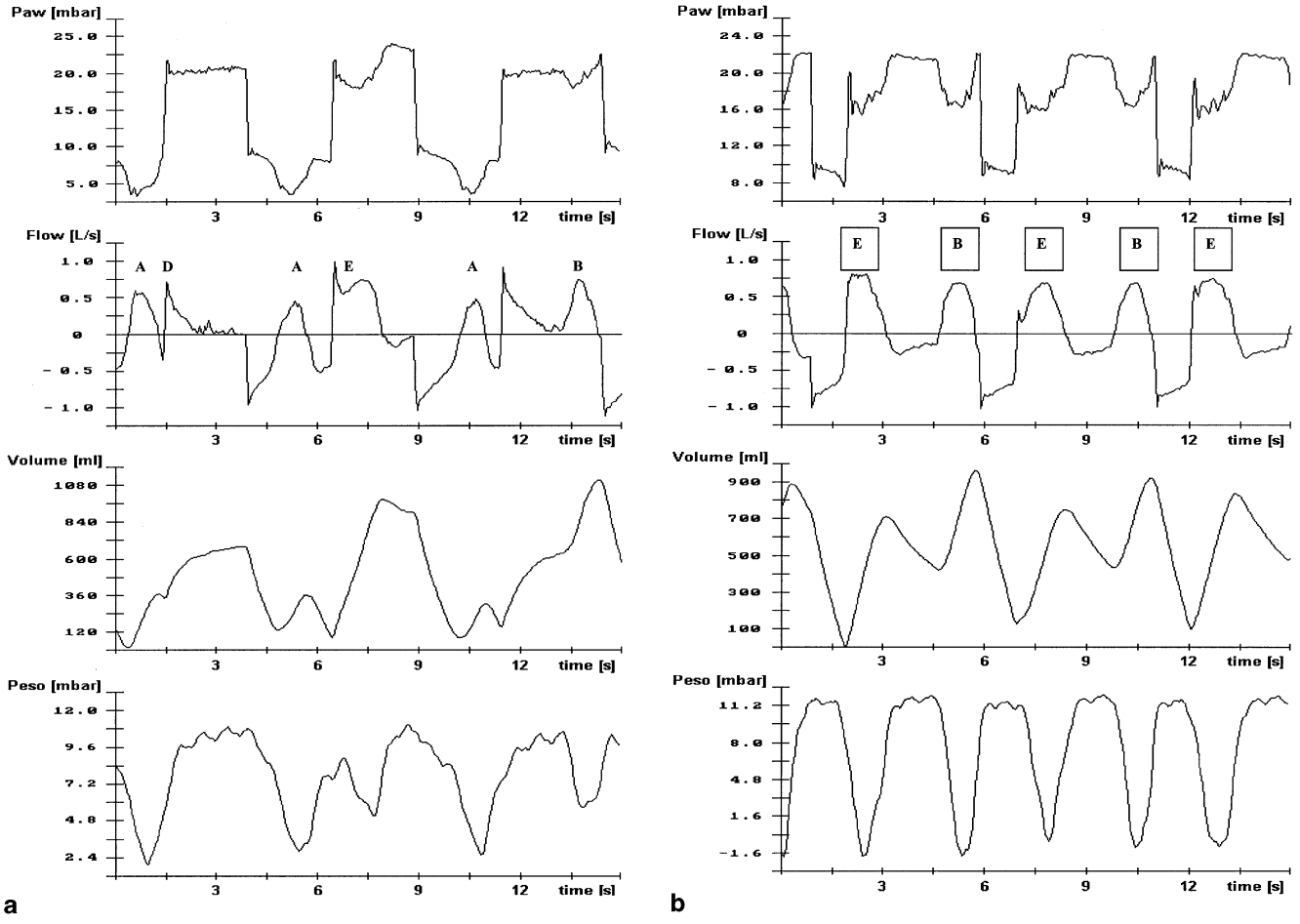

Fig. 1 Airway pressure release ventilation original tracings. A synopsis of airway pressure (Paw), flow, volume and oesophageal pressure (Peso) is shown for (*panel 1a*) time intervals of the upper (P_{high}) and lower airway pressure (P_{low}) set to 2.5 s each, and for (*panel 1b*) time intervals of P_{high} =4.0 s and P_{low} =1.0 s in the same patient. Note, that spontaneous breathing occurred on the upper and lower airway in panel 1a and that tidal volumes varied considerably depending on the pressure level from which an inspiration was started. When P_{low} was decreased to 1.0 s, as shown in panel 1b, spontaneous breaths occurred almost exclusively during P_{high}. This resulted in a more regular breathing pattern as compared to panel 1a. In addition, end-expiratory airway pressure in panel 1b is in the range between 8 and 9 mbar although P_{low} was set to 5 mbar. This indicates incomplete expiration which can also be detected as end-expiratory rest-flow. Breaths were classified as: Type A: spontaneous breath on the lower pressure level, Type B: spontaneous breath on the upper pressure level, Type C: the pressure increase from the lower to the upper pressure level was triggered by an inspiratory effort of the patient, Type D: mechanical breath, Type E: combined mechanical and spontaneous inspiration without a triggered pressure increase from P_{low} to P_{high}

pleural pressure, only the differences of P_{tp} (DP_{tp}) as compared to the ventilatory setting 1 (T_{high} 2.5 s/ T_{low} 2.5 s) are presented below. The spontaneous respiratory rate was calculated from the Peso tracing. Inspiratory and expiratory times as well as the duty-cycle (T_i/T_{tot}) were calculated from the flow signals. During spontaneous breathing in the APRV mode, passive exhalation may not necessarily result in an expiratory flow when the respirator starts a pressure increase from P_{low} to P_{high} exactly at the same moment as the patient wants to exhale. Therefore, inspiratory and expiratory time intervals could not be extracted solely from the flow curve. The individual duty-cycle (T_i/T_{tot}) was consequently determined by visual inspection of flow and Peso tracings. Since this visual interpretation might be somewhat arbitrary, it was independently performed by two investigators.

Measurements of each ventilatory setting were performed for 5min periods after a steady state of the respiratory pattern had been observed (at least 20 min). Blood gas samples were taken after each measurement. All variables were calculated as the average of 5 min per ventilatory setting after exclusion of artifacts such as swallowing or coughing.

The patient-ventilator interaction during APRV may result in different types of spontaneous, mechanical or combined breaths. According to Calzia [13] breaths can be classified as:

Type A spontaneous breath on the lower pressure level
Type B spontaneous breath on the higher pressure level
Type C triggered increase from P_{low} to P_{high}
Type D passive mechanical breath

Using this classification, we categorised each breath during a 5min period by visual inspection of the flow, airway pressure and oesophageal pressure tracings. In order to determine if an inspiratory effort of the patient triggered a change from P_{low} to P_{high}, the time interval of T_{low} was measured. Breaths which occurred as a combination of a spontaneous inspiration together with a pressure increase from P_{low} to P_{high} but which were not triggered, as indicated by a normal interval of T_{low} were classified as a *Type E* breath (see Fig. 1a).

Statistics

Data are presented as means ± SD if not stated otherwise. A two-way analysis of variance (ANOVA) was used for statistical analysis, followed by post hoc testing with Scheffé's test for multiple comparisons. Due to the small sample size, additional non-parametric testing (Friedman-ANOVA for repeated measurements and Kruskal-Wallis-ANOVA for differences among patient groups) was performed for all results found to be significant by parametric testing. Probability values (p) less than 0.05 were considered to be significant. The results are presented to be significant if this was shown by parametric testing. In case parametric and non-parametric testing yielded conflicting results ($p<0.05$ for a parametric test but $p>0.05$ for the non-parametric test) this was explicitly stated in the text. Calculations were performed with the STATISTICA software package (Statsoft, Tulsa, Okla.) on a personal computer.

Results

The main results for all patients are given in Table 2. The progressive diminution of T_{low} and prolongation of T_{high} caused a significant increase of Paw_{mean} and Paw_{min} in all patient groups. Since P_{high} was kept constant throughout the study, Paw_{max} was constant as well. V_e was unaffected by the changes of T_{low} although V_t decreased when T_{low} became shorter than 1.5 s. This was, however, compensated by a parallel increase of the spontaneous respiratory rate. Increasing spontaneous breathing activity associated with less mechanical ventilatory support when T_{low} was shortened resulted in a significant increase of the mean P_{tp}. An original registration of flow, Paw and Peso during the APRV settings 2.5 s/2.5 s and 4.0 s/1.0 s is shown in Fig. 1a and 1b, respectively. Even though the influence of T_{high} and T_{low} on the inspiration time (T_i) and expiration time (T_e) was marginal, less variation of V_t was observed when T_{low} was decreased (Fig. 2).

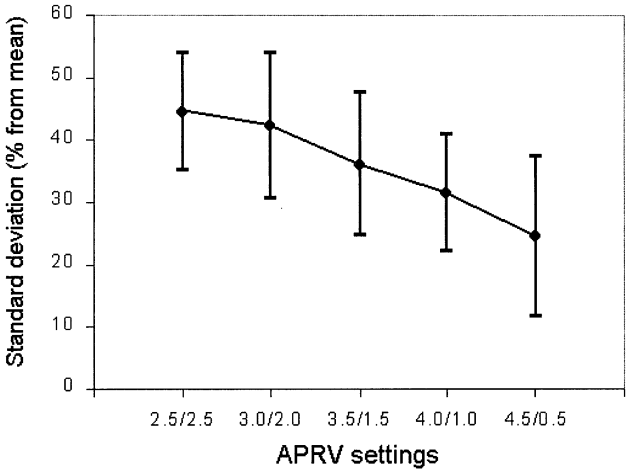

Fig. 2 Variation of tidal volume (V_t) during the airway pressure release ventilation (APRV) settings investigated. The *x-axis* shows the time interval in seconds of the upper (first number) and lower (second number) airway pressures. The *y-axis* shows the standard deviation as percent of the mean V_t during each respiratory setting. Data are given as means ± standard deviation. The variation of Vt decreased with shorter time intervals of the lower airway pressure. As shown in Fig. 1a, V_t differed markedly depending on the pressure level from which inhalation occurred. When the duration of the upper pressure level was increased, more spontaneous breaths occurred during P_{high} and consequently inhaled V_ts became more similar

Table 2 Ventilatory parameters and oxygenation. The upper line represents means ± SD for all patients. The lower line shows the data range. Data of individual patients were averaged over 5min periods during a stable breathing pattern. (*RR* respiratory rate, V_e minute volume, V_t tidal volume, T_e expiratory time, T_i inspiratory time, Paw_{max} peak airway pressure, Paw_{mean} mean airway pressure, Paw_{min} minimal airway pressure, DP_{tp} change of transpulmonary pressure (compared to setting 2.5 s/2.5 s), PaO_2 arterial oxygen partial pressure, $PaCO_2$ arterial carbon dioxide partial pressure)

Setting (T_{high}/T_{low})	2.5 s/2.5 s	3.0 s/2.0 s	3.5 s/1.5 s	4.0 s/1.0 s	4.5 s/0.5 s	
RR (/min)	18.0±4.7 11.9–30.7	19.1±6.0 12.0–33.4	17.8±6.4 11.8–33.0	19.3±7.0 11.9–34.1	22.5±8.0 10.8–46.2	a
V_e (l/min)	11.1±2.8 7.1–18.2	11.3±3.2 7.0–18.5	11.1±3.2 6.5–18.5	11.5±3.4 6.9–19.0	11.5±3.4 6.4–19.1	
V_t (ml)	622±90 463–824	601±100 414–796	619±115 449–913	598±136 230–912	515±122 221–757	a
T_i (s)	1.8±0.5 1.0–2.7	1.8±0.6 0.8–3.1	2.1±0.8 0.8–3.5	1.9±0.9 0.8–3.9	1.4±0.6 0.6–3.2	a
T_e (s)	1.8±0.5 1.0–2.7	1.7±0.5 1.0–2.5	1.7±0.4 1.0–2.8	1.6±0.5 0.8–2.9	1.6±0.6 0.7–3.7	a
Paw_{max} (mbar)	21.5±5.0 12.9–35.1	21.1±4.2 12.9–30.1	21.4±4.4 12.8–30.3	21.3±4.2 13.1–29.9	21.4±4.1 13.9–30.9	b
Paw_{mean} (mbar)	11.6±1.8 8.4–15.9	12.8±2.0 8.8–17.0	14.4±2.5 9.6–20.3	15.8±2.9 10.5–22.0	17.2±3.2 11.2–24.0	a,b
Paw_{min} (mbar)	4.4±0.9 2.7–6.5	5.1±1.1 2.7–7.5	6.1±1.4 3.5–9.1	8.0±1.9 3.7–11.7	10.2±2.1 6.0–14.3	a,b
DP_{tp} (mbar)	0.0 0.0	1.5±1.7 0.2–6.2	2.6±2.7 0.6–6.1	3.1±3.1 1.5–11.2	4.6±0.5 1.7–14.0	a
PaO_2 (mmHg)	109±25 70–169	111±25 76–168	110±23 75–157	112±26 72–164	112±22 72–157	
$PaCO_2$ (mmHg)	40±5 32–50	40±5 32–51	40±5 32–50	41±6 31–54	43±8 31–65	a

[a] significant differences ($p<0.05$) among the ventilatory settings
[b] significant differences ($p<0.05$) among the patient groups

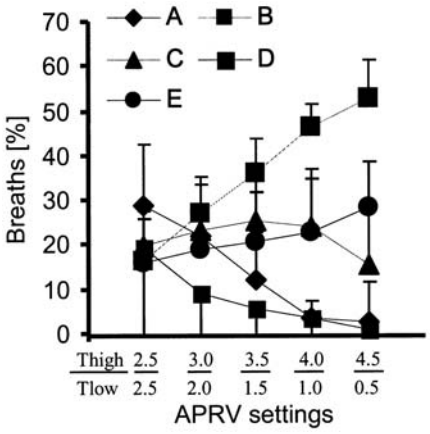

Fig. 3 Type of breaths during the different ventilatory settings. The *x-axis* shows the ventilatory setting, the *y-axis* gives the number of each type of breath in percent of total breaths. Data are shown as means ± SD. Breaths were classified as follows: Type A: spontaneous breath on the lower pressure level, Type B: spontaneous breath on the upper pressure level, Type C: the pressure increase from the lower to the upper pressure level was triggered by an inspiratory effort of the patient, Type D: mechanical breath, Type E: combined mechanical and spontaneous inspiration without a triggered pressure increase from P_{low} to P_{high}

However, the change of T_{high} and T_{low} had a significant impact ($p<0.01$ for the interaction between the respiratory setting and the type of breath) on the type of breaths according to the modified classification proposed by Calzia and co-workers (Fig. 3) [13]. When T_{high} was increased, the number of breaths during P_{high} (type B) increased almost linearly with the prolongation of T_{high} ($p<0.001$ for the difference between all the ventilatory settings), while spontaneous breaths during P_{low} (type A) ($p<0.001$) as well as unsupported mechanical breaths (type D) ($p<0.015$ between T_{low} =2.5 s and T_{low} ≤1.5 s) decreased. Twenty percent of all breaths triggered a pressure increase from P_{low} to P_{high} when T_{low} was set at 2.5 s. With a decrease of T_{low} between 2.0 and 1.0 s, the number of triggered breaths increased to 23–26% and decreased again to 16% when T_{low} was set at 0.5 s (p=0.046 for the difference between T_{low} =1.5 s and T_{low} =0.5 s). When the number of triggered breaths increased, the number of combined spontaneous-mechanical inspirations which were not triggered (type E) decreased and vice versa. No difference among the patient groups (p=0.84) was observed for the interaction between respiratory settings and types of breath.

With regard to gas exchange, changes of T_{high} and T_{low} had only minor effects on oxygenation and carbon dioxide removal (Table 3). In patients with COPD and

Table 3 Ventilatory parameters and oxygenation in patient groups The upper line represents means ± SD, the lower line shows the data range. Data of individual patients were averaged over 5min periods during a stable breathing pattern (*NSP* non-specific pathology, *ALI* acute lung injury, *COPD* chronic obstructive pulmonary disease. For further abbreviations see Table 2)

Setting (T_{high}/T_{low})	2.5 s/2.5 s	3.0 s/2.0 s	3.5 s/1.5 s	4.0 s/1.0 s	4.5 s/0.5 s	
Paw_{mean} (mbar)						
NSP (n=12)	10.8±1.1	12.0±1.4	13.2±1.7	14.6±2.0	15.8±2.3	a
	8.4–12.7	8.8–13.7	9.6–15.8	10.5–17.8	11.2–20.1	
ALI (n=9)	13.5±1.4	15.0±1.2	17.0±1.9	18.9±2.0	20.4±2.4	a
	11.6–15.9	13.8–17.0	14.1–20.3	15.7–22.0	16.7–24.0	
COPD (n=7)	10.6±1.6	11.7±1.7	13.0±1.9	14.1±2.3	15.5±2.3	a
	9.0–13.8	9.8–15.2	10.7–16.7	11.6–18.4	12.5–20.1	
Paw_{min} (mbar)						
NSP	4.5±0.8	4.9±1.0	5.8±1.4	7.4±1.2	9.5±1.4	a
	2.8–5.6	2.7–7.1	3.5–8.7	5.7–9.5	7.2–11.7	
ALI	4.7±0.9	5.8±1.1	7.0±1.4	9.7±1.5	12.2±1.3	a
	3.5–6.5	4.5–7.5	5.2–9.1	6.8–11.7	10.2–14.3	
COPD	3.9±1.1	4.5±1.1	5.4±1.0	7.0±2.1	9.0±2.3	a
	2.7–5.7	3.2–6.5	3.7–6.6	3.7–10.4	6.0–12.2	
PaO_2 (mmHg)						
NSP	125±25	124±24	120±21	123±25	120±17	
	89–169	83–168	82–157	84–164	88–141	
ALI	97±16	100±19	97±17	103±20	106±20	
	74–119	76–128	75–123	72–130	73–128	
COPD	98±23	105±26	114±27	108±36	109±35	
	70–131	81–147	86–149	75–151	72–157	
$PaCO_2$ (mmHg)						
NSP	38±4	38±4	39±4	40±5	40±4	
	32–44	34–44	33–46	31–46	33–46	
ALI	42±6	42±6	43±5	44±5	46±7	a,b
	34–50	32–49	34–50	36–50	31–53	
COPD	39±7	39±7	39±6	40±8	43±13	
	33–50	32–51	32–47	32–54	33–65	

[a] significant differences ($p<0.05$) among the ventilatory settings as tested by a parametric ANOVA
[b] a significant result obtained by parametric testing was not confirmed by non-parametric testing (change of $PaCO_2$ over time in the ALI group: p=0.023 for parametric ANOVA but 0.173 for non-parametric testing using a Friedman-ANOVA)

ALI, the $PaCO_2$ did not change with T_{low} set between 2.5 and 1.5 s, but it increased somewhat in both groups when T_{low} was shortened to 1.0 or 0.5 s, indicating insufficient mechanical ventilatory support in these patients. In patients with NSP, in contrast, the shortened release time had no influence on $PaCO_2$. Interestingly, no significant influence of the ventilatory settings on PaO_2 was found when all the patients were combined, despite the increase of Paw_{mean} and Paw_{min} when T_{low} decreased. However, in ALI patients oxygenation tended to improve (p=0.14) with shorter expiratory time intervals and the resultant increasing Paw_{mean}.

Discussion

The main finding of our study is that patients maintain their "time control" over the respiratory cycle during spontaneous breathing in the APRV mode. Inspiratory and expiratory time intervals were barely influenced by the duration of the upper and lower airway pressures. Thus, the pressure release time does not reflect the actual expiration time during APRV when patients are breathing spontaneously. This may be of importance for the concept of partial mechanical ventilatory support using APRV, because T_{low} can be chosen shorter than the time period necessary for a complete passive exhalation without major effects on V_e. Passive exhalation follows an exponential time course [10]. Consequently, the time period necessary for a nearly complete exhalation can be estimated as 4 times the time constant of the respiratory system (τ) [14].

In support of this concept, Martin and co-workers showed, in an animal model, that minute ventilation and $PaCO_2$ during APRV without spontaneous breathing was stable as long as the expiration time was greater than 4. τ [15]. In patients with acute respiratory failure, τ will be most likely in the range between 0.2 and 1.0 s (compliance approximately 20–50 ml/mbar, resistance approximately 10–20 mbar. s/l) and a passive exhalation will thus last between 0.8 and 4.0 s. However, lung collapse or alveolar flooding has been shown to occur within less than a second when Paw falls below a critical value [9, 10]. In the majority of ventilator-dependent patients, atelectasis may therefore develop during expiration before passive exhalation is complete, unless the lungs are stabilised by high external positive end-expiratory pressure (PEEP) levels. During partial ventilatory support with APRV, in contrast, T_{low} may be set below the time interval of 4. τ without affecting V_e or $PaCO_2$. Thereby cyclic alveolar collapse may be reduced.

Interaction of spontaneous breathing and mechanical ventilation

The driving pressure of pure mechanical breaths (Paw_{max}–Paw_{min}) decreased when T_{low} was reduced. This was caused by an increase of Paw_{min} due to incomplete expirations, indicated by end-expiratory flow, and it resulted in a significant fall of V_t but not of V_e. Thus, patients were able to compensate the reduced mechanical ventilatory support by increasing spontaneous breathing. In support of this assumption, we observed a higher respiratory rate and DP_{tp} when T_{low} was shorter. In addition, a reduction of T_{low} was accompanied by less variation of V_t. With longer release times spontaneous breathing occurred during P_{high} as well as P_{low} (Fig. 3) and V_t differed markedly depending on the pressure level from which inhalation was started (Fig. 1a) or whether a spontaneous inspiration was combined (i.e. supported) by a pressure change from P_{low} to P_{high} or not. With shorter release times, in contrast, spontaneous breaths occurred almost exclusively during P_{high} (Fig. 3) and, in addition, the number of triggered breaths (type C) decreased. Thus, the shorter T_{low} is, the more APRV is similar to CPAP breathing on the upper pressure level.

In the Evita 1 ventilator APRV is not realised as originally described by Stocks and Downs [1], since the changes of airway pressure which occur are not purely time-cycled, but may be triggered by the patient within the last 25% of P_{low} and P_{high}. This has certainly affected the results of the present study, because 15–25% of all breaths were triggered irrespective of the ventilatory settings. Thus, a slightly different breathing pattern may have been observed, if APRV had been perfectly time-cycled in our study. For example, more spontaneous breaths during P_{low} (type A) would most likely have occurred if a change from P_{low} to P_{high} could not have been triggered during the last 25% of T_{low}, and spontaneous inspirations during the phase shift between P_{high} and P_{low} would then all have resulted in type E breaths. Furthermore, the change of Paw_{mean} and Paw_{min} associated with the prolongation of T_{high} was also most likely affected by the trigger, which could potentially have an impact on other results like oxygenation (see below).

Decrease of duration of the ventilator cycle for the lower airway pressure level (T_{low}) and increase of intrapulmonary pressure

If the release time is shorter than 4. τ, alveolar pressure will not equilibrate with ambient pressure or an external PEEP during P_{low}. In this case intrapulmonary pressure is higher than P_{low}, a phenomenon known as hyperinflation or intrinsic PEEP (PEEPi) (for review see [16]). We did not measure hyperinflation, however an end-expiratory rest flow as well as the increase of Peso with decreasing T_{low} indicates increasing lung volume during the release phase and may have the following effects: (1) since APRV is a CPAP system during which the pressure release is a mechanical support of ventilation [1], the mechanical ventilatory support will decrease, (2) in-

creasing intrapulmonary pressure decreases cardiac preload and, thus, might decrease cardiac output. Furthermore, particularly in COPD, increasing lung volume impedes inspiratory muscle activity and might promote respiratory failure. Therefore, the risks and benefits of a short T_{low}, which is potentially associated with an increase in lung volume and decrease in ventilatory support, must be balanced for each individual patient.

Gas exchange

In our patients with mild to moderate respiratory failure the change of the pressure release time had only minor effects on blood gases. This finding was unexpected, since the decrease of T_{low} caused an increase of Paw_{mean} and was associated with increased spontaneous breathing. Paw_{mean} is one important determinant of oxygenation because it is usually closely related to the mean alveolar pressure [17] and interfacing spontaneous breathing and mechanical ventilation in the APRV mode has consistently been shown to improve gas exchange in experimental [7, 8] and clinical [4, 5, 18] conditions of ARF. However, it has also been shown that any improvement in oxygenation may not occur until several hours after changing a respiratory setting in patients with ALI [3]. Thus, the observation period in our study may have been too short to detect the effects of different release times on gas exchange.

In addition, there are several other explanations why we observed only marginal effects of different release times on gas exchange: (1) a lack of power due to the small sample size, (2) an increase of Paw_{mean} due to a sole prolongation of the inspiratory time interval may not always improve gas exchange in ARF [19], (3) in controlled mechanical ventilation oxygenation has been shown to improve when the respiratory rate and tidal volumes were varied throughout ventilation by a computer programme [20], but the breathing pattern became more uniform when T_{high} was prolonged (Figs. 2 and 3), (4) pressure supported breaths have been shown to improve gas exchange less effectively than unsupported spontaneous breaths during APRV [4]. Thus, differences in oxygenation may have been larger among the ventilatory settings in purely time-cycled APRV without the ability to trigger a mechanical inspiration.

In patients with non-specific pathology, $PaCO_2$ remained more or less constant regardless of T_{low}, whereas a moderate increase of the $PaCO_2$ was found in COPD and ALI patients when T_{low} was decreased below 1.5 s. Since the ventilatory settings were not randomised but decreased progressively, a time effect may have influenced these results as well. Nevertheless, the increase of $PaCO_2$ may indicate that ventilatory support was inadequate in patients with a compromised lung function. Thus, if such very short release times are used in critically ill patients, adequate ventilatory support has to be assured. This can either be obtained by an increase of P_{high} to increase the driving pressure of the mechanical breaths or an increase of the release cycles.

Even though we did not observe major adverse affects of a short T_{low} on haemodynamics, ability to breath spontaneously or gas exchange in any of the three patient groups, one has to keep in mind that each ventilatory setting was only used for approximately 30 min. Thus, no conclusion can be drawn about potential long-term effects (e.g. development of respiratory muscle fatigue or improvement of oxygenation) of the respiratory settings used in the present study.

In conclusion, our study demonstrates that APRV is an “open” system which permits a high degree of patient control over the respiratory cycle independent of the pressure release time.

References

1. Stock MC, Downs JB, Frolicher DA (1987) Airway pressure release ventilation. Crit Care Med 15:462–466
2. Stock MC, Downs JB (1987) Airway pressure release ventilation: a new approach to ventilatory support during acute lung injury. Respiratory Care 32:517–521
3. Sydow M, Burchardi H, Ephraim E, Zielmann S, Crozier TA (1994) Long-term effects of two different ventilatory modes on oxygenation in acute lung injury. Comparison of airway pressure release ventilation and volume-controlled inverse ratio ventilation. Am J Respir Crit Care Med 149:1550–1556
4. Putensen C, Mutz NJ, Putensen-Himmer G, Zinserling J (1999) Spontaneous breathing during ventilatory support improves ventilation-perfusion distributions in patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 159:1241–1248
5. Putensen C, Zech S, Wrigge H, Zinserling J, Stüber F, Von Spiegel T, Mutz NJ (2001) Long term effects of spontaneous breathing during ventilatory support in patients with acute lung injury. Am J Respir Crit Care Med 164:43–49
6. Putensen C, Rasanen J, Lopez FA (1995) Interfacing between spontaneous breathing and mechanical ventilation affects ventilation-perfusion distributions in experimental bronchoconstriction. Am J Respir Crit Care Med 151:993–999
7. Putensen C, Rasanen J, Lopez FA (1994) Ventilation-perfusion distributions during mechanical ventilation with superimposed spontaneous breathing in canine lung injury. Am J Respir Crit Care Med 150:101–108
8. Putensen C, Rasanen J, Lopez FA, Downs JB (1994) Effect of interfacing between spontaneous breathing and mechanical cycles on the ventilation-perfusion distribution in canine lung injury. Anesthesiology 81:921–930
9. Neumann P, Berglund JE, Mondejar EF, Magnusson A, Hedenstierna G (1998) Dynamics of lung collapse and recruitment during prolonged breathing in porcine lung injury. J Appl Physiol 85:1533–1543

10. Neumann P, Berglund JE, Mondéjar EF, Magnusson A, Hedenstierna G (1998) Effect of different pressure levels on the dynamics of lung collapse and recruitment in oleic-acid-induced lung injury. Am J Respir Crit Care Med 158:1636–1643
11. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, Lamy M, LeGall JR, Morris A, Spragg R, The Consensus Committee (1994) Report of the American-European consensus conference on ARDS: definitions, mechanisms, relevant outcomes and clinical trial coordination. Intensive Care Med 20:225–232
12. Baydur A, Behrakis PK, Zin WA, Jaeger M, Milic-Emili J (1982) A simple method for assessing the validity of the esophageal balloon technique. Am Rev Respir Dis 126:788–791
13. Calzia E, Lindner KH, Witt S, Schirmer U, Lange H, Stenz R, Georgieff M (1994) Pressure-time product and work of breathing during biphasic continuous positive airway pressure and assisted spontaneous breathing. Am J Respir Crit Care Med 150:904–910
14. Nunn JF (1993) Nunn's applied respiratory physiology. 4:583–593
15. Martin LD, Wetzel RC (1994) Optimal release time during airway pressure release ventilation in neonatal sheep. Crit Care Med 22:486–493
16. Rossi A, Polese G, Brandi G, Conti G (1995) Intrinsic positive end-expiratory pressure (PEEPi). Intensive Care Med 21:522–536
17. Marini JJ, Ravenscraft SA (1992) Mean airway pressure: physiologic determinants and clinical importance – Part 2: Clinical implications. Crit Care Med 20:1604–1616
18. Hormann C, Baum M, Putensen C, Kleinsasser A, Benzer H (1997) Effects of spontaneous breathing with BIPAP on pulmonary gas exchange in patients with ARDS. Acta Anaesthesiol Scand (Suppl) 111:152–155
19. Mercat A, Diehl JL, Michard F, Anguel N, Teboul JL, Labrousse J, Richard C (2001) Extending inspiratory time in acute respiratory distress syndrome. Crit Care Med 29:40–44
20. Lefevre GR, Kowalski SE, Girling LG, Thiessen DB, Mutch WAC (1996) Improved arterial oxygenation after oleic acid lung injury in the pig using a computer-controlled mechanical ventilator. Am J Respir Crit Care Med 154:1567–1572