Improvement of gas exchange during high frequency intermittent oscillation in rabbits

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Objective: Intermittent oscillatory flow has been reported experimentally to improve axial dispersion of respiratory gases by manipulating the flow waveform of oscillatory flow. We clinically investigated the improvement of high-frequency intermittent oscillation (HFIO).
Methods: Seven male rabbits were anesthetized and controlled with conventional ventilation. Arterial blood gas was sampled to analyze PaO_2, $PaCO_2$, and other hemodynamic parameters after conversion to high-frequency oscillation (HFO) or HFIO.
Results: There were no differences in PaO_2 profiles between HFO or HFIO. Arterial CO_2 levels were dependent on the tidal volume and waveforms. At the same tidal volume, HFIO resulted in better CO_2 elimination than did HFO. CO_2 expiration was significantly higher with HFIO.
Conclusions: At a small tidal volume (2.0－2.5 ml/kg), gas exchange on the intermittent waveform is significantly higher than with sinusoidal waveforms. Intermittent waveforms are more efficient than are sinusoidal forms not only under normal conditions but also in the critically diseased lung.

Key words: high-frequency oscillation, high-frequency intermittent oscillation, neonatal respiratory distress

Introduction

It is evident that advances in respiratory care, including development of artificial ventilation methods, have profoundly contributed to the treatment of not only respiratory insufficiency but also the post-surgical management of patients. It has, however, become an issue that artificial ventilation causes complications such as pulmonary barotraumas and bronchopulmonary dysplasia, which greatly affect the prognosis of patients. High-frequency oscillation (HFO) is an excellent artificial ventilation method that was developed to reduce pulmonary barotrauma. This method delivers oscillatory flow of a tidal volume smaller than the anatomical dead space volume into the trachea at a rate of 5－30 Hz. Both inspiration and expiration are active.[1] As anatomical dead space is not considered to directly contribute to gas exchange, the phenomenon that normal ventilation can be performed with delivery of a tidal volume less than the anatomical dead space has attracted considerable attention from the view point of respiratory physiology. This is because it is contradictory to the accepted view that pulmonary gas transport is solely dependent on convection flow.[2] As inspiration and expiration are actively performed with HFO, it is more advantageous compared with other high-frequency ventilation modalities: it reduces the likelihood of air trapping[3] and minimizes respiratory-dependent changes in blood pressure and cerebrospinal pressure.[4] Beginning with the study of Bulter et al.,[5] many clinical studies have reported the efficacious use of HFO, mainly in subjects ranging from newborns with low birth weight to adolescents.[6,7] However, HFO is not always considered to be clinically useful, because there have been some cases in which it does not improve efficiency of gas exchange over that of conventional mechanical ventilation (CV), even in suitable cases. Therefore, its use should be confined to cases whose characteristics are well understood. Axial gas transport is greatly dependent on the ratio of radial mixing to the advection flow in

accelerated dispersion of gases, and this determines the gas transport in HFO.[2,3] Thus, gas transport can be increased if such a ventilation waveform that enhances radial mixing is adopted. Fujioka et al. assessed the axial dispersion of oscillatory flow in a straight tube by using numerical analysis.[8] They demonstrated that interpolation of a stationary phase in the phases in which dispersed molecules moved at the maximum rate increased its axial transport, with a 1.5- to 2.2-fold increase in the effective diffusivity under ventilation conditions where HFO was clinically used.[8] Furthermore, Tanaka et al. demonstrated improvement of axial dispersion by intermittent oscillatory flow in a multi-branched duct based on experimental results obtained with a straight tube and a bronchopulmonary model.[9,10] Tanaka et al. also measured the arterial CO_2 pressure and expired CO_2 concentration during high-frequency intermittent oscillatory flow in rabbits to verify the intermittent augmentation effect on gas exchange from the point of mechanical engineering.[11] The present investigation was conducted to assess the improvement of gas transport from the clinical point of view by the application of high-frequency intermittent oscillation (HFIO) to live animals in which a stationary phase was interpolated in sinusoidal waves used in HFO.

Subjects and Methods

Experimental animals

Rabbits were used in this study because of their similarities in makeup and pulmonary structure to those of human newborns. Their mean body weight was 3.01 ± 0.36 kg (mean ± SD, n = 7). Male rabbits were used throughout the study to avoid the metabolic influences produced by the changes in hormonal conditions in females.

Apparatus

Respiratory circuit: The experimental system is shown schematically in Figure 1. The flow line between a piston generating oscillatory flow and the living body was constructed with hard acrylic tubing and designed to minimize bending and changes in tube caliber and, thereby, to avoid loss of oscillatory components. An electromagnetic vibration generator was used to generate oscillatory flow. Connecting the generator to the piston enabled the output of sinusoidal flow or arbitrary intermittent flow. Displacement of the piston was measured by a laser displacement sensor, and sinusoidal flow and intermittent flow were adjusted and maintained
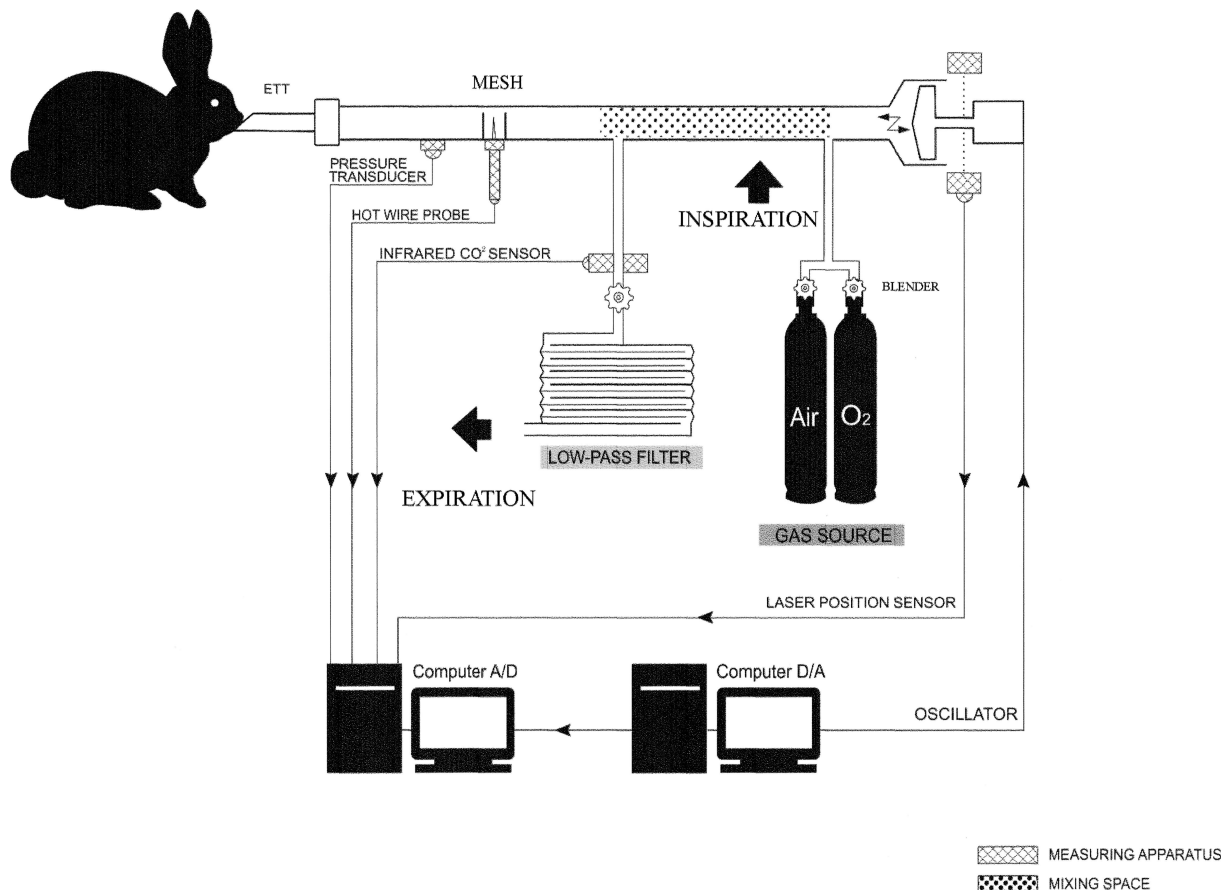

Figure 1. Respiratory circuit of high-frequency intermittent oscillation

in their correct forms by monitoring stroke displacement. Disturbance of ventilation in this artificial respirator was reduced by minimizing anatomical dead space (20 ml) and maximizing a mixing space of inspired gas and fresh air (180 ml). Oxygen supply and carbon dioxide removal were achieved by filling a part of the circuit with fresh air introduced at a constant flow rate (10 l/min) into the circuit. To suppress the loss of oscillatory components and deformation of waveforms by introduction of the constant flow, a low cut filter was placed at the exit port.

Measuring instruments: Ventilation volume was calculated from the flow speed measured by a hot wire anemometer probe. Mesh screens were placed 10 mm anterior and posterior to the probe to generate homogeneous disturbance of the flow across the cross sectional area of the tube to ensure that flow volume could be calculated from the flow speed measured at the center. Airway pressure was measured by a semiconductor pressure transducer. Concentrations of carbon dioxide in expired gas were measured by a far-infrared absorption carbon dioxide sensor. Blood pressure and electrocardiograph were continuously monitored using a polygraph. Concentrations of gases in blood samples were measured by blood gas analyzers (ABL505/OSM3 Radiometer A/S, Denmark).

Experimental procedures
Anesthesia and preparation for experiment: Seven male rabbits were used. Anesthesia was introduced with an injection of pentobarbital sodium (Nembutal®) into the ear vein at an initial dose of 30 mg/kg. Skin hair on the thigh and the neck of a rabbit were then removed and the rabbit was fixed onto a surgical table. After confirming a sufficient degree of anesthesia, a tracheal section was made, and the rabbit was intubated with a 4.5-mm diameter endotracheal tube fixed tightly to prevent air leakage. A muscle relaxant, pancuronium bromide (1 mg), was then injected intravenously to stop spontaneous respiration completely, and catheters were inserted into the femoral artery to collect blood samples and measure blood pressure. After intubation, ventilation was maintained by CV under the following conditions: fractional concentration of oxygen in inspired gas (FiO_2), 0.36; tidal volume (Vt), 10 ml/kg; and frequency of ventilation (f), 25－30 bpm. The rabbits were maintained with CV to stabilize their metabolism and hemodynamics for 10－20 minutes and blood was then collected to determine the basal values of measurement parameters.

Shift from CV to HFO or HFIO: The ventilation mode was switched from CV to HFO or to HFIO by exchanging endotracheal tubes and sustained inflation (SI) was then carried out for about 30 seconds to minimize the influence of switching. SI is a procedure in which airway pressure is maintained higher than usual (20－30 cmH_2O or about 10 cmH_2O higher than the mean airway pressure) for 15－20 seconds to correct the P-V curve, keep pulmonary alveoli open, and facilitate ventilation. It is an effective way for rapid and sustained optimization of gas exchange during HFO.[11] After SI, the tidal volume and mean airway pressure were adjusted. As changes in these two parameters affected each other, they were adjusted several times to control the ventilation conditions, a procedure which took 1－2 minutes.

Measurements during HFO and HFIO: During HFO and HFIO, oscillation frequency and FiO_2 were kept constant at 15 Hz and 0.36, respectively. In the experiments with HFO and HFIO, which were performed at Vts of 2.0, 2.5, or 3.0 ml/kg, blood gases and other parameters were measured 5 minutes, 10 minutes, and every 10 minutes thereafter, following introduction of HFO or HFIO, for not more than 30 minutes if the hemodynamics were stable. If hemodynamic parameters markedly worsened, the ventilation mode was returned to CV. The intermittent ratio (τ) during HFIO was set to 1/2 based on results of previous numerical analysis[8] and experiments in animal models.[9] However, one such study demonstrated that ventilation efficiency was maximal when t was 1/4.[8] This was because collapse of the airway, due to excessive negative pressure around the main and other bronchi caused by shortening of the advection period, was expected under these conditions. After a series of measurements under one ventilation condition was completed, the rabbit was ventilated by CV for 10－20 minutes to stabilize respiratory and hemodynamic parameters. Subsequently, the next series of measurements under the other ventilation condition was started. To avoid an order effect, the series of measurements under different ventilation conditions were performed in a random order. Furthermore, the extracellular fluid was continuously infused to reduce the influence of frequent blood sampling, and body temperature was maintained with a heater to prevent anesthesia-dependent hypothermia caused by decreased metabolism.

Experiment with the lavaged lung-a model of respiratory distress syndrome
Lachmann et al. developed an experimental model of the respiratory distress syndrome (RDS) in which alveolar

surfactant phospholipids were removed by lung lavage with physiological saline.[13] To examine the improvement of gas exchange capacity with HFO or HFIO in the severely diseased lung, experiments were conducted in rabbits subjected to lung lavage. Physiological saline was infused under hydrostatic pressure (about 10 cmH$_2$O) to prevent excessive positive pressure. Lavage fluid was also carefully suctioned to prevent excessive negative pressure. Lung lavage was performed 5 times, each with 30 ml of physiological saline (150 ml in total). During the lavage, the rabbit was ventilated with the appropriate CV under hyperventilation conditions (FiO$_2$, 1.0; Vt, 12 ml/kg; and f, 50 bpm). The lung lavage took 15－20 minutes. Lung lavage was judged to be achieved if PaO$_2$ decreased to less than 100 mmHg under conditions in which FiO$_2$ was 1.0 following lavage.[14] HFO or HFIO was carried out under the following conditions: oscillation cycle, 15 Hz; FiO$_2$, 1.0; and Vt, 2.5 ml/kg. As it was considered that the diseased lung needed a longer time for recovery, the experimental period was set longer than that for the intact lung.

Results

Arterial oxygen tension (PaO$_2$)
The time course of changes in PaO$_2$ ratio during sinusoidal flow ventilation and intermittent flow ventilation are shown in Figure 2. The continuous horizontal line in the figure represents the mean PaO$_2$ during CV. Changes in PaO$_2$ ratio (PaO$_2$ during intermittent flow ventilation/ PaO$_2$ during sinusoidal flow ventilation) are shown in Figures 3 and 4. When Vt was set to 3.0 ml/kg, PaO$_2$ was slightly higher during sinusoidal flow ventilation than that during CV. However, no differences were found in PaO$_2$ between either ventilation condition when Vt was set to 2.0 ml/kg or 2.5 ml/kg. PaO$_2$ was higher during intermittent flow ventilation than that during sinusoidal flow ventilation when Vt was set to 2.0 ml/kg or 2.5 ml/ kg. In particular, at a Vt of 2.5 ml/kg, PaO$_2$ ratios increased to levels comparable to that during sinusoidal flow ventilation at a Vt of 3.0 ml/kg. These results indicate that oxygenation was better improved by intermittent flow ventilation than by sinusoidal flow ventilation under these conditions. When Vt was set to 3.0 ml/kg, however, there were no differences in PaO$_2$ during intermittent and sinusoidal flow ventilation, and PaO$_2$ ratios were slightly lower than those at a Vt of 2.5 ml/kg. Compared with sinusoidal flow ventilation, the improvement in PaO$_2$ with intermittent flow ventilation depended on Vt values: 2.5 ml/kg >2.0 ml/kg >3.0 ml/kg. These results suggest that intermittent flow ventilation improved oxygenation, though the effect was not statistically significant, probably due to the large inter-individual variation in rabbit metabolic activities.
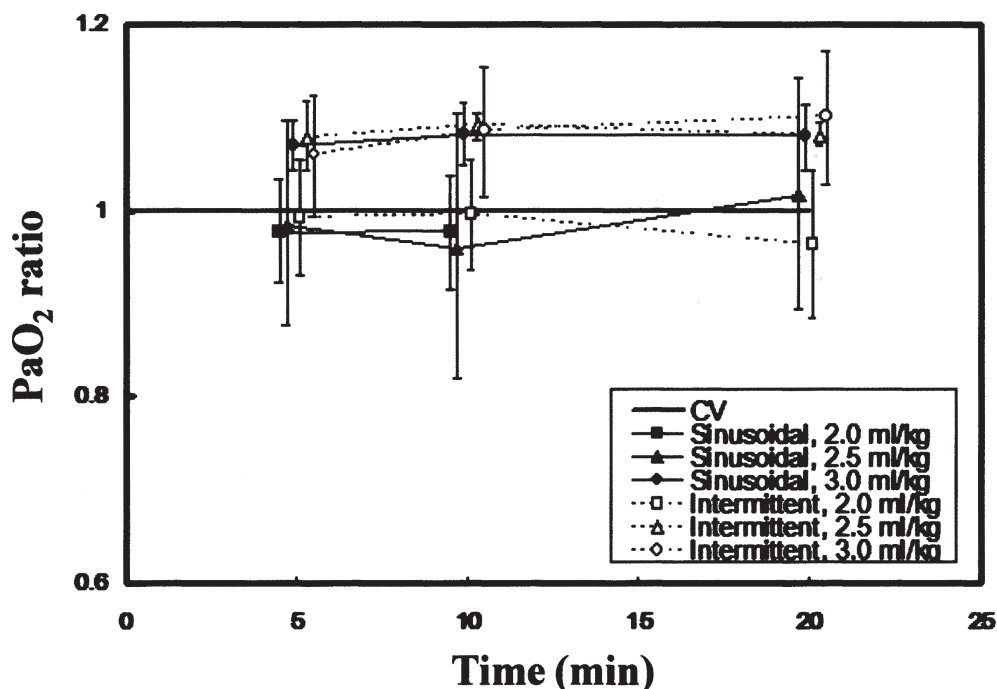

Figure 2. Time course of arterial oxygen tension changes (PaO$_2$ ratio of sinusoidal and intermittent flow to conventional ventilation)

Arterial CO2 tension (PaCO2)

The time course of changes in the PaCO2 ratio during sinusoidal flow ventilation and intermittent flow ventilation are shown in Figure 5, and changes in the PaCO2 ratio (PaCO2 during intermittent flow ventilation/ PaCO2 during sinusoidal flow ventilation) are shown in Figures 6 and 7. During sinusoidal flow ventilation, PaCO2 was lower when Vt was set to 3.0 ml/kg than that during CV. However, it was higher during sinusoidal flow ventilation, with Vts of 2.0 ml/kg and 2.5 ml/kg, than that during CV, indicating retention of carbon dioxide in the blood. It was particularly difficult to continue the experiment for 20 minutes because the animals showed signs of respiratory acidosis with a Vt of 2.0 ml/kg. On the other hand, PaCO2 during intermittent flow ventilation with Vts of 2.0 ml/kg and 2.5 ml/kg was considerably lower than that during sinusoidal flow ventilation. In particular, PaCO2 during intermittent flow ventilation at a Vt of 2.0 ml/kg was lower than that during sinusoidal flow ventilation at a Vt of 2.5 ml/kg (Figures 5, 6). As
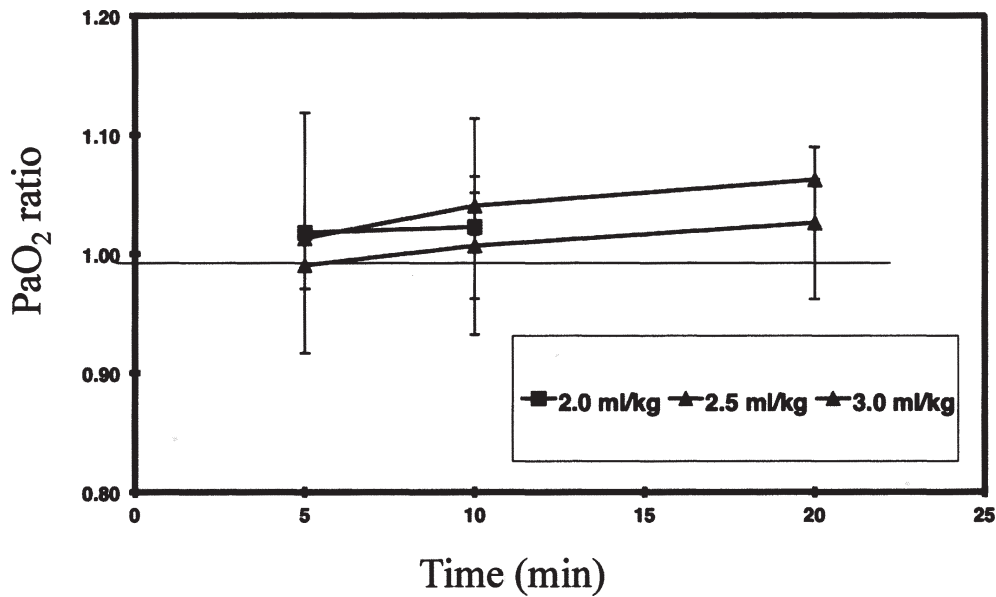

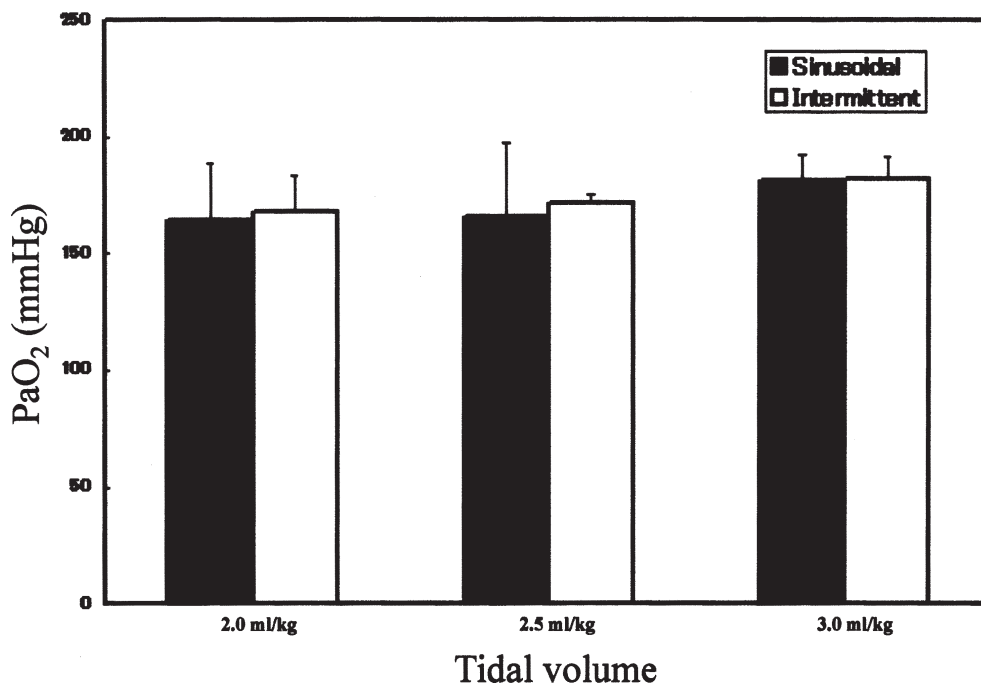**Figure 3.** Time course of change in PaO2 ratio of intermittent flow to sinusoidal flow

Figure 4. PaO2 in sinusoidal and intermittent flow

shown in Figure 7, $PaCO_2$ was most improved at a Vt of 2.0 ml/kg, and $PaCO_2$ during intermittent flow ventilation was 14% lower than that during sinusoidal flow ventilation (P < 0.05). At a Vt of 2.5 ml/kg, $PaCO_2$ was also 10% lower during intermittent flow ventilation than that during sinusoidal flow ventilation (P < 0.05), though $PaCO_2$ at a Vt of 3.0 ml/kg was slightly higher during intermittent flow ventilation. These results indicate that

intermittent flow ventilation dramatically improved gas exchange efficiency over sinusoidal flow ventilation under insufficient ventilation conditions; however, it was very slightly worsened by intermittent flow ventilation at a Vt of 3.0 ml/kg.

CO_2 concentration in expired gas
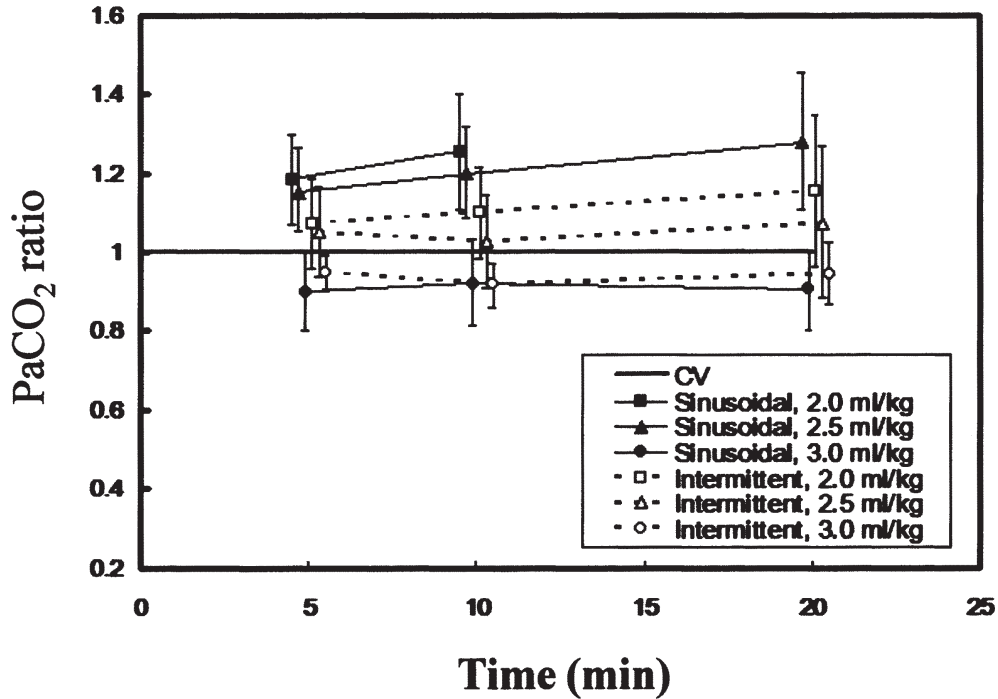
Figure 8 shows the time course of changes in CO_2

Figure 5. Time course of arterial CO_2 tension changes ($PaCO_2$ ratio of sinusoidal and intermittent flow to conventional ventilation)
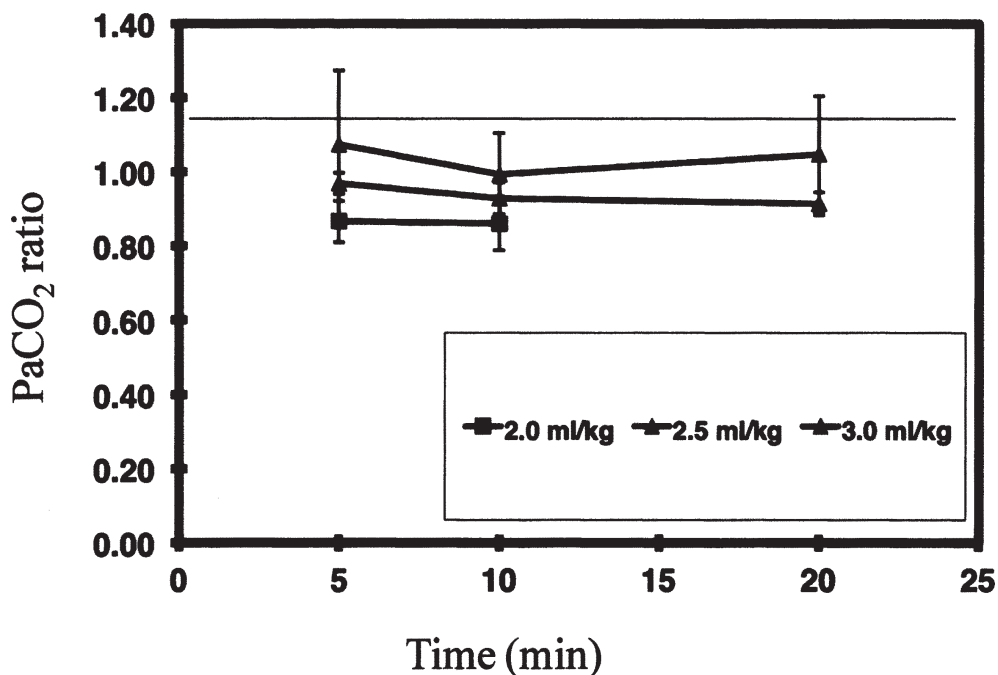

Figure 6. Time course of changes in $PaCO_2$ ratio of intermittent to sinusoidal flow

concentration in expired gas during sinusoidal flow ventilation and intermittent flow ventilation. Figure 9 compares CO_2 concentrations ratio classified by tidal volume between sinusoidal and intermittent flow ventilation, which indicates the improvement in CO_2 expiration with intermittent flow ventilation. Expiratory CO_2 gas concentrations increased with increasing tidal volume, during both sinusoidal and intermittent flow ventilation. CO_2 concentrations in expired gas were inversely related to $PaCO_2$.

Arterial pH and acid-base balance
The time course of changes in pH during sinusoidal flow ventilation and intermittent flow ventilation are shown in Figure 10. The continuous horizontal line in the figure represents the mean pH during CV. pH was higher during
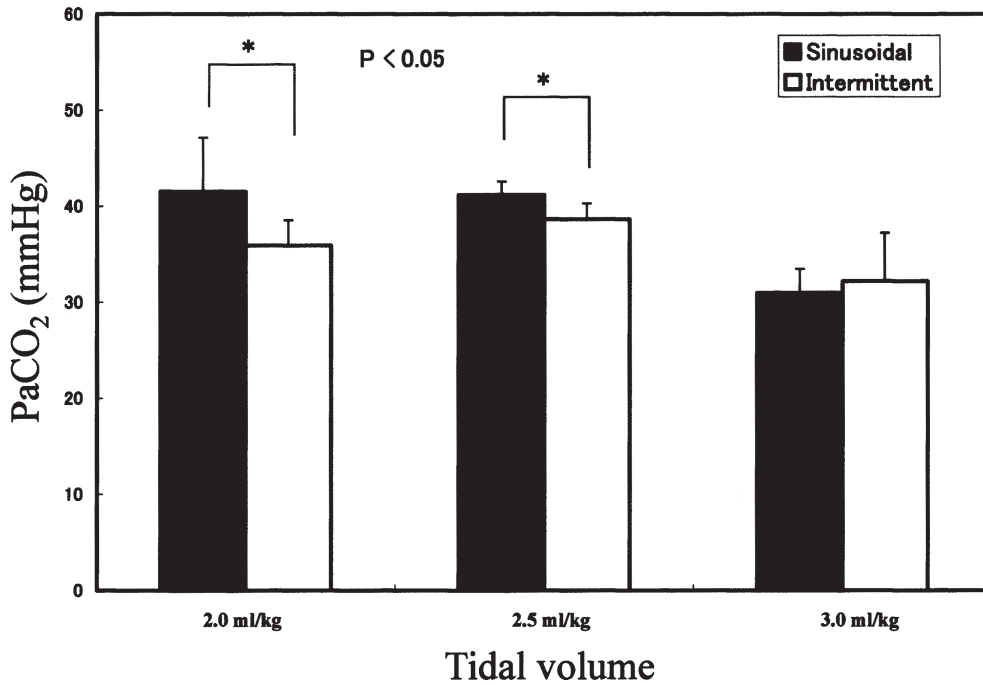

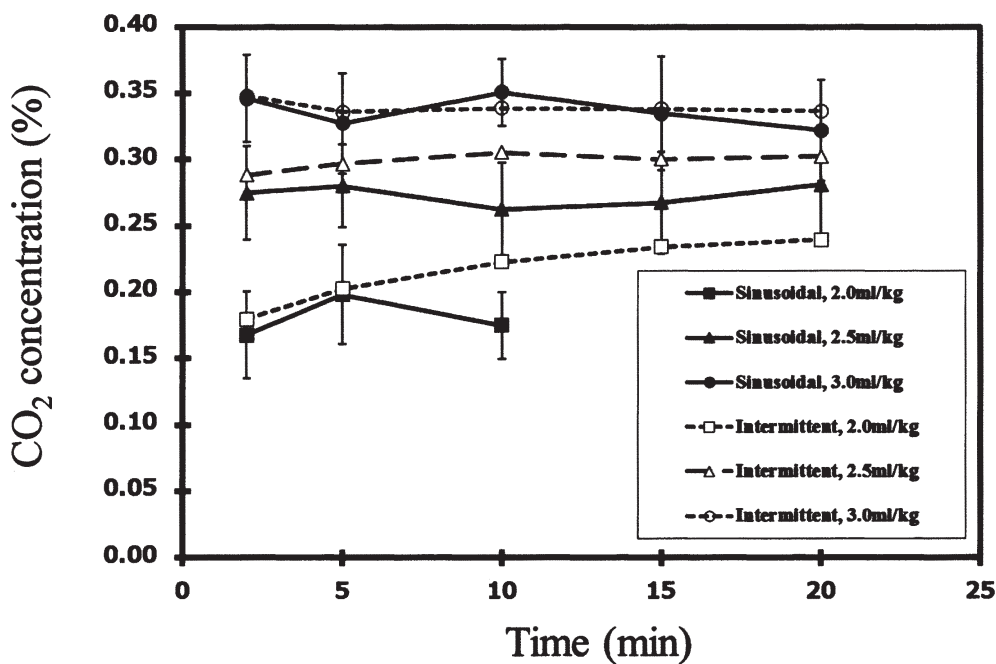**Figure 7.** $PaCO_2$ in sinusoidal and intermittent flow

Figure 8. Time course of expiratory CO_2 concentration changes (sinusoidal and intermittent flow)
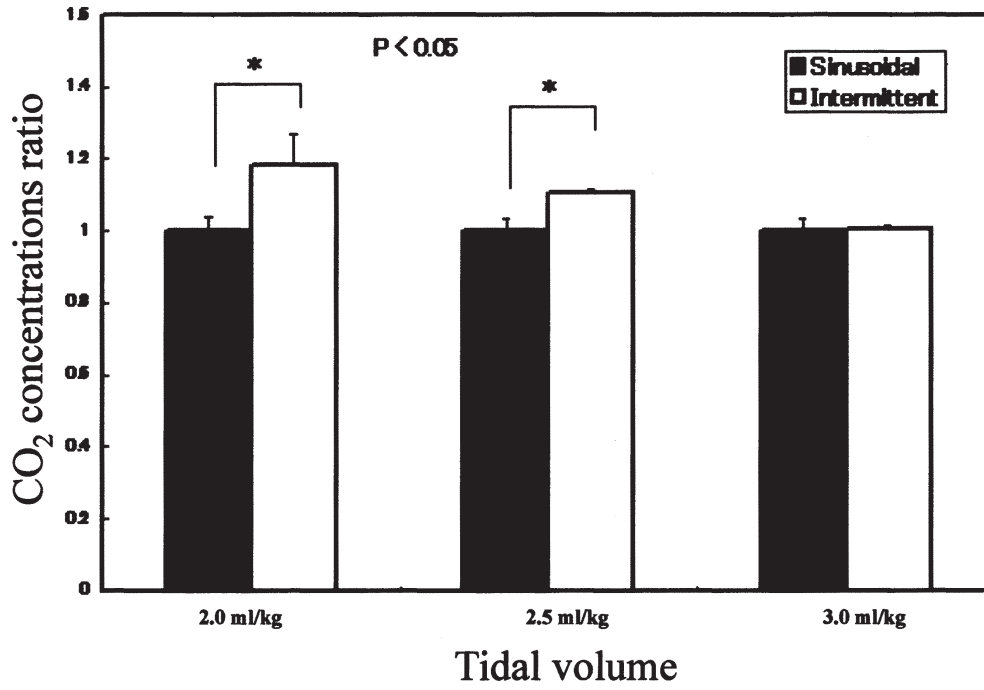
Figure 9. Expiratory CO_2 concentrations ratio of intermittent to sinusoidal flow
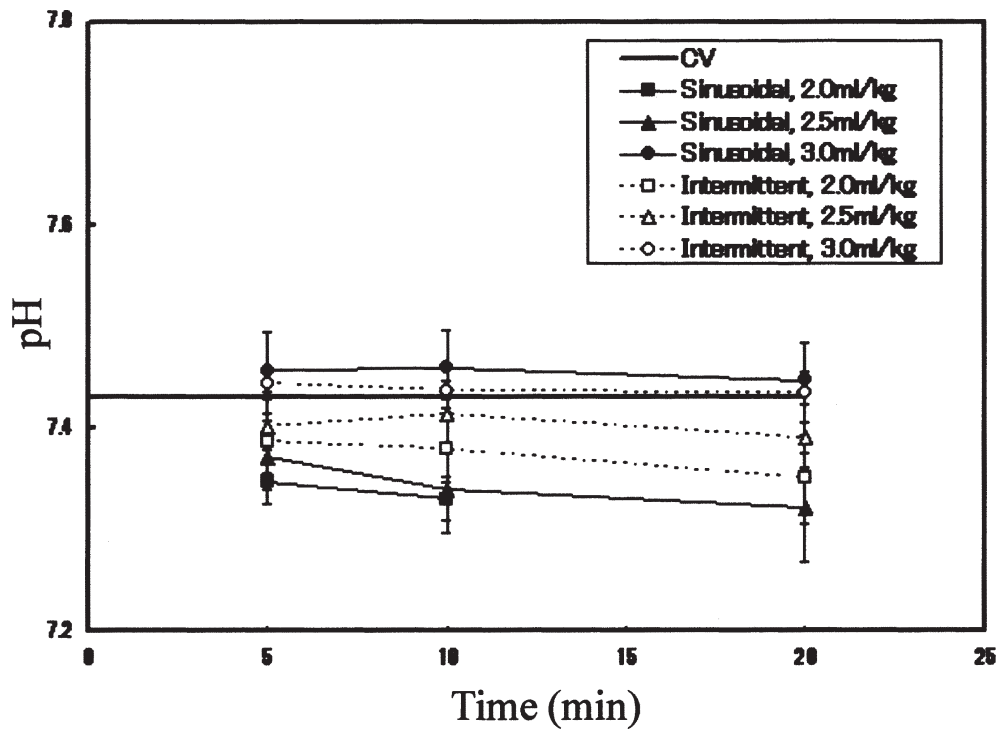

Figure 10. Time course of arterial pH changes (sinusoidal and intermittent flow)
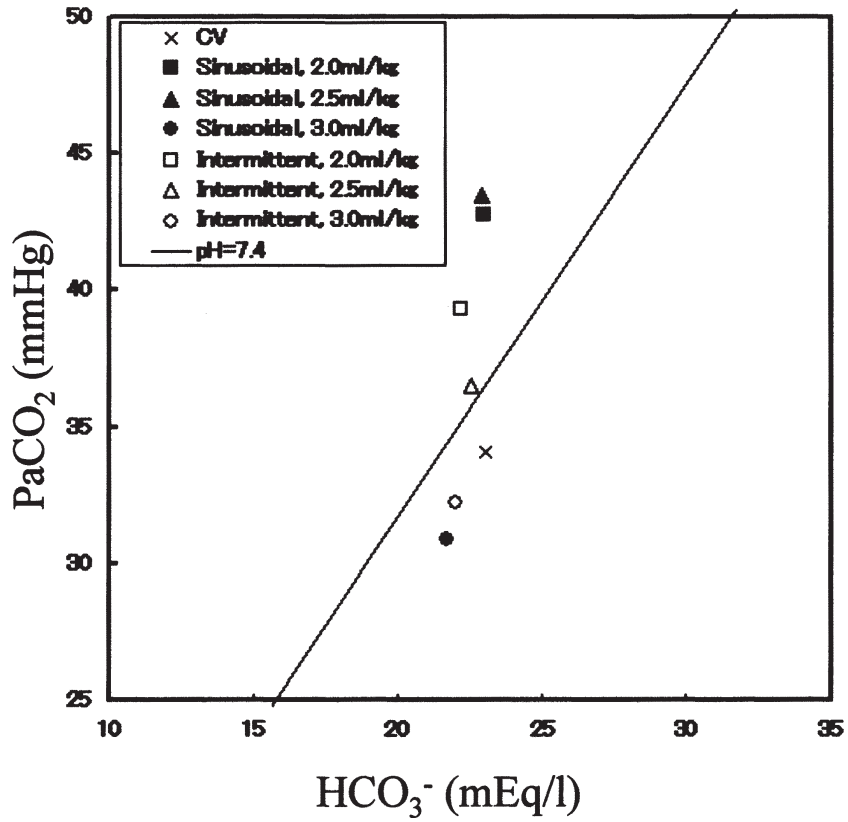
Figure 11. Relationship between arterial HCO₃ concentration and PaCO₂ (sinusoidal and intermittent flow)
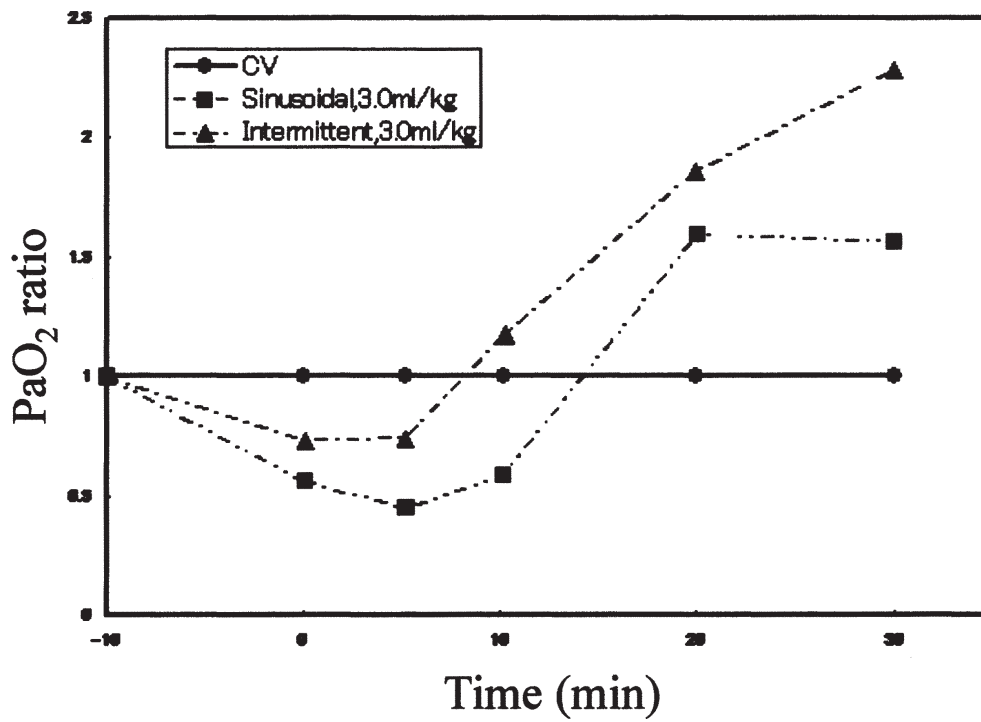

Figure 12. PaO₂ profiles after lung lavage (PaO₂ ratio of sinusoidal and intermittent flow to conventional ventilation)

intermittent flow ventilation than that during sinusoidal flow ventilation when Vt was set to 2.0 ml/kg or 2.5 ml/kg. In particular, pH during intermittent flow ventilation at a Vt of 2.5 ml/kg was about 7.4 and approached to levels comparable to that during CV. When Vt was set to 3.0 ml/kg, however, there were no differences in pH during intermittent and sinusoidal flow ventilation. In this instance, pH in both ventilation conditions exceeds

that during CV. Because sinusoidal flow ventilation is already sufficient, intermittent flow does not have substantial effect.

Figure 11 shows the relationship between arterial HCO_3 concentration and $PaCO_2$ in sinusoidal flow ventilation and intermittent flow ventilation. The solid line represents the condition for a pH of 7.4. The X mark represents the mean value during CV. The plotted data
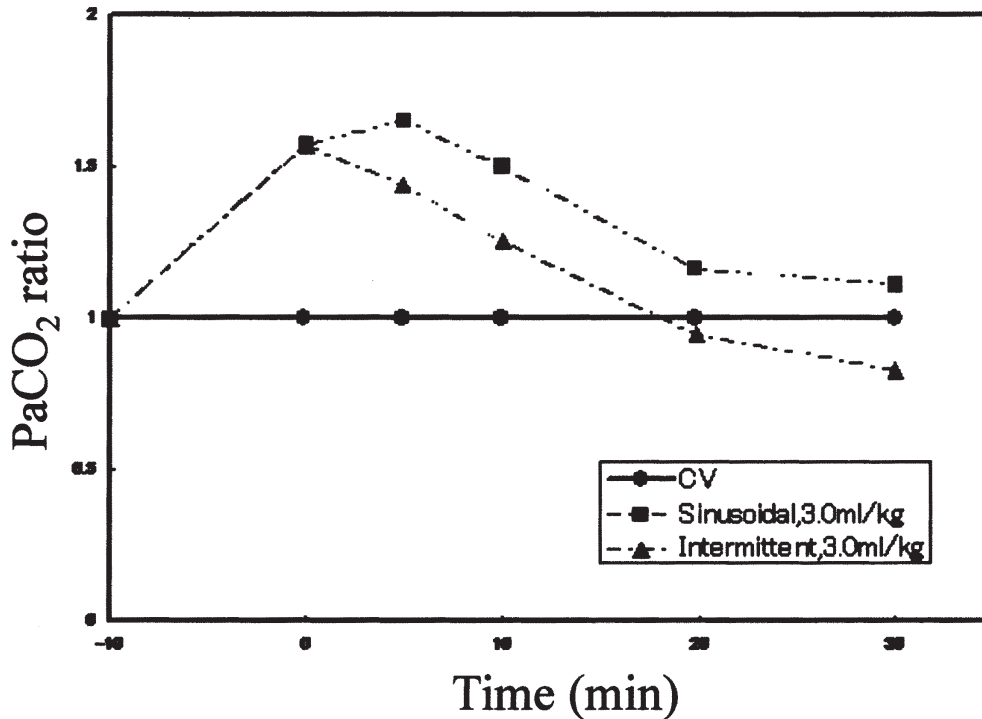

Figure 13. $PaCO_2$ profiles after lung lavage ($PaCO_2$ ratio of sinusoidal and intermittent flow to conventional ventilation)
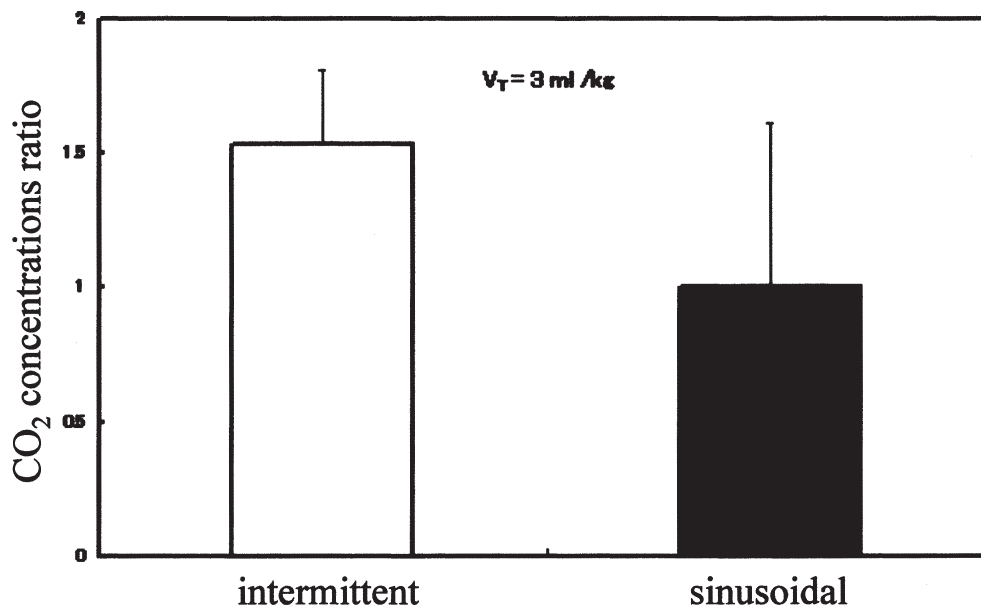

Figure 14. Expiratory CO_2 concentrations ratio of intermittent to sinusoidal flow in lavaged lung

represent the value at 10 minutes in sinusoidal flow ventilation with a Vt of 2.0 ml/kg and those at 20 minutes in the other conditions. As shown in Figure 11B, sinusoidal flow ventilation showed signs of respiratory acidosis with Vts of 2.0 ml/kg and 2.5 ml/kg. On the contrary intermittent flow ventilation showed almost normal conditions with the same Vts. Therefore, the use of intermittent oscillatory flow effectively improves ventilation conditions under insufficient ventilation conditions. On the other hand, CV showed signs of respiratory alkalosis under sufficient ventilation conditions. Also, both the sinusoidal and intermittent flow ventilation showed signs of respiratory alkalosis with Vt of 3.0 ml/kg.

Experiment with lavaged lung: Figures 12 and 13 show the time course of changes in the PaO_2 ratio and the $PaCO_2$ ratio, respectively during artificial ventilation in rabbits subjected to lung lavage. In this experiment, changes in respiratory and hemodynamic parameters were compared between CV and high-frequency oscillatory ventilation under conditions of sinusoidal flow and intermittent flow. PaO_2 in the blood collected at the end of lung lavage was less than 100 mmHg in all the rabbits, indicating that their lung lavage was successfully completed. Under CV, hemodynamics worsened over time after lung lavage, and neither PaO_2 nor $PaCO_2$ recovered throughout the experiment. On the other hand, hemodynamics recovered over time after switching the ventilation mode from CV to sinusoidal flow ventilation or intermittent flow ventilation; under the latter, PaO_2 increased to 80 mmHg, and $PaCO_2$ decreased to 30 mmHg 30 minutes after the start of the experiment.

Discussion

Research on HFO started in Toronto with the objective of developing effective ventilation methods for the fragile lung from the view point of pediatric intensive care management, which has made a significant contribution to neonatal medicine with the completion of the Hummingbird oscillator in 1986.[15] There have been numbers of basic studies on HFO; these demonstrate that, unlike ordinary methods, HFO is an active ventilation method mainly based on gas dispersion. Clinically we have often experienced that, in addition to theoretically established gas exchange, promotion of sputum excretion by vibration improves oxygenation during HFO. Furthermore, HFO is clinically advantageous, because it reduces fighting by enhancement of hypopnea which is attributable to stimulation of the vagal nerves.[5,16]

However, HFO is not always useful, because it cannot show better improvement of gas exchange capacity compared with ordinary CV, even in suitable cases. Therefore, its use should be confined to cases whose characteristics are understood well. Lee concluded from the results of his study that HFO worked to promote dispersion transport by inducing turbulent flow.[17] Furthermore, Fujioka et al. demonstrated that turbulent flow (radial mixing) generated by interpolation of a stationary period in the phase in which dispersion substances move at maximal rate, increased its axial transport.[8] They calculated that effective diffusivity increased by 1.5- to 2.2-fold under ventilation conditions where HFO was clinically used.[8] Tanaka et al. also studied the effect of oscillatory flow on the efficiency of axial dispersion of gases by using a 4th generation multi-branched tube system based on the pulmonary airway model and they demonstrated that axial diffusivity is 1.6 times greater on average in intermittent flow ventilation than that in sinusoidal flow ventilation.[10] As these *in vitro* studies suggested the possible clinical efficacy of intermittent flow ventilation, the present study assessed the *in vivo* efficacy of intermittent flow ventilation in experimental animals.

Arterial oxygen tension: Mean PaO_2 was higher during intermittent flow ventilation than that during sinusoidal flow ventilation in the present study, suggesting the improvement of oxygenation by introduction of intermittent flow. However, the effect was not statistically significant, probably due to great inter-individual variation in animal metabolic activity. As Thompson et al. failed to show a difference in PaO_2 during CV and HFO at an equivalent mean airway pressure in dogs,[18] the effect of HFO may be greatly affected by experimental conditions used. It is considered that statistically significant differences were not found in this study because the oxygen tension in inspired gas was maintained to 0.36, a two-fold higher level than atmospheric pressure.

Arterial carbon dioxide tension: When $PaCO_2$ was compared between ventilation conditions with sinusoidal flow and intermittent flow at equivalent Vts (2.0 ml/kg and 2.5 ml/kg, respectively), $PaCO_2$ during intermittent flow ventilation was significantly lower than that during sinusoidal flow ventilation (Student's t-test). This result also demonstrated a Vt-dependent decrease in $PaCO_2$ that was more evident during intermittent flow ventilation. Tidal volume is generally increased when CO_2 retention is observed during HFO in clinical practice, which we have shown also occurs with intermittent flow ventilation.

CO_2 concentration in expired gas: During sinusoidal flow ventilation, expiratory CO_2 concentrations were markedly lower at a Vt of 2.0 ml/kg than that at Vts of 2.5 ml/kg and 3.0 ml/kg, which are considered to induce respiratory acidosis. On the other hand, expiratory CO_2 concentrations were higher during intermittent flow ventilation than during sinusoidal flow ventilation. Furthermore, these differences were more evident at smaller Vts, and expiratory CO_2 concentrations were 1.2-fold higher during intermittent flow ventilation than that during sinusoidal flow ventilation at a Vt of 2.0 ml/kg. In common with other parameters, expiratory CO_2 concentrations were markedly improved by intermittent flow ventilation compared with sinusoidal flow ventilation. However, these concentrations were the same or even lower than during sinusoidal flow ventilation at a larger Vt, indicating disappearance of the effect of the difference in ventilation waveform under these conditions.

In lung-intact animals, HFIO improved gas exchange capacity compared with HFO under conditions of small Vt, but this effect disappeared at large Vts. The phenomenon may be largely dependent on the flowing state of gas molecules (flow field) in a tube. Intermittent flow used in the present study was thought to increase the radial mixing of gases (thought to be deficient in sinusoidal flow) and was expected to facilitate molecular dispersion in a stationary period. However, under ventilation conditions of sinusoidal flow at a large Vt, or intermittent flow, the flow field may shift to a turbulent flow, which maximally induces radial mixing. That is, as a boundary layer is not sufficiently formed when the advection flow rate is high, radial mixing hits its ceiling and molecules are not axially dispersed, but move back-and-forth in the same place. Therefore, in the present study, intermittent flow ventilation markedly improved gas exchange capacity when the flow field was laminar, because radial mixing facilitates molecular dispersion in such a condition. On the other hand, the improving effect disappeared when the tidal volume became larger because radial mixing was already maximized in that condition.

As previously mentioned, HFO was originally developed to reduce barotraumas by lowering airway pressure. However, it is required to send the same volume of gases into the airway in a shorter time during HFIO than during HFO because the advection period is shorter in HFIO than it is in HFO. Therefore, air pressure naturally becomes higher during HFIO than it does during HFO. This was observed in the present study. Pressure variations at the outlet of the artificial respirator were larger during HFIO than they were during HFO. Therefore, it is understood that pressure in a relatively

large airway becomes higher during HFIO than it does during HFO. However, there may be little likelihood that large variations of pressure induce barotraumas in relatively large airways because the structures are firmer. Pressure variations are larger during HFO with sinusoidal flow than those during CV. Therefore, it is important to minimize pressure variations in the peripheral airways in cases suitable for HFO. The pressure around the pulmonary alveoli depends on the mean airway pressure and the tidal volume. Moreover, the pressure around the pulmonary alveoli is not directly affected by the pressure in the relatively large airways because oscillatory components are interrupted by repeated bifurcation, and the waveforms become less apparent around the pulmonary alveoli. Therefore, pressure variations around the pulmonary alveoli during intermittent flow ventilation are thought to be the same as or smaller than those during sinusoidal flow ventilation, and this is in spite of greater pressure variations in the relatively large airways during intermittent flow ventilation.

Experiment with the lavaged lung: In the experimental animal model of RDS produced by lung lavage, blood gas parameters were worsened during CV along with the worsening of hemodynamics, so it was difficult to continue the experiment. In HFO, PaO_2 became lower immediately after switching the ventilation mode from CV to other ventilation modes, but it gradually recovered reaching 60 mmHg 30 minutes after switching. During HFO and HFIO, pulmonary functions further recovered thereafter. These results indicate that HFO is effective in improving pulmonary functions even in the diseased lung. In particular, greater improvements of hemodynamics and pulmonary functions are expected with the introduction of intermittent flow as a ventilation waveform due to further facilitation of gas exchange.

Conclusions

These results have demonstrated that the introduction of intermittent flow during high-frequency oscillatory ventilation facilitated gas exchange. Particularly, the improvement of $PaCO_2$ and expiratory CO_2 concentrations were evident. These parameters were improved by up to 20% over those during sinusoidal flow ventilation at equivalent Vts. The extent of facilitation of gas exchange was greater at a smaller Vt, indicating that introduction of intermittent flow makes it possible to carry out ventilation with a smaller ventilation volume. The experiment with the diseased lung model demonstrated that HFO and HFIO were also effective in

this condition, and that HFIO gave greater facilitation of gas exchange than did HFO.

Acknowledgements

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