

Determination of resonance frequency of the respiratory system in respiratory distress syndrome

S Lee, J Alexander, R Blowes, D Ingram, A D Milner

Abstract

Aim—To measure tidal volume delivery produced by high frequency oscillation (HFO) at a range of frequencies including the resonance frequency.

Methods—Eighteen infants with respiratory distress syndrome were recruited (median gestation 28.7 weeks). Each was ventilated at frequencies between 8 and 30 Hertz. Phase analysis was performed at various points of the respiratory cycle. HFO was provided by a variable speed piston device. Resonance frequency was determined from the phase relation between the cyclical movements of the piston and pressure changes at the airway opening. Tidal volume was measured using a jacket plethysmograph.

Results—The results were most reproducible when analysis was performed at the end of inspiration (within 1 Hz in nine out of 10 cases). Comparison between tidal volume delivery at 10 Hz and resonance frequency was made in 10 subjects. Delivery was significantly higher at resonance than at 10 Hertz (mean percentage increase 92%, range 9–222%).

Conclusions—These preliminary findings suggest that there is improved volume delivery at resonance frequency.

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Keywords: phase analysis; high frequency oscillation; prematurity; resonance frequency

In recent years, high frequency oscillatory ventilation (HFOV) has increasingly been used in the management of respiratory distress syndrome (RDS) in premature infants. This technique can improve pulmonary and clinical outcome in this group of infants.^{1 2} The frequency used has traditionally been 10 or 15 Hz. This choice is largely governed by the efficiency of the oscillator used.

We speculated that by ventilating these infants at the resonance frequency of their respiratory system, the efficiency of ventilation could be further improved. We therefore set out to devise a practical and reproducible method of measuring the resonance frequency of the respiratory system in such infants, and at the same time, test out our theory that more efficient ventilation could be achieved at this frequency. We began by looking at the changes in tidal volume delivery during oscillation at different frequencies.

In an oscillating system driven by a sine wave pump, the impedance of the respiratory system has to be overcome, for tidal ventilation to occur. If the respiratory system is modelled as a single compartment system, the overall impedance can be regarded as a composite of three main components. These are resistance of the respiratory system, which is largely made up of airway resistance—itsself a function of the radius of the airway; elastance which is the reciprocal of compliance, a function of the stiffness of the pulmonary tissues and chest wall; and inertance, the force necessary to cause acceleration and deceleration of the mass that makes up the respiratory system. The relations of these components are shown in fig 1.

The driving signal, which represents the changes in the piston position, is 90 degrees out of phase with flow. It is therefore, by definition, 90 degrees out of phase with resistance. Elastance is in phase with the driving signal and inertance, on the other hand, operates in opposition, being 180 degrees out of phase with elastance. The magnitude of the inertance impedance is directly proportional to the oscillatory frequency; and the higher the frequency, the greater the magnitude of the inertance becomes. During conventional mechanical ventilation, the inertance component is negligible, but during high frequency ventilation, the inertance increases in magnitude.

The resonance frequency of the respiratory system is the frequency at which the magnitude of the inertance increases to a point where the inertance and elastance components are equal in magnitude and cancel each other out.³ This is an exciting prospect in RDS as, in theory, resistance is then the only impedance left to overcome during delivery of tidal ventilation.

The changes of pressure at airway opening are the net result of the effect of the three main components of impedance, as described above. At frequencies other than resonance, the relative influence of each impedance component to the total causes a phase shift between the pressure at airway opening and flow. At resonance frequency, however, when elastance and inertance cancel each other out, the changes of the pressure signal would therefore be entirely due to the resistance component. The pressure signal at airway opening is now exactly in phase with flow and 90 degrees out of phase with the driving signal. This forms the basis of our method of determining the resonance frequency of the respiratory system.

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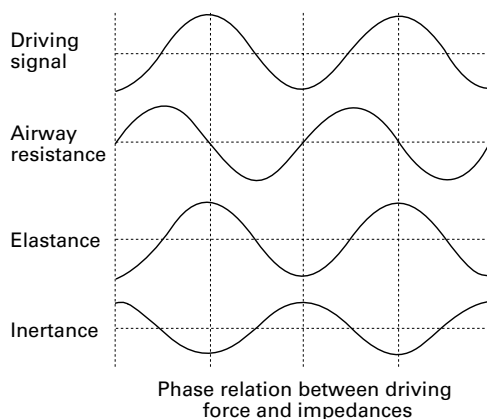


Figure 1 Diagram of phase relation between driving signal and three components of impedance, resistance, elastance, and inertia.

Methods

We recruited 18 ventilated premature infants with RDS within the first 72 hours of life from the neonatal unit at St Thomas's Hospital. Respiratory distress syndrome was diagnosed on the basis of symptoms and *x*-ray appearance at 4 hours of age. Gestational age ranged from 24 to 31 weeks (mean 27.99 weeks, median 28.7 weeks). Birthweight varied from 700 g to 2340 g (mean 1178 g, median 1053 g). Mean FIO_2 during the study period was 0.44. Infants with severe intraventricular haemorrhage, evident on ultrasound scan, who were receiving inotropic support, or otherwise clinically unstable, were excluded from the study. Informed written consent was obtained from at least one parent and the study was approved by the West Lambeth Health Authority ethics committee.

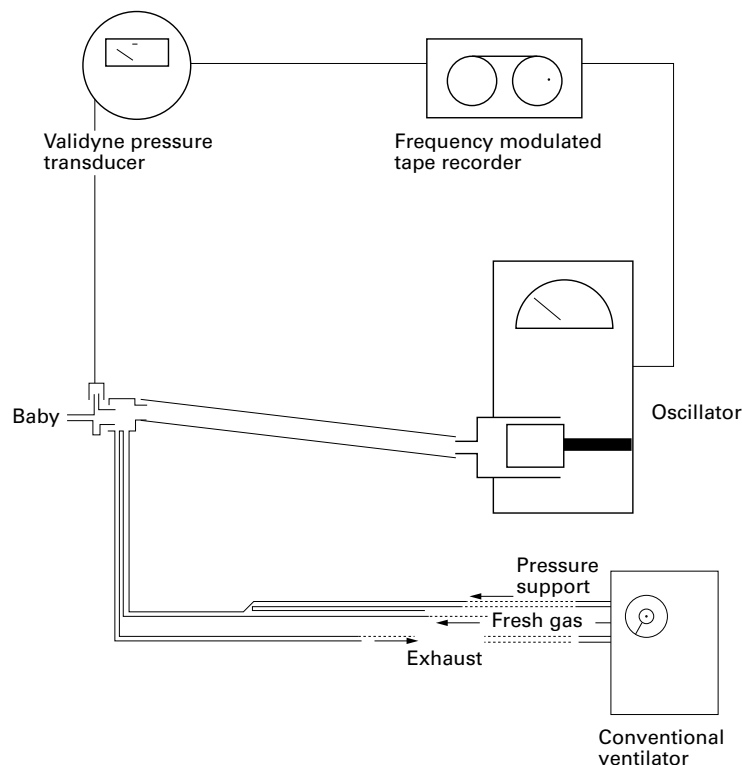


Figure 2 Schematic representation of the ventilatory circuit and recording systems used.

EQUIPMENT AND VALIDATION

Ventilation circuit (fig 2)

High frequency oscillation was provided by a custom built piston based oscillator that had an oscillatory frequency range of 2 to 30 Hz and a capacity of delivering tidal volumes of between 2 to 20 ml. The delivered tidal volume was determined by a movable fulcrum on the cam-shaft, and could be adjusted to the desired volume, but once set, the volume put into the circuit was constant at all frequencies within the range studied. A sine-cosine electrical generator connected to the cam of the system produced a sinusoidal electrical signal that mirrored the changes in piston position. Rotating the sine-cosine generator on its own axis allowed us to alter the phase relation between the electrical output signal and the piston position if necessary. For the purposes of this study, the output signal was rotated 90 degrees from the original position, thereby aligning it in phase with flow.

The effect on the electrical output signal, which represents the driving signal when gas compression within the piston becomes significant, may potentially introduce error into the system. To reduce such error, we fine tuned the sine-cosine generator so that at around 18–19 Hz, the phase difference between the output signal and flow is zero. The phase shift experienced during various frequencies in the study range was then determined. The frequency of 18–19 Hz was chosen simply because it lies close to the mean resonance frequency seen in our group of subjects.

Mean airway pressure (MAP) support was provided by a conventional ventilator (either Sechrist Infant Ventilator, model IV-100B or SLE 2000 Infant Ventilator) on the continuous positive airway pressure (CPAP) mode, with the oscillator connected to the suction port at the patient manifold. MAP used was calculated as 2 cm H_2O above that used during conventional ventilation.

Measurement of changes in pressure at airway opening

This was measured through a side port of the endotracheal tube connector using a Validyne MP15-20 pressure transducer. The frequency response of this pressure transducer has been tested over the range of 14–26 Hz, which was the section we were most interested in; the response was within 7%.

Measurement of tidal volume delivery

This was achieved using respiratory jacket plethysmography.^{4,5} The respiratory jacket was a double layered latex rubber garment which covers the trunk of the baby with the arms outside. Two plastic tubes were attached to its body, allowing communication between the inside of the jacket and the atmosphere. During the study, this jacket was filled with air to a pressure of 2–3 cm H_2O , causing the inner layer to be closely apposed to the baby's chest and abdominal wall. Chest and abdominal wall movements resulted in changes in pressure within the jacket which were measured by a second Validyne pressure transducer (± 2 cm

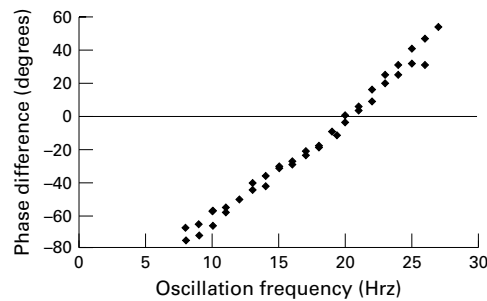


Figure 3 Results of effects of raising and lowering oscillation frequency on phase relation between driving signal and pressure waveform at airway opening in one infant. At frequencies below resonance (when there is zero phase difference), phase difference is negative, while above resonance it is positive.

H₂O). The jacket was calibrated by injecting and withdrawing 10 ml of air using a syringe attached to the second port and measuring the change in end tidal volume during conventional ventilation. The frequency response of the jacket was assessed by filling the jacket with air to 2–3 cm H₂O as in the study. The jacket was then oscillated through one of its tubes at frequencies between 2–30 Hz and the changes in pressure (which is directly proportional to the changes in volume inside the jacket) monitored through its other tube using a Validyne pressure transducer. The pressure changes were within 5% between 2–30 Hz. Although we believe the mechanics of the respiratory jacket will not in any way influence the measurement of resonance frequency, we also carried out measurements in two babies with the jacket inflated and deflated.

Data analysis

The signals from the magnetic tape were sampled at 2000 Hz using a digital data acquisition card with anti-alias filtering device. The data were stored on to the computer hard disk. Phase analyses were performed on four set points of the respiratory cycle—mid-inspiration, end of inspiration, mid-expiration and end of expiration—between the driving signal, which is equivalent to flow after rotation on its own axis through 90 degrees, and the signal caused by changes in pressure at airway opening, using a custom built program. The program identified the corresponding peaks and troughs of the two waveforms and calculated the phase difference at each of the four set points, while simultaneously determining the frequency at which these phase difference occurred.

STUDIES

Measurements were taken within the first 72 hours after birth when the infant established a stable condition on conventional ventilation. The jacket was slipped over the trunk and secured with Velcro attachments at the shoulders. All electrode leads were threaded through either armhole. The jacket was inflated with air to between 2–3 cm H₂O. Volumes of 10 ml of air were introduced into and out of the jacket using a plastic syringe for calibration. Changes in jacket pressure were monitored on an oscil-

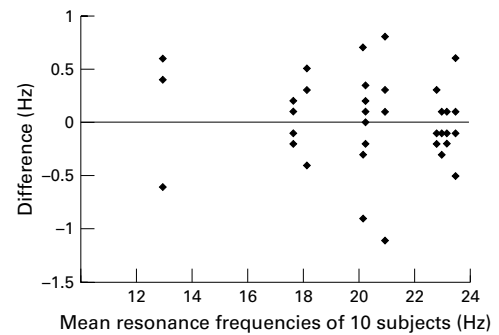


Figure 4 Modified Bland-Altman plot to show reproducibility of repeat measurements of resonance frequency in 10 infants. For these measurements, end inspiratory point was used.

loscope and once the drifting due to warming of the air within the jacket had settled down, the baby was switched from conventional ventilation to HFOV. Mean airway pressure support was set as 2 cm H₂O above that used during conventional ventilation, with the conventional ventilator on CPAP mode.

Tidal volume was set between 4–8 ml and assessed as satisfactory if there were visible oscillations of the chest wall. Frequency was initially set at 8 Hz and was then increased in 2 Hz steps to a maximum of 30 Hz. In 10 out of 18 subjects the frequency was then decreased down to 8 Hz and the entire run was repeated to assess reproducibility.

All three signals—driving, changes of pressure at airway opening, and changes of pressure in the jacket—were recorded on to magnetic tape using a frequency modulated tape recorder for analysis.

The changes in tidal volume delivery with varying oscillation frequencies (8–30 Hz) were observed in 10 infants and the trend plotted. The tidal volume delivery at 10 Hz and at resonance frequency were compared with the maximum tidal volume delivery possible in the studied frequency range.

Results

All infants completed the study successfully. No adverse effects were observed during the study period.

Resonance frequency, measured using phase analysis, was determined in all 18 infants. The frequency varied from 12 to 23 Hz among individual infants, with a mean of 18.6 Hz and a median of 19 Hz. In the two babies studied

Table 1 Comparison of maximum tidal volume (ml/kg) and tidal volumes delivered at 10 Hz and at the resonance frequency

Case No	Maximum	10 Hz	Resonance frequency
1	2.47	0.55	1.77
2	2.76	0.92	2.23
3	1.84	0.83	1.63
4	1.14	0.45	0.89
5	0.85	0.57	0.73
6	1.67	0.97	1.49
7	2.67	1.52	1.66
8	0.74	0.30	0.55
9	2.77	1.11	2.49
10	1.75	0.78	1.28

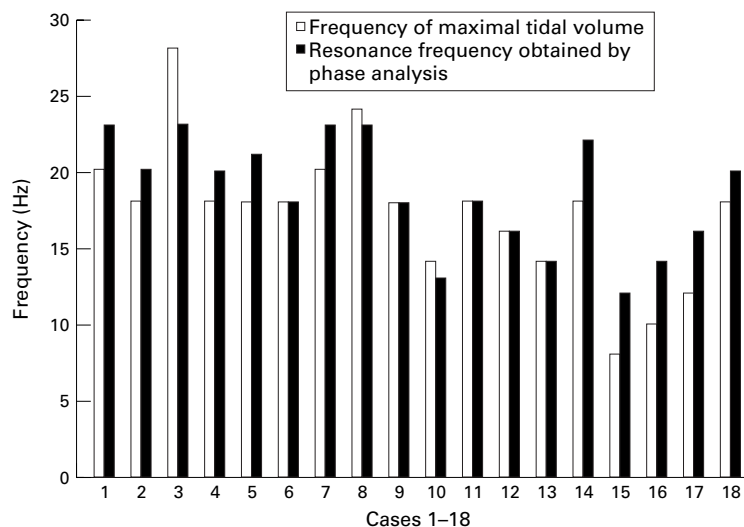


Figure 5 Comparison of maximum tidal volume delivery and tidal volume at resonance in 10 infants.

before and after jacket inflation, the resonance frequency remained unchanged, at 21 Hz in both.

The expected trend of phase difference (fig 3) that is, negative below, becoming less negative when approaching the resonance frequency, and positive above, becoming more positive the further away, was most consistently found when phase analysis was performed at the end of inspiration. The reproducibility of our method was within 1 Hz in nine out of 10 cases (fig 4).

The resonance frequency and frequency at which maximal tidal volume delivery occurred lay within 2 Hz of each other in 10 cases, within 3 in three cases, and within 4 in four cases (fig 5). Figure 6 shows the typical pattern of tidal volume delivery demonstrated, with tidal volume delivery rising steadily to maximum at a specific frequency and decreasing again once that frequency was exceeded. Table 1 shows the comparison between the tidal volume delivery at 10 Hertz, at the resonance frequency as measured using phase analysis, and at maximal tidal volume delivery in these 10 infants. Tidal volume of up to 200% higher could be shown at resonance frequencies.

Discussion

The forced oscillatory method for measuring respiratory resistance was first introduced by DuBois and co-workers in 1955.⁶ In a sinusoidal

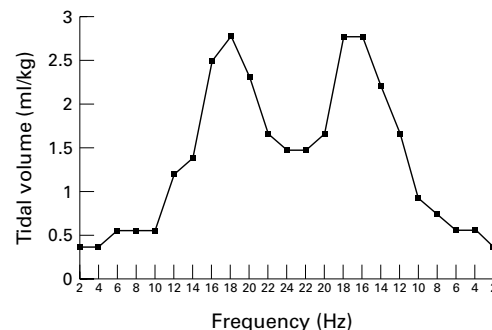


Figure 6 Typical patterns of tidal volume delivery

oscillatory system, elastance and inertance are exactly 180 degrees out of phase. The magnitude of inertance increases with increasing frequency. At a particular frequency, the resonance frequency, elastance, and inertance become exactly equal in magnitude and cancel each other out. At this frequency, pressure and flow are in phase, and their relation describes the flow resistance of the respiratory system.

We based our work essentially on DuBois's theory of oscillatory mechanics which models the lung as a single compartment with single values of resistance, compliance, and inertance. This is by no means a fair representation of the true situation in the diseased lungs in RDS as this illness is characterised by patchy areas of consolidation, atelectasis, and hyperinflation. Nevertheless, our results seem promising. This was further demonstrated when we carried out phase analysis at different points of the respiratory cycle and found that we could only produce consistent results at the end of inspiration.⁷

The range of resonance frequencies observed in our group of premature infants with RDS was 12–23 Hz (mean 18.6 Hz, median 19 Hz). However, studies have shown that healthy adult lungs have a resonance frequency of around 6 Hz⁸ which is considerably lower. The explanation of these findings becomes clear on examining the following equation^{8,9}:

$$I = 1 / (4\pi^2 f^2 C)$$

or

$$f = (1/2\pi)(1/IC)$$

where I = Inertance of the respiratory system; f = resonance frequency of the respiratory system; C = compliance of the respiratory system.

In RDS, the compliance of the surfactant deficient lungs is substantially reduced. As a result, (1/IC) increases and therefore f increases. It would have been interesting to vary the mean airway pressure support, to see if this has an effect on the resonance frequency as over-distension of the lungs will inevitably decrease compliance.¹⁰ However, these infants required ventilatory support for their illness and we did not feel ethically justified to have done this. When comparing the resonance frequency, measured using phase analysis with the frequency at which maximal tidal volume delivery was recorded, only five out of 18 cases coincided exactly. The rest all lay within 3 to 4 Hz of each other. This variation would seem to be a reasonable margin of error. Despite this variation, tidal volume delivery at resonance frequency also showed an increase ranging from 9–222%, compared with tidal volume delivery at the conventional 10 Hz.

Although it might be argued that it is simpler to cross plot the two electrical and pressure signals on an oscilloscope on the X–Y mode and to scan the frequency range, to look for the frequency at which looping is absent,¹¹ our method of determining resonance frequency of the respiratory system using phase analysis is a more accurate and reproducible alternative. It

is also practical and relatively non-invasive in the clinical setting.

These preliminary results suggest optimal volume delivery at resonance frequency and certainly look promising. Nevertheless, further clinical studies are needed to directly compare the efficacy of HFOV at 10 Hz and at the resonance frequency of the respiratory system.

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