Validity of forced expiratory flow volume loops in neonates

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SUMMARY It is claimed that suddenly squeezing a newborn baby's trunk with a pressure of 3–4 kPa produces a flow volume curve that can be used to measure the function of the small airways. If the squeeze is applied during expiration rather than at the end of inspiration, however, anomalous results may be obtained. One possible explanation is that the babies are limiting expiratory flow by making inspiratory efforts in response to the applied external pressure.

The response of 10 healthy term neonates to forced expiration was studied by using an oesophageal balloon. The squeeze was provided by an inflatable jacket, and measurements of oesophageal pressure and jacket pressure were recorded, as well as flow and volume changes at the mouth. Two hundred and twenty one squeezes were performed at different points in the respiratory cycle. In 188 squeezes an inspiratory effort was evident before the oesophageal pressure reached a plateau (mean time to peak pressure = 155 ms). For the remaining squeezes a plateau pressure was associated with closure or narrowing of the upper airway in most of the babies. When the squeeze was applied at low lung volumes the inspiratory effort was significantly earlier and stronger than around end inspiration. Thus a baby makes a reflex inspiratory response to chest compression that may interfere with the measurement of airway function when this technique is used.

Much of our knowledge of lung function is based on the results of tests on forced expiration. The peak flow is the simplest and most commonly used test, but more information can be obtained from a maximum expiratory flow volume curve. In particular, the shape of the curve for lungs with small volumes is altered by changes in the small airways. Flow rates in this part of the curve are independent of effort, and this limitation of flow is a function of the intrinsic mechanical properties of the lungs. As the technique requires the active cooperation of the patient it cannot be used in neonates or young children. A simple, reliable test of lung function in the first three years of life would have obvious benefits in assessing severity and progression of disease and in monitoring effects of treatment.

In 1977 Adler and Wohl described a method for obtaining partial forced expiratory flow volume curves in neonates and infants.¹ This method was later revised and is a useful technique for investigating lung function in this age group.^{2,3} The technique entails compressing the chest and

abdomen suddenly by using an inflatable jacket so that the compression coincides with the beginning of expiration.

The flow volume loop produced by this manoeuvre can be analysed in terms of peak flow, maximum flow at functional residual capacity (V_{max}FRC), and expiratory reserve volume (Fig. 1). The peak flow is not equivalent to that obtained in older children as it is taken after a tidal breath rather than a maximal inspiration to total lung capacity.

The procedure is simple and well tolerated by the infants but has limitations. Firstly, the observed functional residual capacity in the early neonatal period varies from breath to breath and is maintained above the resting volume of the respiratory system, so it will therefore be influenced by the respiratory rate and postinspiratory muscle activity.⁴ There is no measurement of lung volume unless helium dilution is incorporated into the method, and thus any changes in V_{max}FRC and expiratory reserve volume may be due to change in the

Fig. 1 Spontaneous breath before squeeze (continuous line), start of squeeze (arrow¹), and forced expiratory flow volume curve (dotted line). Minimum volume of spontaneous breath defines functional residual capacity and peak flow; $\dot{V}_{max}$ FRC and expiratory reserve volume are marked.

functional residual capacity from which they are calculated. Secondly, the technique assumes that the baby is relaxed during the 'squeeze.' If the baby is trying to breathe in he will be protecting his lungs against the pressure from the jacket, which may prevent the method achieving limitation flow. While using this technique we noticed that if the com-

pression was applied late in expiration the $\dot{V}_{max}$ FRC was often higher than when the compression was applied at the beginning of expiration (Fig. 2). This should not be possible if flow is being limited. We therefore investigated babies' inspiratory efforts during the compression by using oesophageal balloons to measure intrathoracic pressure.

Fig. 2 Flow volume curve from same baby as fig 1, with squeeze applied in mid-expiration (2); $\dot{V}_{max}$ FRC is 30% higher than in fig 1.

Subjects

Ten newborn babies, six boys and four girls aged 1 to 9 days (mean 3.4), were tested after oral informed consent had been obtained from the parents. Mean birth weight was 3480 g (range 2700–3800) and mean gestation 39.6 weeks (range 38–40); all the babies were clinically normal. The studies were carried out half to one hour after a feed when the babies were asleep. No sedation was given, and no attempt was made to assess the sleep state.

Methods

Compressed air was fed into a 140 litre reservoir with a blow off valve set at 4.41 kPa (Fig. 3). This

Fig. 3 Air in reservoir kept at 4.41 kPa above atmospheric pressure by a blow off valve; when valve opened, jacket inflated to about 3.43 kPa.

was connected by an electric solenoid switch through wide bore tubing to a Hammersmith jacket. The jacket comprised an external skin of polyvinyl-chloride plastic that looped round the abdomen and chest with the arms inside, and was secured with Velcro strips. The anterior wall of the chest and abdomen was against the inflatable portion of the jacket, which had thick plastic on the outside and thinner plastic on the inside, resulting in the squeeze pressure being directed inwards. The pressure of the jacket was measured with a strain gauge pressure transducer (SE Laboratories 486) at the point of entry of the air into the jacket. The jacket took 110–210 ms to reach maximum pressure in vivo, and the plateau pressure was 2.74–3.63 kPa. The rise in pressure in the jacket was exponential, 63% of the maximum being reached in 10 ms.

Flow at the mouth was measured with a Fleisch type 0 heated pneumotachograph connected to a soft rubber facemask. The pneumotachograph was linear to about 5% over the range studied (0–25 l/min).

The babies' tidal volumes were measured with a reverse plethysmograph (Fig. 4). Pressure changes in a rigid 100 litre plastic container caused by the babies' inspired and expired volumes were measured with a strain gauge pressure transducer (Pye Ether UP1).

We preferred this method of measuring volume as it was stable over each study period. Integrator drift made it difficult to identify the functional residual capacity when the integrated flow signal from the pneumotachograph was used.

The reverse plethysmograph was calibrated by injecting and withdrawing known volumes of air at

Fig. 4 Air circulated round reverse plethysmograph; pneumotachograph was mounted on face mask held to baby's face.

Fig. 5 Oesophageal pressure shown in relation to jacket pressure, flow, and volume against time.

the babies' approximate respiratory rate to minimise errors due to the adiabatic effect. A fan circulated the air inside the system to reduce the dead space to 22 ml. Intrathoracic pressure was measured by an oesophageal balloon and standard techniques.⁵ In the last five babies the oesophageal pressure was confirmed by occluding air flow in and out of the mask for a few seconds. In such a closed system the oesophageal pressure is the same as the mask pressure and the swings in pressure can be measured as the baby attempts to breathe.⁶ The signals were amplified (SE Laboratories EMMA amplifier) and recorded on a four channel Racal tape recorder. The flow volume data were displayed on an oscilloscope to time the squeeze to the babies' breathing. At the end of the study jacket pressure, oesophageal

pressure, and flow and volume signals were displayed against time by using an oscillograph (SE Laboratories 3006) and flow volume loops were drawn out on an X/Y plotter (Philips PM8041) at 25% of the original speed.

Results

Two hundred and twenty one separate loops were obtained from 10 babies in the study, with the squeeze applied at different points in the respiratory cycle. Peak flow, expiratory reserve volume, and VmaxFRC were measured, and in 213 cases an adequate oesophageal trace was obtained. For the five babies in whom the ratio of oesophageal to mouth pressure was measured the values obtained were all within 10% of unity. Functional residual capacity was defined as the minimum lung volume from the breath before the squeeze. Table 1 shows the results for squeezes at full inspiration. These are similar to the results of other workers. In three babies the VmaxFRC was highest when the squeeze was applied in mid-expiration. By contrast, when the squeeze was applied as the babies breathed in or at functional residue capacity the flow trace was usually erratic and the peak flow much lower than expected.

When the oesophageal pressure traces were examined in relation to the squeeze all traces showed an initial rise in pressure corresponding to the rise in pressure inside the jacket. In 188 cases (88%) there was a peak followed by an immediate fall in oesophageal pressure indicating inspiratory muscle activity against the squeeze (fig 5). The mean (SD) time taken to reach this peak oesophageal pressure was 155 (36) ms (range 53–302). The large variation in the peak oesophageal pressure from 0.05–2.55 kPa above atmospheric pressure meant that in many cases the inspiratory effort must have

Table 1 Analysis of flow volume loops

Case No	No of inflations	Mean (SD) peak flow (l/min)	Mean (SD) expiratory reserve volume (ml)	Mean (SD) VmaxFRC (l/min)	Single highest value of VmaxFRC for each baby
1	6	12.5 (2.2)	12.2 (5.4)	6.8 (2.1)	9.9
2	5	7.4 (1.3)	14.8 (2.6)	5.2 (1.4)	7.3
3	3	18.8 (1.8)	22.2 (3.1)	13.3 (1.8)	15.7
4	10	*	15.4 (4.5)	12.5 (1.3)	14.4
5	2	13.6 (0.8)	22.6 (1.3)	12.2 (0.5)	12.6
6	9	16.3 (1.0)	16.5 (3.6)	11.3 (1.8)	15.5
7	7	8.2 (0.8)	16.9 (5.0)	7.4 (1.3)	11.5
8	7	13.3 (2.0)	17.2 (8.3)	8.3 (2.1)	11.3
9	4	12.0 (1.9)	14.2 (2.8)	9.4 (1.6)	10.9
10	7	14.3 (1.6)	19.7 (5.4)	9.5 (3.4)	15.6

*Mean not available as signal strength exceeded maximum input for several traces.

begun before the peak was reached. The starting point of this effort was obscured by the rise in transmitted pressure from the jacket.

On the 25 other occasions there was a plateau in the oesophageal pressure before the inspiratory effort began. The importance of these traces is that they might represent a truly passive response to the squeeze. In no case, however, was a plateau associated with a satisfactory flow volume curve. The mean (SD) time from the initial rise in the jacket pressure to the start of inspiratory effort was 291 (77) ms (range 190–536). Eighteen of these 25 responses were from two babies. The presence of a plateau was not related to the timing of the squeeze in the respiratory cycle. In the two babies with the repeated plateau traces we looked at the percentage of the squeeze pressure transmitted to the oesophageal balloon. With the exception of one value from each baby the results were reproducible. When those two low results were excluded the mean percentage transmission of pressure across the chest wall was 57.9 and 67 (cases 2 and 5, respectively, in Table 1). The results from case 5 were all associated with zero flow, which implies glottic closure, and this was a common response to inflation of the jacket in this baby (12 out of 22 squeezes). In case 2 all the flow traces showed erratic expiratory flow when an oesophageal plateau was present, implying downstream narrowing (presumably partial glottic closure). During the remaining seven squeezes in three infants one achieved 78% transmission of jacket pressure, which was associated with air flow obstruction, but in the six others the percentage ranged from 9 to 54, indicating some degree of inspiratory effort against the squeeze in most if not all of these plateaus.

To assess whether the timing of inflation pressure in the respiratory cycle influenced the speed and magnitude of the response the mean of the two previous tidal breaths was used to calculate the length of the respiratory cycle. If these two breaths varied by more than 0.3 s the result was discarded; 0.3 seconds represents 20% of the respiratory cycle

in a baby breathing at 40 breaths a minute and was enough to exclude squeezes for which the baby's respiratory pattern was changing appreciably from breath to breath. The time from full inspiration to the start of the jacket squeeze was then expressed as a percentage of a full respiratory cycle, 0% and 100% representing full inspiration. Table 2 shows the results for inflations around full inspiration (80–100% and 0–20%) against inflations around full expiration (30–70%). The time taken for the jacket pressure to rise was similar in the two groups ($t = 0.98$, $p > 0.2$, paired t test). At lower lung volumes the peak oesophageal pressure was significantly earlier and significantly smaller.

Discussion

The object of the forced partial expiratory flow volume technique is to give a transthoracic pressure that is high enough to limit flow. Once this critical pressure is exceeded the flow depends only on the conformation of the airways and the degree of inflation of the lungs. The variation in this flow limitation is then used to indicate abnormalities of the lungs.^{3,7} We have shown a reflex inspiratory response to external compression of the chest that may interfere with these measurements. This would explain the anomalous finding of supramaximal flow when the squeeze is applied during expiration and would mean that values of $V_{max}FRC$ are underestimated and depend partly on the strength of the reflex. The reflex is more obvious at low lung volumes, although accurate timing of onset is not possible when an oesophageal balloon is used as it reflects intrathoracic pressures rather than muscular effort. Diaphragmatic electromyographic recordings are needed to pinpoint the start of the reflex but have the disadvantage of not being quantitative.

This response to chest compression has been observed during the resuscitation of the newborn, when it is a powerful stimulus for a deep inspiratory effort in asphyxiated babies.⁸ Pulmonary rapidly adapting receptors (irritant receptors) stimulate

Table 2 Relation of onset of inspiratory effort and peak oesophageal pressure to time of inflation (values are means (SE))

	Top of tidal breath	Bottom of tidal breath	<i>t</i> test
Time to observable inspiratory effort (ms)	176 (5) (n = 128)	139 (5) (n = 46)	$p = <0.001$ (95% confidence interval for magnitude of difference = 23 to 51 ms)
Peak oesophageal pressure (kPa)	1.69 (0.06) (n = 116)	0.94 (0.08) (n = 42)	$p = <0.001$ (95% confidence interval for magnitude of difference = 0.58 to 0.91 kPa)

phrenic activity in response to lung deflation in rabbits,⁹ and this reflex presumably plays a part in the gasping inspirations of newborn babies.¹⁰ The same mechanism is probably responsible for our results. Babies always make some response to try to limit the effect of the squeeze, using either the diaphragm and chest wall or the glottis, and we conclude that further elucidation is needed before partial forced expiratory flow volume loops can be interpreted easily.

References

- ¹ Adler SM, Wohl MEB. Flow-volume relationship at low lung volumes in healthy term newborn infants. *Pediatrics* 1978;**61**: 636–40.
- ² Taussig LM, Landau LI, Godfrey S, Arad I. Determinants of forced expiratory flows in newborn infants. *J Appl Physiol* 1982;**53**:1220–7.
- ³ Godfrey S, Bar-Yishay E, Arad I, Landau LI, Taussig LM. Flow-volume curves in infants with lung disease. *Pediatrics* 1983;**72**:517–22.
- ⁴ Mortola JP, Milic-Emili J, Norowaj A, Smith B, Fox G, Weeks S. Muscle pressure and flow during expiration in infants. *Am Rev Respir Dis* 1984;**129**:49–53.
- ⁵ Beardsmore CS, Helms P, Stocks J, Hatch D, Silverman M. Improved esophageal balloon technique for use in infants. *J Appl Physiol* 1980;**49**:735–42.
- ⁶ Milner AD, Saunders RA, Hopkin IE. Relationship of intraoesophageal pressure to mouth pressure during the measurement of thoracic gas volume in the newborn. *Biol Neonate* 1978;**33**:314–20.
- ⁷ Prendiville A, Green S, Silverman M. Ipratropium bromide and airways function in wheezy infants. *Arch Dis Child* 1987;**62**: 397–400.
- ⁸ Hull D. Lung expansion and ventilation during resuscitation of asphyxiated newborn infants. *J Pediatr* 1969;**75**:47–58.
- ⁹ Davies A, Sant'Ambrogio F, Sant'Ambrogio G. Onset of inspiration in rabbits during artificial ventilation. *J Physiol* 1981;**318**:17–23.
- ¹⁰ Trzebski A. Respiratory reflexes. In: Pallot DJ, ed. *Control of respiration*. London: Croom Helm, 1983; 108–56.

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