Tidal pressure/volume and flow/volume respiratory loop patterns in human neonates

A. D. MILNER, R. A. SAUNDERS AND I. E. HOPKIN
Department of Child Health, University Medical School, Nottingham, U.K.

(Received 2 November 1976; accepted 8 September 1977)

Summary

1. Tidal pressure/volume and flow/volume respiratory loops were constructed from records obtained during 98 studies on 48 neonates of various ages and gestations. Records were obtained with a total body plethysmograph and an oesophageal balloon. Total pulmonary resistance was computed at five separate levels in the breathing cycle and results were expressed graphically as tidal resistance profiles by plotting total pulmonary resistance against percentage tidal volume above functional residual capacity.

2. Values obtained for standard pulmonary mechanical measurements and thoracic gas volume were similar to those of other workers. In addition six distinctive resistance profile patterns were found and related to different breathing patterns.

3. The technique appeared to be particularly useful in identifying air trapping and also demonstrated that total pulmonary resistance is open to misinterpretation when measured only at the mid-tidal-volume level, as is the present convention.

Key words: air trapping, neonates, pulmonary function, tidal flow/volume loops, tidal pressure/volume loops, total pulmonary resistance.

Abbreviations: $C_D$, dynamic compliance, FRC, functional residual capacity; TGV, thoracic gas volume; TPR, total pulmonary resistance.

Method

Each baby was studied in a specially constructed cylindrical total body plethysmograph (48 litres), externally warmed by a radiant heater servo-controlled from the baby's skin temperature. An oesophageal balloon attached to a 35 cm long x 1.8 mm i.d. feeding tube was passed via the baby's mouth to lie in the lower third of the oesophagus. This siting was achieved by passing the balloon into the stomach and withdrawing it 1 cm beyond the point at which a negative pressure deflection the mechanical characteristics of the lungs of newborn infants who were breathing spontaneously. Since then various modifications have been introduced and the systems have become more elaborate (Karlberg, Cherry, Escardo & Koch, 1960; Nelson, 1966; Hatch & Milner, 1974). The airflow resistance can be measured with a total body plethysmograph (Doershuk & Matthews, 1956; Radford, 1974), but is more usually and more conveniently studied by relating the oesophageal pressure and mouth airflow at the mid-tidal-volume level (Cook et al., 1957). With this technique a considerable volume of normal data has been accumulated and infants with a wide variety of pulmonary problems have been studied (Karlberg & Koch, 1962; Dahms, Krauss & Auld, 1974). This measurement, however, is informative only if the resistance remains constant throughout the tidal breath and if flow is essentially laminar. We have evaluated this technique further by measuring the total pulmonary resistance over 90% of the tidal volume range by analysis of tidal pressure/volume and flow/volume loops.

Introduction

In 1957, Cook, Sutherland, Segal, Cherry, Mead, McIlroy & Smith described a method for studying
was obtained during inspiration. This site was normally 13 cm from the mouth in full-term infants, but as little as 9 cm in infants of less than 1.5 kg body weight. The balloon was made of thin latex and measured 3.0 cm long \times 0.7 cm diameter fully inflated. In use it contained only 0.15 ml of air and then the pressure system had a combined elastance \( (dP/dV) \) of 0.38 kPa/ml, which remained constant within \( \pm 1\% \) in the range 0.03–0.35 ml of balloon volume. This provided adequate matching to the tube and pressure transducer, which has a total dead space of 0.8 ml. Measurement error was therefore less than 0.93% for balloon volume change of 0.35 ml, corresponding to pressures between \(-24\) kPa and \(+18\) kPa. Previous studies with such balloons in this way have shown that the pressures recorded correlate closely with intrapleural pressure changes (Dinwiddie & Russell, 1972), particularly when, as in our studies, the infants are nursed in the right-lateral position (Russell & Dinwiddie, 1973). For calculation of dynamic lung compliance \( (C_D) \) and mid-volume total pulmonary resistance \( (TPR_{50}) \) transpulmonary pressure was derived by simultaneously measuring face-mask pressure.

The baby's tidal flow patterns modulated a steady bias air flow from a high-impedance source at 0.05 litre/s, which was warmed and fed via a tube and shutter system to a modified Rendell-Baker neonatal size 0 face mask with a latex-coated, sponge-rubber, airtight flange, an inflow tube and a pneumotachograph in the outflow line. The pneumotachograph consisted of a 1.3 cm diameter disc of fine-mesh gauze with pressure-flow linearity within \(+3.0\%\) at flow rates up to 0.18 litre/s. Except during crying, the total pneumotachograph flow never exceeded 0.15 litre/s during the studies. Warming the inflow air prevented condensation on the gauze. The total resistance added by the measuring circuit remained constant between 0.54 and 0.60 kPa \( \cdot \) litre \( ^{-1} \) \( \cdot \) s. The total dead space of the mask, tubing and transducers was 10 ml.

Mask and balloon pressures were measured by strain-gauge transducers (SE Laboratories, SEM 4–86). The pressure drop across the pneumotachograph and pressure changes within the plethysmograph were measured by differential pressure transducers (Elema-Schonander, EMT 32C). All signals were fed to a modified amplification system (SE Laboratories EMMA). Tidal volume was measured by integration of the amplified flow signal. Selected signals were relayed to a four-channel, F.M. tape recorder (SE Laboratories, SE 8–4), with replay of signals to an \( X-Y \) plotter at 25% of recorded speed, thus improving its effective amplitude/frequency response to 90% amplitude between 0 and 21.2 Hz for loops of up to 40 mm diameter. Of the recording systems the worst-case (balloon) amplitude/frequency response was flat from 0 to 5.5 Hz, falling to 90% response at 11 Hz. Fourier analysis of 13 pairs of pressure and flow traces, including 'uniform', 'grunting', 'crying' and 'air-trapping' types, showed the worst-case total harmonic content to be 27%, related to the fundamental, of which 20.5% was second harmonic and 5% third (equivalent to 1.8 Hz and 2.7 Hz respectively). Thus the total significant harmonic content of the waveforms was within the linear measurement range of our system. Phase lag between pressure and flow signals introduced by our measuring devices was small, and linear at 0.43°/Hz.

The mask and oesophageal pressure transducers were calibrated against a water column. A Rotameter was used to calibrate the pneumotachograph and an air-filled syringe to calibrate the electronic integrator. The plethysmograph transducer was calibrated by cycling 5 ml of air into and out of the plethysmograph at approximately the baby's own respiratory frequency to minimize adiabatic error.

Mask pressure, oesophageal pressure, tidal flow and tidal volume were measured during quiet breathing, crying or grunting where applicable. Plethysmograph chamber pressure and mask pressure were also recorded with the shutter closed for periods of up to 5 s in order to calculate thoracic gas volume.

**Analysis of the record**

The traces were replayed on to a 6 inch U-V recorder (SE Laboratories, SE 3006). Dynamic compliance \( (C_D) \), mid-volume total pulmonary resistance \( (TPR_{50}) \) and thoracic gas volume \( (TGV) \) were calculated by standard techniques (Cook *et al.*, 1957; Dubois, Botelho, Bedell, Marshall & Comroe, 1956; Auld, Nelson, Cherry, Rudolph & Smith, 1963). At least six breaths were analysed for each calculation. Coefficients of variation in a sample of 15 sets of measurements ranged from 5.0% to 22.2% for \( C_D \) (mean: 12.7%), from 4.3% to 27.3% for \( TPR_{50} \) (mean 17.9%) and from 3.6% to 17.2% for \( TGV \) (mean 10.8%). Parts of the recording free from oesophageal and integrator drift were selected for replay on an \( X-Y \) plotter (SE
Tidal pressure/volume and flow/volume loops

Inspiration

$V_T$ 22.3 ml

Flow ($\dot{V}$) 0.05 litre/s

FIG. 1. Tidal pressure/volume and flow/volume loops constructed from a single breath. Isovolume lines were drawn horizontally at values of 5, 25, 50, 75 and 95% of tidal volume ($V_T$) above functional residual capacity (FRC). Total pulmonary resistance (TPR) was calculated at each level, e.g. TPR$_{75} = \frac{dP}{dV}$.

225), pressure/volume and flow/volume loops of individual tidal breaths being plotted side by side. Lines were then drawn horizontally across the tidal pressure/volume and flow/volume loops at levels 5, 25, 50, 75 and 95% of the tidal volume ($V_T$) above functional residual capacity (FRC) (Fig. 1). In the worst case the full-scale error was ±2-0%. The TPR was then calculated at each level by dividing the algebraic inspiratory/expiratory pressure difference by the corresponding flow difference. Since cardiac impulses produced artifacts on the oesophageal pressure trace, four consecutive breaths were recorded and the results averaged. Scatter was worst at the 5% and 95% $V_T$ values. Critical analysis of each profile showed that the total scatter around the mean was always less than 20% in 87 of the 98 profiles. The corresponding coefficients of variation were less than 20% in 92 of the 98 profiles. The mean TPR values from each of four breaths were plotted against $V_T$, giving a 'tidal resistance profile'.

Subjects

Our study population was highly selective, and included many with respiratory problems. To obtain data on pulmonary mechanics in normal babies we initially analysed records of 48 unselected babies whose gestational ages ranged from 34 to 41 weeks, weighing from 1.68 to 4.45 kg, and so derived mean ±SD for $C_D$, TPR$_{50}$ and TGV/body weight in a normally distributed group.

All the babies studied were either born at the City Hospital, Nottingham, or admitted to the neonatal unit from other maternity units. Their gestations varied from 28 to 42 weeks and their birth weights from 800 g to 4.8 kg. The project was approved by the North Nottinghamshire Ethical Committee, and informed maternal consent was obtained before each investigation. No sedation was given for any of the studies.

Results

Forty-eight babies were studied on 98 occasions. This does not represent a cross-section of the infant population, since some degree of selection was inevitable owing to availability of infants for study in special units. Our preliminary analysis of the 48 random studies, however, gave the following values: $C_D$: mean 0.0484 litre/kPa, SD 0.0316; TPR$_{50}$: mean 5.92 kPa l$^{-1}$ s, SD 3.86; TGV/body weight: mean 33.4 ml/kg, SD 9.1.

The patterns revealed by examination of resistance profiles fell into six distinct groups.

1. Uniform resistance pattern

The most commonly seen pattern in normal infants in our study is shown in Fig. 2, TPR being virtually unchanged throughout the tidal range measured. This was seen on 38 occasions in 33 babies of various gestation times (Table 1).

2. Flow-related pattern

On 28 occasions in 19 of the normal infants a second pattern was seen, wherein TPR was higher over the mid-portion of the profile than at the extremes (Fig. 3). Closer analysis of the records showed that during every group of four breaths the TPR was highly correlated with algebraic inspiratory–expiratory airflow difference ($r > 0.80$ in all instances, $P < 0.001$). This correlation was never seen in any other group. However, the peak inspiratory–expiratory flow difference was not particularly high in this group (mean 0.082 litre/s, SD 0.014) compared with those in group 1 (mean 0.081 litre/s, SD 0.022, $P = 0.42$), but TPR$_{50}$ was significantly higher (group 1 mean: 5.49 kPa l$^{-1}$ s,
TABLE 1. General details and basic lung mechanics of babies studied, grouped according to resistance profile

Mean values for the group are shown, with the range in parentheses. C\textsubscript{D}, Dynamic lung compliance; TPR\textsubscript{0}, mid-volume total pulmonary resistance; TGV, thoracic gas volume.

<table>
<thead>
<tr>
<th>Profile pattern</th>
<th>No. of studies</th>
<th>No. of babies</th>
<th>Gestation (weeks)</th>
<th>Weight at study (kg)</th>
<th>Age at study (days)</th>
<th>C\textsubscript{D} (1/kPa)</th>
<th>TPR\textsubscript{0} (kPa l\textsuperscript{-1}s)</th>
<th>TGV/weight (ml/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Uniform resistance</td>
<td>38/33</td>
<td>28/19</td>
<td>37.0 (28-42)</td>
<td>2.59</td>
<td>12</td>
<td>0.052</td>
<td>5.5 (1.5-15.3)</td>
<td>33.4</td>
</tr>
<tr>
<td>2 Flow-related</td>
<td>28/19</td>
<td>19/11</td>
<td>35.5 (28-42)</td>
<td>2.58</td>
<td>22</td>
<td>0.048</td>
<td>7.4 (2.4-13.8)</td>
<td>35.5</td>
</tr>
<tr>
<td>3 Crying</td>
<td>4/4</td>
<td>4/4</td>
<td>39.2 (28-42)</td>
<td>3.37</td>
<td>0.5</td>
<td>0.062</td>
<td>3 (1.8-5.5)</td>
<td>34.4</td>
</tr>
<tr>
<td>4 Grunting</td>
<td>6/6</td>
<td>6/6</td>
<td>33.7 (28-40)</td>
<td>2.24</td>
<td>11</td>
<td>0.044</td>
<td>7.9 (2.4-42.2)</td>
<td>36.6</td>
</tr>
<tr>
<td>5 Air-trapping</td>
<td>11/8</td>
<td>8/8</td>
<td>35.1 (28-40)</td>
<td>2.29</td>
<td>31</td>
<td>0.027</td>
<td>11 (2-40.4)</td>
<td>49.0</td>
</tr>
<tr>
<td>6 \textsuperscript{N}_{2}-related</td>
<td>11/9</td>
<td>9/9</td>
<td>37.4 (28-40)</td>
<td>3.15</td>
<td>9</td>
<td>0.058</td>
<td>6 (2.8-10.4)</td>
<td>28.1</td>
</tr>
</tbody>
</table>

Fig. 2. Uniform resistance pattern. Total pulmonary resistance (TPR) was plotted against the isovolume levels at which it was calculated, and remained virtually constant between 5% and 95% of the tidal volume (\(T_v\)) above functional residual capacity (FRC). Seven representative examples are illustrated; the babies were all clinically normal.

Fig. 3. Flow-related pattern. This was another pattern seen in clinically normal infants, wherein there was a moderate rise in total pulmonary resistance (TPR) over the mid-portion of the tidal breath. In all cases there was a high correlation between flow and resistance for each group of breaths (\(r \geq 0.80, P < 0.001\)).

3. Crying pattern

Loops were constructed on four occasions from records obtained during crying (Table 1). The profiles had a characteristic pattern with high TPR near the inspiratory and expiratory limits of the tidal breath and a relatively lower TPR during the mid-portion (Fig. 4).

4. Grunting pattern

Loops and profiles were constructed in six babies who had audible expiratory grunting. This form of ventilation was easy to identify on the tidal flow trace and the tidal flow/volume curve, as there was always a sudden increase in flow towards the end of expiration (Fig. 5), corresponding to the end of the grunt. A characteristic resistance profile was again seen with a relatively low TPR near the inspiratory and expiratory limits of the breath, rising to high values over the mid-portion. In addition the lowest TPR was always recorded at the 5% level (Fig. 6). This pattern was thus a two-dimensional image of that seen during crying.
5. Air-trapping pattern

Four studies on four babies who had meconium aspiration and six studies on three babies who had Wilson-Mikity syndrome revealed a strikingly different pattern during the times when they showed clinical and radiological evidence of hyperinflation. On recovery this resolved to a uniform or flow-related pattern. In all these instances TPR was progressively higher at successively lower tidal values during quiet breathing (Fig. 7). This pattern was seen in seven ill, hyperinflated babies, and in one baby studied 5 h after caesarean section, who had a low TGV (21.5 ml/kg body weight). Apart from this one instance, all the TGV values measured were greater than 1 SD and four of the 11 were greater than 2 SD above the normal mean value (Table 1). All TGV values returned to the normal range on clinical recovery and resolution of the profiles to types 1 or 2.

6. Tidal-volume-related pattern

In a further nine infants on 11 occasions we found a pattern in which, in contrast to the air-trapping pattern, there was a positive relationship between TPR and tidal value (Fig. 8). The mean values of slope \( \frac{dTPR}{dV} \) in different babies varied and were not measured numerically. The criterion for inclusion in this group was a progressive rise in TPR between successive tidal values. We found no consistent features to explain these profiles, but all babies were clinically well.

It is obvious from the above that some infants demonstrated different types of profile on different occasions. In some cases the variation was associated with the presence or absence of disease, but often one pattern seen in normal infants was replaced by a different 'normal' pattern when next studied.

Discussion

Initial analysis of randomly selected healthy babies gave results for \( C_D \), TPR, and TGV which were reproducible and comparable with those of others (Auld et al., 1963; Cook et al., 1957; Klaus,
FIG. 6. Grunting pattern. The total pulmonary resistance (TPR) was highest over the mid-portion of the breath and in addition was lower at the 5% level than the 95% level in all cases. This profile pattern is thus a two-dimensional image of the crying pattern.

FIG. 7. Air-trapping pattern. Total pulmonary resistance (TPR) was lowest at the highest tidal volume measured. Profiles in this group always showed a higher resistance value at each successively lower tidal volume.

FIG. 8. Tidal volume-related pattern. This pattern was seen on 11 occasions in nine apparently normal babies. In these profiles, the total pulmonary resistance (TPR) was higher at successively higher tidal volumes. The significance of this pattern is not clear.

Tooley, Weaver & Clements, 1962; Nelson, 1966; Polgar & Promadhat, 1970). However, the measurement of TPR is often considered to be unsatisfactory and sometimes misleading. It is not purely representative of the state of the airways, but contains contributions from capacitive and inertial 'reactances' of lung tissue. In addition, dynamic compression of gas during breathing alters the Reynolds number (in turn modifying the Coanda and Bernoulli effects) and may alter the proportions of laminar, streamline and turbulent flows. In the present study we attempt to analyse this variable more closely to see if the shortcomings of this measurement could be overcome and the information obtained from it made more reliable.

We compared TPR at different values within single tidal breaths in order to obtain a profile of the resistance during the tidal range. In each individual, reproducibility from breath to breath was found to be good and as a result six distinct tidal resistance profile patterns were identified.

The first two patterns described were seen most often in clinically healthy babies. In the first, the resistance was essentially constant throughout the breath, suggesting that airflow is predominantly laminar in many full-term neonates during quiet breathing. Resistance is inversely related to lung volume, so that a fall in resistance might have been expected as the lung volume rose in these babies. However, the change in lung volume during a quiet, tidal breath was small compared with thoracic gas volume and any change in resistance was evidently too small to be detected by our form of analysis.

The flow-related pattern was interesting, particularly with respect to the frequency with which it was seen in healthy babies. The high degree of correlation of resistance with airflow suggested that
there was a significant degree of turbulence in the airways, since pressure is related to the square of flow velocity when flow is non-laminar. As there was statistically no difference in the flow rates measured in this group compared with those in group 1, the pattern was thought to be unrelated to absolute flow rates. However, there was a highly significant difference in the mid-volume total pulmonary resistance between the two groups, indicating a higher than normal resistance in the mid-portion of the breath, supporting the concept of turbulent flow. Surprisingly there was no difference between the groups in terms of gestation or weight ($P = 0.39$ and $0.47$ respectively by paired $t$-test), and indeed 11 babies demonstrated both patterns at some stage. Both groups of babies appeared clinically well and were indistinguishable. However, taken in isolation the mid-volume total pulmonary resistance (TPR$_{50}$) in group 2 obviously underestimated the babies' breathing ability in terms of airflow, whereas the resistance profile revealed the true potential.

The crying pattern was surprisingly consistent. Resistance was highest at the extremes of the tidal volume, at the points at which tidal flow was lowest. Measurements of TPR$_{50}$ are likely to be unrepresentative of 'resting' resistance if obtained while the baby is crying. This crying can be missed quite easily when the baby is wrapped up in the plethysmograph with a face mask in situ. Recognition of the crying pattern will avoid introduction of this error.

The grunting pattern was also very reproducible in terms of the variables measured, and on reflection could have been predicted from clinical observation of a grunting baby. Once again TPR$_{50}$ would have given no indication of the 'resting' resistance since grunting represents a deliberate increase in airways resistance during part of the expiratory phase. Resistance profiles revealed that many of the babies in this group demonstrated normal conductance at low lung volume, suggesting normal airways. Grunting is frequently seen in healthy neonates, particularly within the first 6 h after birth and indeed none of the six babies studied had the idiopathic respiratory distress syndrome with which grunting is usually associated.

The most important finding in our study was the consistent pattern seen in group 5. We did not measure trapped gas by comparing gas-dilution measurements with plethysmographic measurements of lung volume (Nelson, 1963), but all these babies were diagnosed as having air trapping on the basis of (a) specific clinical disease, (b) radiological evidence of pulmonary hyperinflation and (c) plethysmographic evidence of large lung volumes. All TGV values were greater than 46 ml/kg body weight when the air-trapping pattern was present, with the exception of the infant born by caesarean section. In addition six babies of this group were studied when clinical, radiological and plethysmographic criteria were normal and in all cases the air-trapping profile had resolved to one of the 'normal' patterns. We therefore considered our method to be reliable in detecting air trapping without the need to measure lung volumes. The reason for the pattern appearing in the infant born by caesarean section remains speculative, but on re-test at 24 h the pattern had resolved to a uniform profile and the TGV had risen from 21.5 to 34.7 ml/kg body weight. This suggested to us that during the first study the airways were closing or narrowing on expiration either because of excessive quantities of lung fluid or as a direct result of the low lung volume.

It is clear from these profiles that when air trapping is present the TPR at the mid-volume level will depend on the size of the tidal volume. Any increase in tidal volume will result in an apparent reduction of the airways obstruction and give a false impression of improvement. We have no explanation for the tidal-volume-related pattern. All the babies in this group were clinically well. Their gestation times and weights spanned almost the entire range. Their TGV values, though low, were not significantly different from our normal values (paired $t$-test gave $P = 0.10$).

The ability of many of the infants to demonstrate more than one resistance profile is evident, and is of no fundamental importance in itself. The points that are important in support of our method of analysis are that grunting or crying infants always had the appropriate profiles, that TPR was always related to flow ($r > 0.80$, $P < 0.001$) in group 2, but never in other groups, and most particularly that there was a striking association between our air-trapping profiles and other evidence of air trapping in these babies, together with resolution to normal patterns on recovery.

We therefore conclude that the tidal resistance profile adds a significant improvement to the interpretation of total pulmonary resistance in the neonatal period.

Acknowledgments

We are very grateful to the Action Research for the Crippled Child's Fund, who have provided financial support for this project.
References


