Respiratory timing in intubated neonates with respiratory distress syndrome

M South, C J Morley

Abstract
Respiratory timing was studied in 100 babies ventilated for respiratory distress syndrome (RDS) during a brief period of continuous positive airway pressure. For the 76 spontaneously breathing babies the mean (SD) inspiratory and expiratory times were 0.31 (0.06) and 0.41 (0.12) seconds. Respiratory rate was predominantly modulated by expiratory time. The severity of RDS was the main influence on expiratory time.

There have been a number of studies of respiratory rate in well neonates, both term and preterm.1-3 Little is known, however, about respiratory rate in preterm babies with respiratory disease.

A baby’s respiratory rate is determined by the duration of each breath, which, in turn, is fixed by the time spent in inspiration (Ti) and expiration (TEx). How changes in respiratory rate are modulated by changes in Ti and TEx, in sick babies with respiratory disease, is not known. Hird and Greenough measured inspiratory time in intubated babies with respiratory distress syndrome (RDS) during disconnection from the ventilator, but the expiratory time was not measured.4

The aim of this study was to examine the relationships between respiratory rate and Ti and TEx, in a group of intubated babies with RDS.

Patients and methods
Over a nine month period, 100 intubated and ventilated babies with a clinical and radiological diagnosis of RDS were selected at random within six to 24 hours of birth. Babies were not enrolled in the study if they had been treated with sedative or paralysing drugs.

The respiratory pattern was studied at the time of enrolment, and classified as either ‘apnoeic’ or ‘breathing’. If the baby was breathing, measurements were made of respiratory rate, Ti, and TEx. ‘Breathing’ babies were studied again at 2 and 7 days of age, provided that they were still being ventilated, were not apnoeic, nor receiving sedative or paralysing drugs at the time.

A pneumotachograph (Mercury F2L, dead space 1.7 ml, resistance 0.04 mm H2O/l/second) was inserted between the endotracheal tube and the ventilator circuit. The flow signal obtained was recorded on paper at a speed of 25 mm/second. Measurements of Ti and TEx were made from the flow trace between points of zero air flow. The respiratory rate was calculated from these measurements. This pneumotachograph system has been demonstrated not to affect respiratory rate, or arterial blood gas tensions, when used for periods of up to 30 minutes in ventilated preterm babies.5

The babies were studied in the supine position, when quiet and making no gross body movements. No other assessment of arousal state was made. Arterial blood was analysed at the time of the study.

The mechanical ventilator was switched from the ventilating mode to provide 5 cm H2O continuous positive airway pressure (CPAP) only. The inspiratory and expiratory flow pattern was observed for 30 seconds. Babies who made no breathing efforts in this period were classified as apnoeic, and mechanical ventilation was resumed. Babies who were breathing then had a further 30 second recording of the flow trace before ventilation was resumed. The flow traces from each breathing baby were examined, and a sequence of five consecutive regular breaths was selected for timing analysis. The mean measurement in these five breaths were taken as respiratory rate, Ti, and TEx.

Results were expressed as mean (SD). The effects of other factors on respiratory timing were explored using stepwise multiple regression analysis. The relationships between timing variables were examined using Spearman’s rank correlation coefficient. The relationships between respiratory rate and Ti and TEx were examined across the group on day 1, and in individual babies who had been followed sequentially. The slopes of the regression lines for rate versus Ti, and rate versus TEx, were calculated for each baby that had been followed in this way, and the means of these slopes were taken.

The study was approved by the hospital human ethics committee.

Results
The data recorded from 100 babies enrolled on the first day of life shown as mean (SD), were: gestation 28-7 (2-8) weeks and birth weight 1259 (571) g; there were 58 boys and 42 girls. Hydrogen ion concentration was 48-1 (10) mmol/l, carbon dioxide tension (PCO2) 5-6 (1-6) kPa, oxygen tension (PO2) 9-3 (3-4) kPa, and alveolar–arterial oxygen gradient (A–aDo2) 4-6 (2-7) kPa.

Of the 100 babies, 76 were classified as breathing, and 24 as apnoeic, when studied on the first day. Of the 76 breathing babies, 20 were also studied on day two, and of these, 11 were studied again on day seven.
There were no significant differences in sex ratio, hydrogen ion concentration, $P_{CO_2}$, $P_{O_2}$, or $A-aDO_2$ between the apnoeic and breathing groups. The apnoeic babies were less mature than the breathing babies (26.6 (2-3) v 29.1 (2-8) weeks’ gestation, $p=<0.05$).

Timing analysis from the 76 records on day 1 gave the following results: respiratory rate 88.5 (17-6), range 48-138, breaths/minute (bpm); $T_{in}$ 0-31 (0-06) seconds; and $T_{ex}$ 0-41 (0-12) seconds. Coefficient of variation for the five breaths analysed was 9-2% for $T_{in}$ and 8-7% for $T_{ex}$. The figure shows the relationships between respiratory rate and $T_{in}$ and $T_{ex}$ for all 76 babies studied on day 1. The slopes of the regression lines were: $-2.5$ ms/breath for $T_{in}$ and $-6.2$ ms/breath for $T_{ex}$. The mean slopes of the regression lines for those babies followed sequentially were: $-2.8$ ms/breath for $T_{in}$ and $-13$ ms/breath for $T_{ex}$.

Stepwise multiple linear regression showed no statistically significant effect on day 1 respiratory rate, $T_{in}$, or $T_{ex}$ for the variables: gestation, birth weight, hydrogen ion concentration, $P_{CO_2}$, or $P_{O_2}$. $A-aDO_2$ was significantly related to respiratory rate ($r=0.43$, $p=<0.001$), $T_{in}$ ($r=-0.03$, $p=<0.05$), and $T_{ex}$ ($r=-0.41$, $p=<0.001$). Thus the higher $A-aDO_2$, the faster the respiratory rate and the shorter $T_{in}$ and $T_{ex}$.

**Discussion**

Of 100 unsedated ventilated babies with RDS, 76% were found to be breathing, and 24% apnoeic, during a brief period when ventilation was stopped in the period 6 to 24 hours of age. There were no differences in hydrogen ion concentration, $P_{CO_2}$, or $P_{O_2}$ which might have caused this. The apnoeic babies were significantly less mature than those who were breathing. Other clinical factors which could have influenced the babies’ tendency to breathe (for example, sepsis or intraventricular haemorrhage) were not recorded.

The mean respiratory rate found in this study was fast (88.5 bpm), with a short $T_{in}$ (0-31 s) and $T_{ex}$ (0-41 s). Bourbouline-Young and Smith found a mean respiratory rate of 33 bpm in well preterm babies. Seguin et al., in a study of six preterm babies with RDS (who were not intubated and ventilated) found a mean respiratory rate of 73 bpm, with $T_{in}$ of 0-35 seconds, and $T_{ex}$ of 0-48 seconds. Hird and Greengough found the median $T_{in}$ of intubated preterm babies with RDS to be 0-275 seconds when disconnected from the ventilator and 0-35 when on endotracheal CPAP. They did not study expiratory time.

Maintenance of adequate lung volume in preterm babies with lung disease is dependent on dynamic mechanisms. Such mechanisms include continued contraction of inspiratory muscles, and partial glottic closure, during expiration. Glottic closure produces the familiar grunting respirations, and retards expiratory gas flow. Once intubated, a baby is deprived of this mechanism for preserving lung volume. Rapid respirations with short expiratory times may lead to gas trapping which may in turn help to preserve an adequate functional residual capacity. The mean $T_{ex}$ of 0-41 seconds found in this study may indicate that some babies had expiratory times of less than the three respiratory time constants said to be necessary for complete expiration.

Respiratory rate was found to be modulated predominantly by changes in $T_{ex}$, with $T_{in}$ playing a lesser part. This was found in the breathing babies as a group on day 1, and in individual babies followed up over a period of time. Irritant receptors in the bronchial tree are stimulated by atelectasis, and this, via a vagally mediated reflex, is probably what leads to shortening of $T_{ex}$, which, in turn, will raise end expiratory lung volume and reverse atelectasis.

Interestingly, $P_{CO_2}$, $P_{O_2}$, arterial hydrogen ion concentration, and gestation had no significant independent effects on respiratory timing. The influence of arterial blood gas tensions was studied in the group as a whole. The effects were not studied in individual babies. The only factor studied which did influence timing was $A-aDO_2$, which is a measure of oxygen diffusion ability. Thus the more severe the lung disease, the faster the respiratory rate, and the shorter $T_{in}$ and $T_{ex}$, with $T_{ex}$ again being affected more than $T_{in}$. How $A-aDO_2$ influences respiratory timing without affecting $P_{O_2}$ is not clear. It is likely that abnormal $A-aDO_2$ measurements were associated with other abnormalities of lung function (for example, compliance) that were not measured in this study.

In conclusion, intubated babies with RDS tend to breathe quickly, with short inspiratory and expiratory times. Respiratory rate is predominantly modulated by changes in expiratory duration and this, in turn, is influenced by the severity of the lung disease. An understanding of why, and how, preterm babies with RDS become tachypnoeic should help in their management.

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Intraventricular haemorrhage after aspiration of ventricular reservoirs

N E Moghal, M W Quinn, M I Levene, J W L Punits

Abstract
A previously unrecognised complication of aspirating ventricular reservoirs is described. Four infants developed fresh bleeding into the cerebrospinal fluid after reservoir taps; ultrasound confirmed intraventricular blood clot in one case. The technique for aspirating the reservoir may have an important bearing on the incidence of this complication.

The use of ventricular reservoirs in the management of the newborn infant with posthaemorrhagic hydrocephalus was first described in 1980. It has since been shown to be an effective method for ‘buying time’. It allows time to stabilise the infant, prevents multiple lumbar punctures and ventricular taps, allows more aggressive management of raised intracranial pressure, and enables clearance from the cerebrospinal fluid (CSF) of blood and protein before insertion of a ventriculoperitoneal shunt. In addition, the incidence of shunt infection is significantly reduced when reservoirs are used initially with later shunting as compared with early primary insertion of a shunt. We review our experience of 10 cases who had reservoirs inserted over a three year period and describe a previously unrecognised complication—late intraventricular haemorrhage.

Patients and methods
Between January 1988 and December 1990, 10 infants had reservoirs inserted at the Leeds General Infirmary for posthaemorrhagic hydrocephalus. Eight of the infants were ventilated for hyaline membrane disease and all suffered at least a grade II intraventricular haemorrhage in the first week of life. This was followed by progressive ventricular dilatation. Indications for inserting a reservoir were an occipitofrontal head circumference which was larger than the 97th centile, difficulty with lumbar punctures and/or symptoms of raised intracranial pressure. The reservoir was inserted in the parieto-occipital region with the tip lying in the occipital horns of the lateral ventricles and the dome lying subcutaneously.

Subsequently, the reservoir was tapped sufficiently often to control excessive head growth or symptoms of raised intracranial pressure (most commonly apnoea and or bradycardia). The CSF was removed through a 23 gauge butterfly needle usually by free drainage. Occasionally gentle suction was applied by a syringe when CSF flow was sluggish. All patients had regular cranial ultrasound examinations and the CSF sent for microscopy and culture. Shunt insertion was performed when the CSF became clear of red blood cells and the protein concentration was less than 2 g/l.

Results
The median (range) weight of the infants treated with a reservoir was 1100 g (675–3560 g). The gestation ranged from 23 to 41 weeks. The reservoirs were inserted at 6 to 68 days postnatal age (median 27 days).

There were no reservoir infections. Two infants became hyponatraemic, probably due to CSF removal as their serum sodium was normal before this removal; this was corrected with sodium supplements in the feeds. No infant became hypoalbuminaemic. One reservoir became blocked and required revision: no specific cause was identified but infection was excluded.

There were four cases of late intraventricular haemorrhage after reservoir insertion. These episodes occurred at 13, 17, 24, and 33 days after insertion. The CSF had become clear just before these bleeds. Fresh blood suddenly appeared in the CSF and red cell counts rose to between 10^7/l and 10^8/l. In one case a new blood clot was seen on cranial ultrasound scan at the time of the haemorrhage. This bleed occurred into a porencephalic cyst on the opposite side to the reservoir (fig). Clotting studies at the time of the haemorrhage were normal.

The method and amount of cerebrospinal fluid removed is compared in the table with

<table>
<thead>
<tr>
<th>Details of CSF removal</th>
<th>Gashill et al.</th>
<th>Lombardi et al.</th>
<th>Leeds General Infirmary</th>
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<td>Median (range) volume removed (ml) at each tap</td>
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<td>Median (range) tap frequency/day</td>
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<td>25–27</td>
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*Median not stated.