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Longitudinal assessment of infant lung function following pregnancies complicated by prolonged and preterm rupture of the membranes

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Abstract. Serial measurements of functional residual capacity (FRC) were made in 22 infants (median gestational age at delivery 32 weeks, range 25–40) during the first 2 years of life. All infants had been delivered from pregnancies complicated by prolonged and preterm rupture of the membranes (PPROM) of at least 1 week in duration. The onset of membrane rupture was at a median of 26 weeks (range 15–32) with a median duration of 5.5 weeks (range 1–21). The mean FRC at all postnatal ages studied: 25 ml/kg at 6 and 12 months and 24 ml/kg at 18 and 24 months did not differ significantly from the control population (mean 24 ml/kg). There was, however, a wider scatter of results in the study population: four infants born very preterm consistently had FRC results above the 95% confidence limits of the controls but only two infants had FRCs consistently below this range. These results suggest PPROM may not be an invariable association of abnormal antenatal lung growth.

Key words: Pulmonary hypoplasia – Functional residual capacity – Prematurity

Introduction

Fatal neonatal pulmonary hypoplasia has been reported in 21%–33% of neonates following preterm and prolonged rupture of the membranes (PPROM) [8, 11]. Infants, however, despite early onset and prolonged duration of membrane rupture do survive [1] and relatively few are symptomatic at follow up [12]. These results [1, 12] suggest PPROM is not an invariable association of abnormal antenatal lung growth, unfortunately data on lung function of PPROM survivors outside the neonatal period does not exist to test this hypothesis. We have now, therefore, performed serial lung function studies, to assess if a proportion of infants following PPROM survive without chronic lung function abnormality.

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Abbreviations: FRC = functional residual capacity; KCH = King's College Hospital; PPROM = prolonged and premature rupture of the membranes

Patients

Twenty-two infants were recruited into the study. These patients represent 22 of 26 survivors of 51 patients with PPROM prior to 32 weeks gestation, consecutively referred to King's College Hospital (KCH). In all cases the mothers had been referred to KCH for antenatal investigation. All patients were referred to KCH because of suspected PPROM and the diagnosis was confirmed from the maternal history and a sterile speculum examination demonstrating leakage of amniotic fluid. Leakage of amniotic fluid continued in all cases until delivery. All patients had oligohydramnios at presentation to KCH which persisted until delivery. Oligohydramnios, demonstrated at sequential antenatal ultrasound examinations, was defined as the absence of a pool of amniotic fluid of greater than 1 cm in diameter in a vertical plane [1, 3]. The other 25 pregnancies ended in spontaneous abortion ($n = 2$), intrauterine death ($n = 1$) and neonatal death ($n = 22$). Four survivors were lost to follow up, two of the four having emigrated. The onset of membrane rupture of the 22 study patients was at a median of 26 weeks (range 15–32 weeks) and the duration was 5.5 weeks (range 1–21). Antenatal dexamethasone was administered to all patients in an attempt to promote lung maturation, however, neither prophylactic antibiotics or tocolytics were prescribed. Their median gestational age at delivery was 32 weeks (range 25–40), two infants were small for gestational age. Seven infants had required ventilation in the neonatal period for a median of 7 days (range 2–15), the appearance of their chest roentgenogram was compatible with respiratory distress syndrome. Eight infants required an increase in their inspired oxygen concentration, their median oxygen dependency was 5 days (range 1–75). No infant developed a chest roentgenogram appearance compatible with bronchopulmonary dysplasia [5]. The median length of follow up was 23 months (range 5–32). One infant was only seen at 5 months of age, as she unfortunately died the following month of sudden infant death syndrome.

Ethical permission for this study was granted by the KCH Ethical Committee.

Methods

Infants were recalled for lung function measurements at approximately 6-monthly intervals. The infants were seen in the Paediatric

Respiratory Laboratory where their history was taken and they were weighed and examined. Lung function measurements were only performed when the infants had been asymptomatic for at least a 48-h period. Lung function was then assessed by measurement of functional residual capacity (FRC), using a helium gas dilution technique [15]. Measurements were made with the child sitting comfortably on his or her mother's knee after 1 of age and before this age in the semi-prone position. The infant breathed through a face mask, held firmly in place to prevent air leaks, into a water sealed spirometer (Gould Pulmonet III, Gould Electronics Ltd, Ilford, Essex, UK). The accuracy of the spirometer was checked daily with calibrated syringes. The spirometer incorporates a digital display of FRC, which was recorded above the respiratory trace at 15 s intervals. When the display remained unchanged for 30 s, equilibration was assumed to have occurred and the measurement discontinued. These traces were coded and analysed blind of clinical details. From the trace the end expiratory level was determined and the FRC calculated. The results were converted from ambient to body temperature, pressure saturated conditions.

To assess the reproducibility of the measurement of FRC in young children, two separate measurements were made in 20 children with a similar gestational and postnatal age range to the study population. The mean of the differences between the 20 paired measurements was 2.0 ml/kg. The intrasubject reproducibility was determined by calculating the coefficient of variation of these measurements and was found to be 7.3% [15]. The mean FRC of 50 healthy infants (controls), measured in our own laboratory of similar postnatal age to the study population, was 24 ml/kg (SD 1.9 ml/kg).

Results

Due to distances involved in travelling to KCH, a proportion of infants were unable to attend for every appointment (Table 1). The mean FRC at all postnatal ages studied did not differ significantly from that of our control population, being 25 ml/kg at 6 and 12 months and 24 ml/kg at 18 and 24 months. There was, however, a wider scatter of results amongst the study patients compared to the control population. Four infants (patients 1–4 in the Table) had FRC results consistently above the 95% confidence limits of our controls, three of the four infants had been ventilated in the neonatal period and had been born significantly earlier than the remaining infants ($P < 0.05$, Wilcoxon rank sum test). Two of the four hyperinflated infants had recurrent chest symptoms and one had suffered from bronchiolitis, all three had been ventilated in the neonatal period, the fourth infant was asymptomatic and had not required neonatal ventilation. Only two of the infants (patients 21 and 22), who were measured on more than one occasion, had FRCs consistently lower than the 95% confidence limits of the reference range.

Discussion

We have demonstrated the mean FRC of the survivors of PPROM to be similar to the control population throughout the first 2 years of life. Impairment of antenatal lung growth results in abnormal lung function postnatally and in particular small volume lungs [7]. Thus assessment of lung volume by measurement of FRC seemed likely to give an indication of antenatal lung growth. The measurement of FRC may not always accu-

Table 1. Schedule of follow up attendances for individual patients (Individual lung function data demonstrated as ml/kg)

Patient number	Gestation (weeks)		Duration of membrane rupture (weeks)	FRC (ml/kg) at postnatal age (months)			
	Onset of membrane rupture	Delivery		6	12	18	24
1	18	29	11	32	30		
2	22	31	9	42		35	32
3	24	26	2	35	38		
4	18	28	10	32	47	36	42
5	28	40	12		23	23	19
6	17	32	15	27	26	24	30
7	24	27	3	23		21	32
8	30	33	3	18			21
9	27	30	3	24			24
10	26	30	4	29	25	23	16
11	25	27	2	25	20		
12	28	32	4	25		29	25
13	21	36	15	22	25	27	
14	17	31	14	34	29		21
15	15	35	20	17	21		17
16	24	25	1	20	17	16	25
17	32	39	7	17		25	
18	27	32	5	15	Died		
19	32	34	2		17	Emigrated	
20	31	32	1		15		
21	29	35	6			18	13
22	20	41	21		16	16	

rately reflect lung volume, however, as errors can arise in infants with high airways resistance. Such infants suffer from gas trapping and are usually symptomatic [14], these abnormalities occur in severe asthmatic children [6]. Reassuringly, very few of our study population were symptomatic [12] and it has previously been demonstrated that infants with pulmonary hypoplasia are more likely to have a low rather than a high airways resistance [7]. Thus, in infants following PPROM, FRC is likely to give an accurate reflection of lung volume. Lung volume may also be assessed by plethysmographic estimation of thoracic gas volume. Unfortunately, unlike assessment of FRC, infants must be sedated for the measurement of thoracic gas volume, thus rendering this measurement inappropriate for repeated sequential assessment of asymptomatic infants.

Postnatal lung function following antenatal interventions suspected to interfere with fetal lung growth has been assessed by other investigators by measurement of crying vital capacity [13]. That test [13], however, relies on measuring the infant's response to a stimulus and it is not possible to guarantee the same strength stimulus in all infants. In contrast, measurement of FRC is highly reproducible in that population [15]. Respiratory symptoms have also been used as an indication of impaired antenatal lung growth [1, 9]. Lung function abnormalities, however, may be asymptomatic [15] and thus recording clinical respiratory problems only would be a relatively insensitive indicator of abnormal lung growth.

Several authors [4, 10] have expressed the measurement of FRC in relation to both body length and weight. In this study FRC measurements were related to weight, as length could not be accurately measured. Certain of our infants initially had postural deformities [1] and others had congenital dislocated hips and were in harnesses. In this group the infants were weighed, while being appropriately treated and the weight of a similar harness was removed from the weight of the baby measured in harness. The FRC results of our control population were very similar to other reference ranges when related to body weight: mean FRC 24.5 ml/kg (SD 2.8) [4] and 24.2 ml/kg (SD 5.7) for males and 23.2 ml/kg (SD 4.3) for females [10].

Four infants had FRC results consistently elevated above the 95% confidence limits of the reference range. All of these infants had been born at a very early gestation and three had required neonatal ventilation. Elevation of FRC above the reference range has been previously demonstrated in ventilated infants born preterm but without PPROM [15]. This suggests this apparent hyperinflation may be reflection of the neonatal rather than the antenatal insult.

Only two infants had consistently low FRC results. This finding and the low incidence of respiratory symptoms at follow up [12] suggest antenatal lung growth and development is not necessarily impaired by oligohydramnios due to PPROM. The present results further encourage expectant management of pregnancies complicated by PPROM [1, 2, 3] if infection is absent.

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