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Fetal breathing movements in pregnancies complicated by premature membrane rupture in the second trimester

M. Blott, A. Greenough and K.H. Nicolaides

Departments of Child Health and the Harris Birthright Research Centre for Fetal Medicine, Department of Obstetrics and Gynaecology, Kings' College School of Medicine, Kings' College Hospital, Denmark Hill, London SE5 (U.K.)

Summary

Forty pregnancies complicated by oligohydramnios in the second trimester due to prolonged and premature membrane rupture (PPROM) were followed prospectively to determine factors influencing fetal breathing activity and the relationship of fetal breathing movements (FBM) to outcome. The patients were retrospectively divided into three groups according to the presence or absence of FBM. Membrane rupture occurred at a significantly earlier gestation in those pregnancies in which FBM were absent. Duration of membrane rupture only differed significantly between pregnancies in which FBM were intermittent or consistently present.

In the group in which FBM were always absent ($N = 12$) all the infants died in utero or in the neonatal period due to pulmonary hypoplasia. In the group with FBM always present ($N = 17$) all infants survived. In the third group FBM were observed in some, but not all, ultrasound examinations ($N = 11$). Some infants survived ($N = 6$), while others died either due to pulmonary hypoplasia or neonatal sepsis. These results show the necessity for several serial ultrasound examinations, all demonstrating the absence of fetal breathing movements, before pulmonary hypoplasia in PPROM can be predicted confidently.

fetal breathing movements; pulmonary hypoplasia; oligohydramnios; premature rupture of the membranes.

Introduction

Fetal chest movements have been observed from as early as 8 weeks gestation in human pregnancies [10]. Regular fetal breathing movements (FBM) are established

by 20 weeks and the duration of breathing activity increases with advancing gestation [10,17]. Fetal breathing movements (FBM) have a diurnal variation and are affected by maternal glucose levels, ingestion of sedative drugs or alcohol and cigarette smoking [9,8,13,20,22].

Animal studies have shown an association between FBM and pulmonary development [27]. Cessation of FBM by cervical cord transection in the fetal rabbit and reduction of FBM by thoracoplasty in the fetal lamb both result in pulmonary hypoplasia [1,12]. In human fetuses congenital abnormalities which result in limitation of FBM, such as myotonic muscular dystrophy, are also associated with pulmonary hypoplasia [23].

In a preliminary study we found that in some pregnancies complicated by premature and prolonged membrane rupture (PPROM) FBM were absent, and in these cases the perinatal outcome was poor due to abnormal lung growth. In contrast, when FBM persisted the outcome was good [6]. In a much larger series we have now assessed fetal breathing activity and determined the validity of our preliminary observations.

Patients and methods

Selection of patients

Patients with a history of PPROM, occurring before 30 weeks gestation and with a duration of longer than 1 week, were eligible to enter the study. In all cases the diagnosis had been confirmed by a positive nitrazine test of the fluid in the posterior vaginal fornix.

Clinical management

The patients were admitted to hospital from the time of diagnosis to delivery. All were screened for infection: by daily recording of maternal pulse and temperature, and weekly measurement of blood leucocytes and microbiological examination of a low vaginal swab. Prophylactic antibiotics were not given in the antenatal period and only prescribed in the immediate postnatal period for documented infection. Dexamethasone was administered at fortnightly intervals, with the aim of stimulating fetal pulmonary maturation. The spontaneous onset of labour was not inhibited and patients were electively delivered at 32—34 weeks gestation, in an attempt to reduce the incidence and severity of orthopaedic deformities.

Ultrasound examinations

At the time of referral to our unit an ultrasound scan was performed for the exclusion of major congenital abnormalities, assessment of amniotic fluid volume and quantification of FBM. Oligohydramnios was defined as the absence of any pool of amniotic fluid measured in a vertical plane of greater than 1 cm [14]. Subsequent ultrasound scans were performed at one- or two-weekly intervals until delivery.

Fetal breathing movements

A real-time ultrasound examination was performed for 30 min and any fetal chest wall movements were recorded using a two-track chart recorder. FBM were defined as being present if a continuous period of chest wall movements lasting for at least 60 s, with a breath-to-breath interval of 6 s or less, was seen [14,21,24,25]. If no FBM were present the scan time was extended to 60 min. All patients were scanned within 2 h of a standard hospital meal, and were asked to refrain from smoking on the day of the scan.

On the basis of fetal breathing activity, the patients were retrospectively divided into three groups.

Group 1. FBM present at all ultrasound examinations.
Group 2. FBM present at some and absent at other ultrasound examinations.
Group 3. FBM absent at all ultrasound examinations.

Neonatal management

Details of respiratory support required in the neonatal period were recorded. A clinical diagnosis of pulmonary hypoplasia was made if the infant required artificial ventilation with high positive pressures (> 30 cm H_2O), both for resuscitation and subsequent respiratory support and had a chest radiograph compatible with small volume lungs. In addition, all infants were examined at 6 months of age to document any continuing chronic respiratory problems. In the event of a fetal or neonatal death, permission for postmortem examination was requested, at which the diagnosis of pulmonary hypoplasia was made if the lung to body weight ratio was less than 0.012 and the radial alveolar count was less than or equal to 4.1 [2].

Statistical analysis

A Wilcoxon rank sum test was used to establish if differences between the three groups of patients in the gestation at which membrane rupture occurred, the duration of oligohydramnios or the gestation at delivery were significant. Differences in the neonatal outcome according to the presence or absence of FBM were assessed for statistical significance using a χ^2 test.

Results

During an 18-month period, 40 patients with singleton pregnancies were seen and all agreed to be included in the study. The mean gestational age at membrane rupture was 21.3 weeks (range 15—29 weeks) and the mean gestational age at delivery was 28.6 weeks (range 23—35 weeks).

The onset and duration of oligohydramnios and the outcome of the pregnancies is shown in Table I. Statistically significant differences between the three groups were found for: gestational age at membrane rupture (groups 1 and 2 were earlier

TABLE I

Outcome of 40 pregnancies complicated by premature rupture of the membranes according to the presence or absence of fetal breathing movements.

Group	N	Gestation age				TOP	IUD/ SA	NND	Alive
		PROM		Delivery					
		Mean	Range	Mean	Range				
1	12	19.5	15—26	26.7	23—30	1	1	10ᵃ	0*
2	11	18.6	15—25	29.4	25—35	0	1	4ᵃ	6
3	17	24.8	17—29	29.9	24—35	0	0	0	17*

TOP, termination of pregnancy; IUD, intrauterine death; SA, spontaneous abortion; NND, neonatal death.
ᵃPulmonary hypoplasia, $N = 10$.
ᵇPulmonary hypoplasia, $N = 1$; neonatal sepsis, $N = 3$.
*χ^2 test, $P\,0.01$.

than group 3; $P < 0.01$) and duration of membrane rupture (longer in group 2 than group 3; $P < 0.01$).

Group 1. FBM absent (N = 12)

Each patient was scanned for 1 h on at least four separate occasions. Although in three pregnancies there were occasional fetal gasping movements they were not regular and did not last for 60 s. In the remaining 9 cases there was no fetal respiratory activity.

One pregnancy ended in an intrauterine death at 24 weeks, and another was terminated at the mother's request at 23 weeks gestation. The remaining 10 patients delivered at 24—34 weeks gestation. All 10 infants required high peak inspiratory pressures both for resuscitation and subsequent respiratory support. However, satisfactory oxygenation was never achieved and the babies died within 48 h. Postmortem examination was performed in 11 cases, confirming pulmonary hypoplasia. A postmortem examination was not performed on the fetus that was electively aborted.

Group 2. FBM intermittent (N = 11)

The gestation of ultrasound examinations and the presence or absence of FBM of this group are shown in Table II. There was no uniformity of gestational age at which FBM were either absent or present.

One pregnancy aborted spontaneously at 23 weeks gestation (case 1); FBM were present at 20 and 21 weeks but absent at 22 and 23 weeks. No postmortem examination was performed. Three infants (cases 2—4) died in the neonatal period from

TABLE II

The gestational ages at which FBM were present or absent in the six pregnancies with a favourable neonatal outcome in group 2.

Gestation (weeks)	Case										
	1	2	3	4	5	6	7	8	9	10	11
17							−				
18	−									−	−
19							−	−			
20	+				−			−	−	−	−
21	+				+		−	−	+	−	−
22	−				−		−	−	+	+	−
23	−	+			−	−	−	+		−	−
24		−		+	−	+	+	+	−	+	−
25		−		+	+	+	+	−		+	−
26				−	−	+			+	+	−
27				−	−	+	−				
28			+		−	+	−		+	−	
29			+		−	−	+		+		+
30			−		−	−	+		+		+
31					−		+		+		
32									+		
33									+		

+ Fetal breathing movements present.
− Fetal breathing movements absent.

overwhelming sepsis. In these cases FBM were originally present but disappeared 1 —2 weeks before the onset of spontaneous labour and delivery. Antenatally, there was a suspicion of choriamnionitis in only one of these cases (a maternal pyrexia and the presence of leucocytes in the amniotic fluid obtained at amniocentesis).

One infant (case 5), delivered at 31 weeks gestation, died of respiratory failure due to unilateral pulmonary hypoplasia. Antenatally FBM were present in two of this patient's twelve ultrasound examinations.

The remaining six pregnancies (cases 6—11) were delivered between 25 and 35 weeks gestation and all the infants survived. One infant born at 25 weeks gestation required respiratory support for respiratory distress syndrome but the other five infants had no neonatal respiratory problems. All six infants were reviewed at 6 months of age and none had chronic respiratory problems.

Group 3. FBM present (N = 17)

A total of 70 ultrasound examinations were performed in this group and on all occasions FBM were present. The patients were delivered at 24—35 weeks gestation and all the infants survived. Although 6 babies required support from artificial ventilation for respiratory distress syndrome, the peak inspiratory pressures required

were less than 30 cm H_2O (range 15—25 cm H_2O). One of the babies required ventilatory support for 4 weeks because she had a persistent ductus arteriosus that required surgical ligation. The remaining 11 infants had no neonatal respiratory problems. Fourteen of the 17 infants were reviewed at 6 months of age and they did not have chronic respiratory problems. One infant was not examined because she lived abroad and the remaining two were less than 6 months of age.

Discussion

The findings of this study confirm that in pregnancies with oligohydramnios due to PPROM the absence of FBM is associated with neonatal death due to pulmonary hypoplasia, while the presence of FBM is associated with a good perinatal outcome. These results are in contrast to those reported by Moessinger et al. who used a different definition of FBM and found no difference in outcome [15]. The more stringent definition in this study has been used extensively in the literature [14,24—26] because it differentiates FBM from fetal gaspings, which are often seen in compromised fetuses [18,3].

These results and our previous results confirm animal data linking absent FBM and pulmonary hypoplasia. It has been reported that infants with pulmonary hypoplasia due to renal abnormalities [15] do breathe and we have demonstrated FBM in fetuses with idiopathic pulmonary hypoplasia. These findings suggest infants with pulmonary hypoplasia can make breathing movements and suggest that in PPROM the absence of FBM has a causal association with abnormal lung growth.

The outcome of pregnancies with intermittent FBM is varied, with some infants dying of sepsis or respiratory failure and others surviving with no apparent pulmonary problems. In this study we only considered FBM to be present or absent, and the outcome in terms of survival or death. Variations in the quantity and quality of FBM may explain the differences in outcome between apparently similar patients. Furthermore, it is possible that in the group of survivors there were minor degrees of pulmonary hypoplasia which were masked by respiratory distress syndrome. Detailed lung function both at birth and in later life is necessary to determine whether minor differences in lung growth can be related to the quantity and quality of FBM.

Possible factors affecting both FBM and pulmonary hypoplasia include the gestational age at membrane rupture, the degree of oligohydramnios and the presence of subclinical infection or uterine activity.

The group in which FBM were absent had a significantly earlier gestational age at membrane rupture than the group with FBM present. Oligohydramnios and extrathoracic compression of the fetal chest before 24 weeks gestation may have prevented FBM during this critical stage of lung development [19]. However, there was some degree of overlap in the gestational age of membrane rupture between the two groups, and therefore this cannot be the sole factor for the development of pulmonary hypoplasia.

Antenatally, both fetal breathing activity and the development of pulmonary hypoplasia may be dependent on the degree of oligohydramnios. Although in this

series all three groups had fulfilled the criterion for oligohydramnios, assessment of amniotic fluid volume by ultrasonographic techniques does not allow accurate quantification.

A change in fetal breathing activity is a sensitive indicator of intrauterine infection [24], and is claimed to be more reliable than analysis of amniotic fluid [26]. This is confirmed by the findings of the present series in that all three fetuses who developed early neonatal sepsis had ceased making breathing movements 1—2 weeks before delivery. It is possible that in these fetuses cessation of FBM was indicative of intrauterine infection. However, it is unlikely that a chronic low-grade infection was responsible in all the other pregnancies in which FBM were absent or intermittent, as none of these infants developed neonatal sepsis or indeed had any evidence of bacterial colonisation. Our results demonstrate that neonatal sepsis is rare even in cases of very prolonged duration of membrane rupture, suggesting expectant management of such pregnancies is a safe alternative.

Absence of FBM has been shown to be an apparently accurate predictor of preterm labour [4,7]. Cessation of FBM occurs 48 h before the onset of labour [11], and this has been attributed to a direct effect of the rising prostaglandin levels on central fetal respiratory centres [5]. In fetal lambs, infusion of prostaglandin E2 results in inhibition of FBM whereas the administration of prostaglandin inhibitors increases the frequency of FBM [16]. In this series all patients delivered prematurely and it is therefore possible that although the gestational age at delivery was similar in the three groups, differences in prostaglandin levels may have been responsible for differences in the fetal breathing activity.

In pregnancies complicated by PPROM the persistent absence of FBM was strongly associated with perinatal death due to pulmonary hypoplasia. The mechanisms for the absence of FBM remain to be elucidated.

Acknowledgement

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