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PULMONARY INTERSTITIAL EMPHYSEMA IN LOW BIRTH WEIGHT INFANTS: CHARACTERISTICS OF SURVIVORS

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Twenty out of 303 ventilated low birth weight infants, hospitalized in the Beilinson Medical Center's Intensive Care Unit, during the years 1984-1986, developed pulmonary interstitial emphysema. Eighteen infants had very low birth weight (less than 1500 grams) and 17 were less than 30 weeks' gestation. The mean birth weight was 987 $\pm$ 311 and mean gestational age 27.7 $\pm$ 2.5. Eight infants survived the pulmonary disease. There were no significant differences in the neonatal parameters between infants who died or survived. However, the survivors had a significantly lower maximal peak inspiratory pressure and FiO_2 on the first day of ventilation. The incidence of pneumothorax and asphyxia was the same in both groups.

INTRODUCTION

Pulmonary interstitial emphysema (PIE) is a complication of mechanical ventilation especially in low birth weight, premature infants. This complication causes deterioration of the infant's condition and increases mortality rate to 57 % - 89 % /1-3/.

Low birth weight, prematurity, hyaline membrane disease and mechanical ventilation are risk factors associated with the development of PIE /5,7,10/. PIE developing on the first day of life carries a grave prognosis /5,8/ and there is a positive correlation between high ventilatory pressures and mortality /3/. A retrospective study was carried out in order to examine the differences between infants with PIE who survived or succumbed.

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PATIENTS AND METHODS

The medical records of all ventilated low birth weight infants hospitalized in the Neonatal Intensive Care Unit of the Beilinson Medical Center during the years 1984 - 1986, were reviewed retrospectively for the presence of PIE.

Indications for institution of mechanical ventilation were based on standard criteria /8/. The respiratory support was aimed at maintaining a pH greater than 7.25, and PaO_2 of 50 to 80 torr with a minimal mean airway pressure (MAP).

PIE was diagnosed by a pediatric radiologist when a coarse reticular pattern of linear and rounded radiolucencies was seen extending out of the hilum /13/.

Twenty infants with radiologically confirmed PIE were identified. Their clinical records were examined with attention to gestational age, birth weight, mode of birth, Apgar score, mechanical ventilation parameters and oxygen requirements prior and during airleak, presence of other perinatal complications and outcome. The serial chest X-rays were reviewed with attention to the development of hyaline membrane disease, PIE, pneumothorax, pneumomediastinum and bronchopulmonary dysplasia.

PIE was managed conservatively. When PIE was unilateral the infant was placed in the lateral decubitus position, affected side down /3/. Positive pressure ventilation was reduced as much as clinically permissible. In 3 severely ill infants, high frequency ventilation was attempted /6/ ("Infant star" neonatal ventilator).

Statistical analysis: surviving premature infants with PIE were compared to infants who died of this pulmonary disease. Results were expressed as mean $\pm$ standard deviation. Differences between groups were analyzed by the Student's t-test. Comparisons among groups for frequency of an event were analyzed by the Chisquare test. Statistical significance was accepted at $p < 0.05$.

RESULTS

During the study period 303 low birth weight infants required mechanical ventilation in the first days of life. Twenty infants developed PIE (6.6 %). The primary respiratory diagnosis of all infants was hyaline membrane disease. Nineteen infants were ventilated on the first day of life and all were ventilated before developing PIE. The main neonatal parameters are summarized in Table I. The mean birth weight was 987.5 $\pm$ 311 grams (range 640 gr - 1790 gr). Eighteen infants had a very low birth weight ($<$ 1500 gram). Mean gestational age was 27.7 $\pm$ 2.5 weeks (range 24 - 34 weeks). Seventeen patients were less than 30 weeks of gestation, eleven developed pneumothorax, that was bilateral in 5.

TABLE I

Neonatal parameters of 20 patients with PIE (mean ± SD)

Birth weight (grams)	987.5 ± 311.7
Gestational age (weeks)	27.7 ± 2.5
Apgar score at 1 minute	3.9 ± 2.9
Day PIE developed	3.0 ± 1.8
Location of PIE	
Bilateral	15 (75 %)
Unilateral	5 (25 %)
Incidence of pneumothoraces	11 (55 %)
Mortality	12 (60 %)

Mean Apgar score at one minute was 3.9 ± 2.9. PIE developed on the first day of life in 5 infants. The mean day at which PIE developed was 3.0 ± 1.8 (range 1-7 days). PIE was bilateral in 15 patients.

Twelve infants died of respiratory failure with a chest roentgenogram consistent with PIE on the day of death. Eight infants survived and their chest roentgenograms were clear of PIE. One infant of the latter group died on the 18th day of life of non-respiratory cause. The main neonatal parameters of both groups are summarized in Table II.

As can be seen, there were no significant differences between the 2 groups. However, the infants who died tended to be smaller (899 ± 202 grams vs 1120 ± 408 grams) and of younger gestational age (27.2 ± 2.0 weeks vs 28.4 ± 3.2 weeks).

The main ventilatory parameters for the 2 groups are summarized in Table III. As can be seen there were significant differences in the ventilatory characteristics of both groups. Maximal peak inspiratory pressure (PIP) used on the first day of ventilation was higher as were the first and last FiO_2 used on this day. The maximal PIP used during ventilation was also significantly higher.

Outcome: 7 infants survived the neonatal period. Bronchopulmonary dysplasia developed in 6 (85 %).

TABLE II

Comparison of neonatal parameters of patients who survived versus those who died (mean ± SD)

	Survived n = 8	Died n = 12	p*
Birth weight (grams)	1120 ± 407.8	899 ± 202	NS
Gestational age (weeks)	28.4 ± 3.2	27.2 ± 2.0	NS
Apgar score at 1 minute	3.3 ± 3.4	4.25 ± 2.7	NS
Day PIE developed	3.7 ± 1.8	2.7 ± 1.8	NS
Location of PIE			
Bilateral	5 (62 %)	10 (83 %)	NS
Unilateral	3 (38 %)	2 (27 %)	NS
Incidence of pneumothoraces	4 (50 %)	7 (58 %)	NS

*Significant $p < 0.05$

TABLE III

Ventilatory characteristics (mean ± SD)

	Total	Survivors	Dead	p*
First day of ventilation	(n = 20)	(n = 8)	(n = 12)	
First PIP (cm H_2O)	20.7 ± 3.3	19.7 ± 2.9	21.2 ± 3.4	NS
Last PIP (cm H_2O)	24.2 ± 5.4	22.3 ± 3.5	26.0 ± 6.6	<0.025
First FiO_2	0.85 ± 20	0.72 ± 18	0.93 ± 18	<0.01
Last FiO_2	0.79 ± 23	0.66 ± 23	0.88 ± 19	<0.025
% infant with PIP > 25 cm H_2O		14 %	60 %	<0.05
Maximal PIP (cm H_2O)	33.4 ± 10.2	23.8 ± 5.7	38.6 ± 8.1	<0.001

*Significant $p < 0.05$
PIP = Peak inspiratory pressure
FiO_2 = Fractionized inspiratory oxygen

DISCUSSION

Pulmonary interstitial emphysema occurs when gas ruptures through the alveoli into the perivascular spaces and becomes trapped in the connective tissue of the peri-bronchovascular sheaths, the interlobular septa and the visceral pleura /7/. The small premature infant is especially prone to development of PIE and there is a strong association with hyaline membrane disease and mechanical ventilation /7,10/. The mortality rate is very high, but there has been an improvement from 89 % in 1978 /10/ to 38 % /8/ in 1987. Among the survivors, bronchopulmonary dysplasia is very frequent /5,8/.

Risk factors for PIE are prematurity, low birthweight, HMD, and high peak inspiratory pressures on the first day of ventilation /5,10/. Gaylord et al /5/ believe that mortality can be predicted early in the infant's course with a 70 % confidence level using a formula constructed with the variables birthweight and highest PIP on day 1. This formula was not predictive in our group of infants. PIE developing on the first day is more severe and has a fatal outcome: 77 % mortality as opposed to 45 % when PIE develops later /5/, or 49 % versus 16 % (8).

Prolongation of inspiratory time was found to be a major risk factor in pathogenesis of pulmonary air leaks, overshadowing other ventilatory settings /11/ but the relative importance of this factor in PIE has not been evaluated. However, it is possible that the improved outcome reported by Heneghan et al /8/ can be attributed to ventilation of their infants at a maximal inspiratory time of 0.7 seconds.

Gaylord et al /5/ found that infants who died were significantly smaller and younger than those who survived. In our work there was the same tendency but the differences did not reach statistical significance (probably due to the small study group). In both works Apgar scores, location of the PIE, and incidence of pneumothorax were not significant. The ventilatory characteristics were significantly different: highest peak inspiratory pressures and higher oxygen requirement on the first day in infants who died.

Medical treatment of infants with PIE is usually conservative: physiotherapy and maintenance of the lowest possible mean airway pressure with high rate and short inspiratory time. However, in recent years new methods have been developed. High frequency ventilation seems promising in treatment of bilateral PIE /6/. Gaylord et al reduced mortality with this method from 82 % to 44 % in a very high risk group of very low birth infants with PIE. When PIE is unilateral the best approach is to position the infant on the affected side /3,12/ so that the emphysematous lung is underventilated compared with the contralateral lung. This simple method is effective and safer than selective bronchial intubation /2/ or surgical resection /1,9/.

Extracorporal membrane oxygenation is a method developed to treat acute cardiopulmonary failure. Frattallone et al /4/ tried using it for infants with severe PIE but the situation worsened, after adding apnea and full lung rest, the method worked and after 2 or 3 days there was a resolution of air leaks. This method was used mainly in full term babies /5,6/ so that its application in sick, very low birth weight infants is still unclear.

PIE is a severe complication of the respiratory distress syndrome, especially in small premature infants, but new treatment approaches give promise of a better outcome in the future.

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