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Original article

Pneumothorax in premature infants with respiratory distress syndrome: focus on risk factors

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Abstract

Introduction: Pneumothorax is a life threatening condition, more often seen in immature infants receiving mechanical ventilation. It carries a significant risk of death and impaired outcome.

Objective: To determine predictive factors for the occurrence of pneumothorax in preterm infants with respiratory distress syndrome (RDS).

Patients and methods: The present study was conducted in a tertiary research and educational hospital, NICU, Pediatric Clinic UKC Sarajevo, from January 2010 to December 2013. All infants had chest X-ray at admission, and were treated due to RDS with nasal continuous positive airway pressure (CPAP), mechanical ventilation, or high frequency oscillatory ventilation. At admission we registered data regarding birth weight, gestational age, Apgar score, prenatally given steroids. Inclusion criteria were fulfilled by 417 infants. Data about timing, circumstances, side and treatment of pneumothorax were gathered from medical records.

Results: Mean birth weight was 1,477 g, mean gestational age 29.6 weeks. We report 98 infants who did not survive. We also report incidence of pneumothorax in 5% of the infants with RDS. In this study pneumothorax and non-pneumothorax groups didn't differ regarding sex, gestational age (median 29 and 30) nor birth weight ($p = 0.818$). Apgar score at the 1st and 5th minute of life had no influence in genesis of pulmonary air leak, neither prenatally given steroids ($p = 0.639$), nor surfactant administration. There was a low coverage of preterm infants with prenatal steroids (overall 28.29%). We found that $FiO_2 \geq 0.4$ in the first 12 hours of life, and need for mechanical ventilation are predicting factors for developing pneumothorax ($p < 0.05$).

Conclusion: Together with mechanical ventilation, inspired fraction of oxygen higher than 40%, needed to provide adequate oxygenation in the first 12 hours of life in preterm infants, could be a predictive factor in selecting the highest risk babies for development of neonatal pneumothorax.

Keywords

Preterm infant, respiratory distress syndrome, pneumothorax, risk factors.

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Introduction

Pneumothorax is a life threatening condition, more often seen in immature infants receiving mechanical ventilation. According to a report from the Vermont Oxford Network database in 1999, incidence of pneumothorax is 6.3% in the group of infants with birth weight from 500 to 1,500 grams, and decreases to 4.1% in 2013 [1]. It begins with the rupture of an over-distended alveoli. The air escapes along the perivascular connective tissue sheath into the pleural space, causing a pneumothorax. Less common sites of air loss are hilum, pericardial space, subcutaneous tissue, or peritoneal space, resulting in pneumomediastinum, pneumopericardium, subcutaneous emphysema, and pneumoperitoneum, altogether known as air leak syndromes. Due to inadequate gas exchange, mediastinal shift and compromise of cardiovascular system it carries a significant risk of death and impaired outcome. Tension pneumothorax causes rise in intrapleural pressure and subsequent lung collapse, as well as impaired venous return to the heart that can cause systemic hypotension, respiratory and cardiac arrest. It is, therefore, essential to recognize high risk infants and treat them properly in order to avoid undesirable results. Risk factors for pneumothorax include immaturity, respiratory distress syndrome (RDS), invasive and non-invasive respiratory support, chorioamnionitis, out-born status. For moderate-late preterm infants risk factors also include higher birth weight, male sex, and rupture of membranes > 24 hours [2]. The most common therapeutic approach to pneumothorax is chest tube placement. Needle aspiration is also an option, especially in cases of mild to moderate pneumothorax, or while waiting for experienced team. However, management of this condition is not always clearly defined, especially when the infant is hemodynamically stable. In such cases expectant management is an option as it was first reported by Litmanovitz and Carlo [3]. Objective of this study is to determine predictive factors for the occurrence of pneumothorax in preterm infants with RDS.

Patients and methods

This study was conducted at Neonatal Intensive Care Unit, Pediatric Clinic UKC Sarajevo, Bosnia and Herzegovina. It included 417 infants with diagnosed RDS, treated in the period 01.01.2010-31.12.2013. Chest X-ray was performed in all infants at admission. RDS was treated according to current European guidelines for management of RDS (2013 update) [4] using nasal continuous positive airway pressure (CPAP), conventional mechanical ventilation, or high frequency oscillatory ventilation. Bovine surfactant (Survanta®) in one or more doses was given to infants requiring $FiO_2 \geq 0.4$. At the time of occurrence of pneumothorax, X-ray was done to every infant immediately after clinical deterioration. All infants with confirmed pneumothorax were treated with chest tube placement. We tested distribution by Kolmogorov-Smirnov test, Chi square when comparing frequencies, we used Fisher's exact test for groups with less then 5. Analyses of continuous variables was done by Mann-Whitney. Statistical tests were carried out at the 5% significance level.

Results

Our study included 417 infants, of whom 236 were male (56.59%). Their mean gestational age was 29.6 weeks (± 2.98), mean birth weight 1,477 g (± 521), range 520-3,330 g. There were 98/417 of infants who died. Patients are divided in two groups: pneumothorax (21) and non-pneumothorax (396).

In 21 (5%) out of 417 patients with RDS, air leak occurred. Group of patients with diagnosed pneumothorax is compared with the group of patients without pneumothorax (**Tab. 1**). There were no significant differences between groups in sex distribution, gestational age, birth weight, Apgar scores at 1st and 5th minutes and coverage with antenatal steroids.

Comparing these two groups in FiO_2 requirement and mode of ventilation, statistical significance was found between groups ($p < 0.05$) in max FiO_2 in the first 12 hours, need for mechanical ventilation or nasal CPAP, and lethal outcome, while

there was no statistical difference in incidence of mayor intraventricular/periventricular hemorrhage (IVH-PVH) and bronchopulmonary dysplasia (BPD) between groups (**Tab. 2**).

Discussion

The aim of this study was to determine predictive factors for the occurrence of pneumothorax in preterm infants with RDS in order to avoid catastrophic events that can be a consequence of an unexpected situation. Pneumothorax has been reported to occur in 3-9% of very low birth weight infants [5-7] and we confirmed its incidence in our study (5%). We didn't find sex predominance in occurrence of pneumothorax, although some authors found male prevalence in a group of moderate to late preterm and term infants [2]. In our study groups of infants with and without pneumothorax didn't differ regarding gestational age (median 29 and 30) nor birth weight (p = 0.818). When divided into subgroups (ELBW, VLBW, LBW) they showed a slight difference, without a statistical significance. Neither Apgar score at the 1st and 5th minute of life has influence in genesis of pulmonary air leak, according to the conclusions of other authors [8], nor prenatally given steroids (p = 0.639). Despite clear efficiency of prenatally given steroids on lung maturation, incidence and severity of RDS, improved survival and outcome, unfortunately the mean coverage in 75 countries with > 90% of maternal coverage, newborn and child deaths is estimated at around only 10% [9]. Even in middle-income countries, antenatal steroids may

Table 1. Descriptive statistics of two study groups (pneumothorax and non-pneumothorax).

	Pneumothorax				Non-pneumothorax				p
n (%)	21 (5%)				396 (95%)				
Sex, n (%)	**F**		**M**		**F**		**M**		0.394
	11 (52.4%)		10 (47.6%)		170 (57.1%)		226 (42.9%)		
Gestational age (weeks), Me (Iq)	29 (26-34)				30 (28-32)				0.875
Birth weight (grams), Me (Iq)	1,400 (845-1,950)				1,430 (1,090-1,800)				0.818
Birth weight, n (%)	**< 1,000**	**1,000-1,500**	**1,501-2,500**	**> 2,500**	**< 1,000**	**1,000-1,500**	**1,501-2,500**	**> 2,500**	0.122
	6 (28.6%)	6 (28.6%)	6 (28.6%)	3 (14.3%)	70 (17.7%)	149 (37.6%)	158 (39.9%)	19 (4.8%)	
Apgar score 1st minute, Me (Iq)	5 (3-7)				6 (4-7)				0.249
Apgar score 5th min, Me (Iq)	7 (5-7)				7 (6-8)				0.171
Prenatal steroids, n (%)	5 (23.8%)				113 (28.5%)				0.639

Me: median; Iq: interquartile range.

Table 2. Respiratory distress syndrome (RDS) treatment, oxygen dependency, and outcome.

	Pneumothorax		Non-pneumothorax		p
Surfactant, n (%)	12 (57.1%)		211 (53.3%)		0.730
Dependency on mechanical ventilation, n (%)	18 (85.7%)		249 (62.9%)		**0.034**
Days on mechanical ventilation, Me (Iq)	5 (2.7-9.0)		3 (1.0-6.0)		0.07
Dependency on nasal CPAP, n (%)	9 (42.9)		264 (66.7)		**0.025**
Days on nasal CPAP, Me (Iq)	2 (1.5-3.0)		2 (1.0-4.0)		0.904
Overall oxygen dependency, Me (Iq)	4 (2.0-20.5)		2 (1.0-5.0)		0.099
Max FiO_2 (first 12 hours), Me (Iq)	55% (47-90%)		35.5% (28-52.25%)		**< 0.001**
Max FiO_2 (first 12 hours) (40%), n (%)	**< 40%**	**≥ 40%**	**< 40%**	**≥ 40%**	**0.008**
	2 (9.5%)	13 (61.9%)	138 (34.8%)	124 (31.3%)	
Death, n (%)	10 (47.6%)		88 (22.2%)		**0.014**
BPD, n (%)	2 (9.5%)		37 (9.3%)		0.604
IVH (grade III-IV), n (%)	2 (9.5%)		22 (5.6%)		0.344

Me: median; Iq: interquartile range.
CPAP: continuous positive airway pressure; BPD: bronchopulmonary dysplasia; IVH: intraventricular hemorrhage.

not be routinely administered, and overall maternal coverage in a few countries is less than 20% of those indicated [10]. In our study we also noticed a low coverage with prenatal steroids in preterm infants (overall 28.29%). We did not show surfactant administration to be a statistically significant factor in escaping pneumothorax in preterm infants with RDS ($p = 0.73$), compared to other authors who found that surfactant replacement therapy significantly reduces the risk of pneumothorax in ventilated newborns. An explanation for that can be the fact that we have analyzed surfactant use not only in ventilated infants, but also in infants who were extubated immediately after surfactant application (INSURE strategy: INtubate, SURfactant, Extubate). In our study, approximately half patients in both groups, with and without pneumothorax, were treated with surfactant. One similar study showed that 32.4% of newborns with pneumothorax received surfactant compared to 60.4% ventilated infants without pneumothorax [12]. Mechanically ventilated infants more frequently develop air leaks. We found that babies with pneumothorax were more dependent on mechanical ventilation, so mechanical ventilation was identified as a risk factor ($p < 0.05$). Babies who needed higher FiO_2 in the first 12 hours of life, irrespectively of the mode of oxygen delivery, were more likely to develop pneumothorax ($p < 0.001$), with a cut-off value of 40% ($p = 0.008$). In the present study there was no significant difference in the two groups (pneumothorax and non-pneumothorax) regarding presence of BPD and IVH grade ≥ 3. The average time of diagnosis of pneumothorax was 2.5 days, and 72% was diagnosed by the end of the 3rd day. There was no pneumothorax after the 5th day. Similar results were published by Ramash et al. [11]: about 84% of pneumothorax occurred within 48 hours of life. Our patients had 12/21 (57.14%) right-sided air leaks; 7/21 (33.3%) were on the left side; 2/21 (9.52%) were bilateral. Malek et al. [12] found pneumothorax in the following percentages: 66.6% in the right side, 12.8% in the left side and 0.6% bilateral. Pulmonary hemorrhage and airway suction, surfactant application and resuscitation due to asphyxia were events that happened prior to air leak in 8/21 patients. Management of neonatal pneumothorax is not clearly defined and depends on presence of mediastinal shift, hemodynamic stability of the patient, experience of the staff, their skill in solving complications, etc. The most common option is chest tube placement, and according to hospital policy all of our patients got a chest tube. Needle aspiration has been recommended in infants with mild to moderate symptoms [13-15]. Therapeutic option is also an expectant therapy, which is a gentle and conservative treatment, previously being reserved for non-ventilated patients. Litmanovitz and Carlo [3] did a retrospective analysis of expectant management in ventilated neonates with symptomatic pneumothorax and for the first time proved the safety of this approach. There is a significant difference in outcome between our groups: 47.6% of patients in pneumothorax group died comparing to 22.2% of non-pneumothorax group ($p = 0.014$). Other authors published similar results 40.8% vs. 32% [12]. Together with other risk factors like birth weight, gestational age, base excess, Apgar score, RDS and hemodynamic instability [16], pneumothorax has to be considered as a risk factor for neonatal death [17].

Conclusion

Neonatal pneumothorax is a life threatening condition, and carries significant risk for neonatal death. Preterm babies with RDS receiving mechanical ventilation are at a notable risk. FiO_2 higher than 40%, needed to provide adequate oxygenation in the first 12 hours of life, could be a significant predictive factor in selecting the highest risk babies.

Declaration of interest

The Authors declare no conflict of interest.

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