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Pulmonary air leak syndrome in term and late preterm neonates

Плућни синдром цурења ваздуха код терминске и предтерминске новорођенчади

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SUMMARY

Introduction/Objective Air leak syndrome is more frequent in neonatal period than at any other period of life. Its timely recognition and treatment is a medical emergency. We present results of a tertiary medical center in treatment of air leak syndrome in term and late preterm neonates.

Methods Neonates born between 34 0/7 and 41 6/7 gestational weeks (g.w.) who were treated for air leak syndrome in Neonatal Intensive Care Unit of Mother and Child Health Care Institute, from 2005 to 2015 were included in the study. Anthropometric data, perinatal history, type of respiratory support prior to admission, chest radiography, type of pulmonary air leak syndrome and its management, underlying etiology and final outcome were analyzed.

Results Eighty-seven neonates of an average gestational age 38.1 ± 1.9 g.w. were included in the study. The average birth weight was 3182.5 ± 55.5 g. Fourty-seven (54%) were born by cesarean section and 40 (46%) were born by vaginal delivery. Prior to admission, 62.1% received supplemental oxygen, 4.6% were on nasal continuous positive airway pressure, and 21.8% were on conventional mechanical ventilation. Type of delivery did not significantly affect the appearance of pneumothorax, nor did the type of respiratory support received prior to admission ($p > 0.05$). The majority (93.1%) had pneumothorax, which was unilateral in 79%. The length of mechanical ventilation significantly affected the appearance of pneumothorax ($p = 0.015$). Low Apgar score in 1st minute and the presence of pneumopericardium were significant factors predisposing for an unfavorable outcome.

Conclusion Improving mechanical ventilation strategies and decreasing the rate of perinatal asphyxia in term and late preterm neonates could diminish the incidence of pulmonary air leak syndrome in this age group.

Keywords: pneumothorax; newborn; respiratory insufficiency; mechanical ventilation

САЖЕТАК

Увод/Циљ Плућни синдром цурења ваздуха је чешћи у неонаталном узрасту него у било ком периоду живота и његово благовремено препознавање и лечење спада у најхитнија стања у медицини. Приказујемо резултате терцијарног медицинског центра у лечењу плућног синдрома цурења ваздуха код терминске и предтерминске новорођенчади.

Методе Студијом су обухваћена сва новорођенчад рођена између 34 0/7 и 41 6/7 гестацијске недеље која су током периода 2005–2015. лечена од плућног синдрома цурења ваздуха у Одељењу неонаталне интензивне неге Института за здравствену заштиту мајке и детета Србије. Анализиране су антропометријске карактеристике, присуство перинаталне асфикије, примена и тип респираторне потпоре пре пријема, радиографија грудног коша, тип плућног синдрома цурења ваздуха начин лечења, примарна етиологија болести и коначан исход.

Резултати Анализирано је 87 новорођенчади просечне гестацијске старости 38.1 ± 1.9 гестацијске недеље, просечне порођајне телесне масе 3182.5 ± 55.5 г. Четрдесет седам (54%) је рођено царским резом, док је 40 (46%) рођено природним путем. Пре пријема, оксигенотерапија примењивана је код 62.1%, назални континуирани позитивни ваздушни притисак код 4.6%, а конвенционална механичка вентилација код 21.8%. Начин порођаја као ни врста респиратоне потпоре примењиавана пре пријема у неонаталну интензивну негу нису статистички значајно утицали на појаву знакова плућног синдрома цурења ваздуха ($p > 0.05$). Највећи број болесника имао је пнеумоторакс (93.1%), који је најчешће био једнострани (79%). Дужина трајања механичке вентилације статистички је значајно утицала на појаву плућног синдрома цурења ваздуха ($p = 0.015$). Низак Апгар скор у првом минуту и присуство пнеумоперикарда су предиктивни фактори за неповољан коначни исход лечења.

Закључак Побољшање стратегије механичке вентилације и смањење учесталости перинаталне асфиксије код терминске и предтерминске новоорођенчади могли би да допринесу смањењу учесталости плућног синдрома цурења ваздуха у овој групи болесника.

Кључне речи: пнеумоторакс; новорођенче; респираторна инсуфицијенција; механичка вентилација

INTRODUCTION

Pulmonary air leak syndrome (PALS) comprises several different clinical conditions resulting from alveolar over distension and air leakage outside the lungs. It appears more frequently in neonatal period than in any other period of life [1]. This is due to some particularities of respiratory system and its physiology in neonates [poorly compliant lungs, absence of collateral ventilation, highly compliant chest wall, poor respiratory reserve etc.] [2]. Frequency of PALS is determined by gestational age, mode of delivery, underlying lung disease, therapeutic interventions, mechanical respiratory support [3–5].

The aim of the study was to present the frequency, pathogenesis and treatment of PALS in a group of term and late preterm neonates treated in a tertiary medical center. Risk factors, clinical course and outcome of neonates treated for PALS were also analyzed.

METHODS

We present a group of 87 neonates treated for PALS in Neonatal Intensive Care Unit (NICU) of Mother and Child Health Care Institute, Belgrade, from January 2005 to December 2015. All patients were born between 34 0/7 to 41 6/7 gestational weeks (g.w.). The following data were analyzed from medical records: gestational age, birth weight, mode of delivery, Apgar score, need for resuscitation and respiratory support after birth, type of PALS [pulmonary interstitial emphysema - PIE, pneumomediastinum, pneumothorax, pneumopericadium], clinical and radiographic findings, accompanying disorders, mechanical ventilation [mode, parameters and duration], treatment of PALS [spontaneous resolution or chest tube drainage] and final outcome. Diagnosis was based on plain chest radiography. If thoracic drainage was indicated for treatment of pneumothorax, chest tube was inserted by a pediatric surgeon, according to common hospital practice. Neonates who required mechanical ventilation were ventilated using conventional mechanical ventilation modes. The final outcome was considered favorable if the patient recovered and was discharged home without need for supplemental oxygen. A patient's death was considered an unfavorable outcome.

Categorical variables were identified and reported in percentage. Data were analyzed using SPSS (Kolmogorov-Smirnov Chi-square test for testing the normal distribution, Pearson's chi-square test for testing the association of variables, Student's t-test for testing

the difference between groups, univariate logistic regression). A p-value of < 0.05 was considered statistically significant.

The protocol and publication of the results were approved by the Ethics Committee of the Mother and Child Health Institute of Serbia (number 8/10).

RESULTS

During the observed ten-year period, out of 3484 neonates hospitalized in NICU, 91 were diagnosed with PALS, which makes 2.6% of all hospitalized neonates. Four neonates were born before 34 g.w. Since the study aimed to analyze term and late preterm neonates, these four patients were excluded and further analysis was based on 87 patients. Patients' demographic characteristics are presented in table 1. The average gestational age was 38.1 ± 1.9 g.w. The average birth weight was 3182.5 ± 55.5 g. In late preterm subgroup the average birth weight was 2791 ± 441.9 g, while in term subgroup it was 3349.0 ± 456.0 g. There is a statistically significant difference in birth weight in these two subgroups of neonates ($t=5.264$; $p<0.001$).

Mean Apgar score was 7.1 ± 2.4 at 1st minute and 7.9 ± 2.1 at 5th minute. There is a statistically significant difference in Apgar score at 1st and 5th minute ($t=6.700$; $p<0.001$). Apgar score significantly increased at 5th minute.

Forty-seven neonates (54.1%) were born by cesarean section, while 40 (45.9%) were born by vaginal delivery. There is no statistically significant difference in the mode of delivery ($p>0.005$).

Type of respiratory support prior to admission to our hospital and type of PALS neonates developed are presented in table 2.

On admission to NICU, 77 (88.5%) neonates had pathological auscultatory findings on chest auscultation, 61 (70.1%) had signs of respiratory distress and 53 (60.9%) had tachypnea.

Chest radiography was a part of initial workup and was described by an experienced radiologist as pathologic in 85.1% of neonates, while in 14.9% it was described as normal.

Signs of PALS were present in 45 (51.7%) of patients. The distribution of PALS type on admission is presented in table 2.

In 10 patients there were signs of air leakage in more than one thoracic cavity. Distribution of PALS type in those ten patients is presented in table 3. Of five patients with pneumopericardium, one was symptom-free and had only thin continuous band of lucency encircling the heart with no clinical significance, while four patients had pneumopericardium along with pneumothorax. Three of five patients with pneumopericardium deceased.

In patients with pneumothorax, there was a complete pneumothorax in 54 (66.6%) and partial pneumothorax in 27 (33.3%) patients. Pneumothorax was unilateral in 64 patients, most commonly right-sided (60.9%). Patients' distribution in regard to pneumothorax type and its resolution is presented in table 4.

Spontaneous resolution of pneumothorax was observed in 31% of patients, while 69% needed thoracic drainage. Median thoracic drainage length was 4 days (range 1-14 days). Median thoracic drainage in patients with unilateral pneumothorax was 4 days (1-14 days), while it was 6 days (1-13 days) in patient with bilateral pneumothorax. There is a statistically significant difference in the length of thoracic drainage in regard to the type of pneumothorax ($U=195.5$; $p=0.014$). After the insertion of thoracic chest tube, the chest radiography showed pulmonary expansion in 85% of patients, whereas thoracic tube revision was needed in 15% of patients.

During the 10-year period of this study, mechanical ventilation (MV) was used in treatment of 726 neonates. Signs of PALS appeared in 7.2% of all ventilated neonates. Of 87 patients analyzed in the study, radiographic signs of PALS were present in 40.2% of patients who previously did not receive MV. Most commonly used type of MV was SIMV (synchronized intermittent mandatory ventilation), which was used in 81.5%, while IPPV (intermittent positive pressure ventilation) was used in 18.5% of patients. During the study period high frequency ventilation was not available in our hospital. The average length of MV was 3.8 ± 7.2 days. In patients with spontaneous pneumothorax the average length MV was 1.9 ± 2.9 days, whereas in those patients with an underlying pulmonary disease who developed pneumothorax in clinical course the average length of MV was 5.2 ± 9.1 days. There is a statistically significant difference in the length of MV in regard to an underlying condition (U- test 543,5; $p < 0.05$).

The underlying etiology of patients with PALS is presented in table 5.

Most of our patients (78.2%) had favorable outcome, while 21.8% deceased. Univariant logistic regression model showed that the variable associated with greater risk for adverse outcome was lower Apgar score at 1st minute (p= 0.001). The presence of pneumopericardium was at the limit of statistical significance (p= 0.056). In group of patients with an unfavorable outcome 63.1% neonates had severe perinatal asphyxia, 26.3% MAS and PPHN, 26.3% had sepsis and/or pneumonia. There were 21% neonates with intracranial hemorrhage (ICH), 21% with complex congenital heart disease (CHD), 15% with congenital anomalies (e.g. Sy Pierre-Robin, polycystic renal dysplasia, tracheoesophageal fistula) and one patient with severe nonimmune fetal hydrops.

DISCUSSION

Pulmonary air leak syndrome appears more commonly in the first month of life than in any other period of life. The overall incidence is estimated to be about 1% of all neonates, although only 10% of patients are symptomatic [1,3,6]. It is more common in premature neonates, because of the increased incidence of RDS and need for MV. Pneumothorax is by far the most common type of PALS.

More than two-thirds of all premature labors occur between 34 0/7 and 36 6/7 g.w [7]. This group of neonates, referred to as “late preterm”, stands somewhere between term, mature neonates and those extremely premature, whose prematurity caries well known risks and long-time complications. This group of neonates experience significantly more morbidity than infants born at term [7,8]. It is known that these patients have increased incidence of respiratory distress syndrome (RDS), transitional tachypnoea of newborn (TTN), meconium aspiration syndrome (MAS) with/without persistent pulmonary hypertension of the newborn (PPHN), hypoglycemia, hyperbilirubinemia. When prolonged premature rupture of membranes occurs between 34 and 37 g.w, corticosteroids are not used for fetal lung maturation [7]. An updated Committee Opinion from the American College of Obstetricians and Gynecologists (ACOG), published in the August 2017 expands antenatal corticosteroid recommendations to support betamethasone administration to women at high risk for late preterm birth (34 0/7 - 36 6/7 weeks) [9] . This is an important point since there is a significant incidence of RDS and TTN in neonates born at this gestational age. It will be of

clinical interest to follow the incidence of respiratory problems in this group of neonates in the next years, as we expect it to decrease with the latest update of ACOG recommendations.

In the absence of spontaneous initiation of delivery there is a lack of multiple hormonal changes, in the fetus and the mother, which induce lung maturation and fetal lung fluid clearance [7,8,10]. Thus neonatal adaptation to extrauterine life is more difficult, respiratory physiology is changed and the incidence of RDS and TTN is increased, along with its possible complications such as PALS, respiratory insufficiency and pneumonia [8]. It is well documented that delivery by cesarean section is associated with increased risk for pneumothorax, regardless gestational age, especially in the absence of spontaneous initiation of delivery [11]. The fact that there is no significant difference in the mode of delivery in our group of neonates and that there is as much as 54% neonates were delivered by cesarean section is probably due to the fact that all neonates treated in our hospital are transfers (there is no maternity within hospital), so the structure of patients is random.

Higher birth weight carries greater risk of spontaneous pneumothorax in term neonates [12]. This is probably because larger neonates are more commonly born by interventional delivery (vacuum or forceps) and interventions are used prior to complete clearance of lung fluid. During the first few breaths uneven distribution of transpulmonary pressure might precipitate pneumothorax. In our study group we showed a statically significant difference in birth weight between term and late preterm subgroup of neonates.

It was in late 70's of last century when it was noticed that primary spontaneous pneumothorax appears more often in term and postterm neonates, especially in the presence of perinatal asphyxia, difficult and prolonged vaginal delivery, resuscitation after birth, presence of blood in airways, meconium in the airways at first aspiration after birth [13]. Therapeutic measures such as bag and mask ventilation in delivery room and resuscitation are well known risk factors for PALS [14]. Most of the patients with primary spontaneous pneumothorax don't have symptoms or have only mild symptoms and require no treatment. In clinical practice most of these neonates are managed by supplemental oxygen. Most of our patients (62.2%) received oxygenotherapy prior to admission to our hospital. The presence of signs of respiratory distress in the maternity wards resulted in supplying oxygen as the first step of respiratory support in these neonates. This stands along with the fact that 70.1% of them had signs of increased work of breathing and 60.9% were tachypnoeic. Canadian group

of authors showed an interesting result that oxygenotherapy in term neonates with primary spontaneous pneumothorax does not shorten time to its complete resolution [15].

Respiratory insufficiency occurs in late preterm and term neonates as one of complications of perinatal asphyxia [8]. In the most severe cases of perinatal asphyxia chronic mechanical ventilation might be needed. In our group of patients 65.5% were diagnosed with perinatal asphyxia.

Unfavorable outcome was observed in 21.8% of our patients, which can be explained by high percentage of patients with severe perinatal asphyxia and associated conditions that increase the risk of death. In group of patients with unfavorable outcome, as much as 63% had severe perinatal asphyxia. This result stands in favor of the fact that a lot of effort must be made in preventing perinatal asphyxia in developing countries, as this is an important risk factor for both respiratory insufficiency, complications but also for and an unfavorable outcome.

Several pulmonary diseases such as RDS, TTN, MAS, pulmonary hypoplasia, pneumonia, increase the risk of PALS [16,17]. Some of these were the most common underlying pulmonary diseases in our group of neonates, as they are frequent respiratory pathology in neonates born at term or late preterm gestation.

Mechanical ventilation increases the risk for PALS. The use of surfactant in prevention and treatment of RDS along with modern concept of “gentle” mechanical ventilation significantly decrease the risk of PALS during MV of a neonate [18]. The wide use of nasal continuous positive airway pressure (nCPAP) and nonivasive ventilation diminishes number of neonates who require intubation and conventional MV, thus decreasing the risk of PALS. The use of high frequency ventilation in prevention and treatment of PALS is attracting more attention of neonatologists in the last years [19]. Conventional MV was the only MV mode available in our hospital for most of the time during the ten years period of this study, so we could not compare the incidence of PALS in regard to different respiratory support types.

Neonates with asymptomatic pneumothorax without underlying pulmonary disease do not require specific treatment. Needle aspiration with angiocatheter would be an acceptable, less invasive but efficient treatment modality, especially in a patient with mild symptoms, but there is, so far, only one small randomized trial to support its use in neonates [20]. In 69% of our patients pneumothorax was treated by thoracic underwater drainage. Duration of thoracic

drainage was statistically significantly longer in patients with pneumothorax due to an underlying disease in regard to those with spontaneous pneumothorax. Other invasive procedures commonly used in children and adults, such as video-assisted thoracoscopic surgery, are not used in neonates [21].

Statistical analysis distinguished two factors which are connected to high risk of unfavorable outcome: low Apgar score in 1st minute and the presence of pneumopericardium. We believe that the former result is of great clinical importance, as pneumopericardium is seen almost exclusively in patients on mechanical ventilation, so its appearance would demand increased vigilance of clinicians. We believe that our results are to be interpreted in context of our study design which did not include the control group so the true incidence of PALS in larger group of neonates could not be estimated.

CONCLUSION

Pulmonary air leak syndrome in neonates is a life-threatening condition and a medical emergency that requires prompt treatment. Wide use of surfactant in prevention and treatment of RDS, modern concept of noninvasive respiratory support and "gentle" mechanical ventilation lead to an important decrease in the incidence of PALS. A lot of effort should be made in prevention of perinatal asphyxia, as it is an important risk factor for PALS in group of term and late preterm neonates.

Conflict of interest: None declared.

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Table 1. Patients' characteristics

Sex		
Male	54 (62.1%)	p > 0.005
Female	33 (37.9)	
Gestational age at birth (g.w.)		
37 0/7–41 6/7	61 (70/1%)	p < 0.005
34 0/7–37 0/7	26 (29.9%)	
Mode of delivery		
Vaginal	40 (46%)	p > 0.005
Cesarean section	47 (54%)	
Average birth weight (g ± SD)		
Term neonates	3349.0 ± 456.0	p < 0.001
Late preterm neonates	2791.0 ± 441.9	
Average Apgar score		
1st minute	7.1 ± 2.4	p < 0.001
5th minute	7.9 ± 2.1	
Perinatal asphyxia		
Present	57 (65.5%)	p < 0.005
Absent	30 (34.5%)	

g.w. – gestational weeks

Table 2. Distribution of patients in regard to type of respiratory support and type of PALS

Type of respiratory support	
None	9 (10.3%)
Oxygen	54 (62.1%)
nCPAP	4 (4.6%)
MV	19 (21.8%)
Type of PALS	
PIE	3 (3.4%)
Pneumothorax	81 (93.1%)
Pneumomediastinum	10 (11.5%)
Pneumopericardium	5 (5.7%)

nCPAP – nasal continous possitive airway pressure; MV – mechanical ventilation; PALS – pulmonary air leak syndrome, PIE – pulmonary interstitial emphysema

Table 3. Distribution of PALS type in patients with air leakage in several thoracic cavities

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8	Pt 9	Pt 10
PIE	X	X							X	
PM			X	X	X	X			X	
PT	X	X	X	X	X	X	X	X	X	
PP						X	X	X	X	X
Final outcome	**+**	**+**	**+**	**+**	**+**	**-**	**-**	**+**	**-**	**+**

Pt – patient, PIE – pulmonary interstitial emphysema; PM – pneumomediastinum; PT – pneumothorax; PP – pneumopericardium; "+" – recovered and discharged home without supplemental oxygen; "-" – deceased

Table 4. Distribution of patients with pneumothorax in regard to its type and resolution

Pneumothorax			
Unilateral	64 (79%)	right-sided	39 (60.9%)
		left-sided	25 (30.1%)
Bilateral	17 (21%)		
Pneumothorax resolution			
Spontaneous	25 (30.9%)		
Thoracic drainage	56 (69.1%)		

Table 5. The underlying etiology in patients with PALS

Underlying disease	n
Perinatal asphyxia	57
TTN	24
MAS	18
Sepsis	15
Pneumonia	10
RDS	9
Complex CHD	4
ICH gr III–IV	4
Multiple congenital anomalies	3
Fetal hydrops	1

TTN – transitional tachypnoea of newborn; MAS – meconium aspiration syndrome; RDS – respiratory distress syndrome; CHD – congenital heart defect; ICH – intracranial hemorrhage

