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ORIGINAL ARTICLE

Pneumothorax in Neonates during Respiratory Support: Incidence, Timing, and Association with Mortality and Invasive Ventilation

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Abstract:

Aim: Pneumothorax , while a serious adverse event primarily associated with positive pressure respiratory support, is not well documented. Our aim was to document the incidence and timing of pneumothorax, as well as its association with initial mode of ventilation (invasive or noninvasive) and mortality. Methods: We analyzed a database documenting the course of care and outcome of every neonate requiring noninvasive or invasive ventilation in one region of Poland (18 centers) over a 7-year period (5,551 cases). Results: The incidence in all infants was 5.1%. It was 7.2% in those initially treated with invasive ventilation, and 3.6% for those initially treated with noninvasive ventilation (p<0.001). The incidence of pneumothorax was also associated with an increased risk of mortality (11.4% vs 4.5% p<0.001). These both remained significant after controlling for baseline risk factors. Except for the intubated neonates >36 weeks EGA, the pneumothorax primarily occurred during the initial mode of ventilation and in the early days of respiratory support. Conclusion: Significant pneumothorax tends to occur early in the course of respiratory support. It is more likely to be associated with invasive than noninvasive ventilation and is associated with a marked increased risk of mortality.

Keywords: *Noninvasive ventilation, pneumothorax, mechanical ventilation, neonatal outcome*

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Introduction

Pneumothorax is an important clinically relevant, sometimes lethal, complication in neonatal care. Although "spontaneous pneumothorax" does occasionally occur, it is most commonly associated with positive pressure respiratory support.

There is some documentation of the incidence of pneumothorax in the neonatal ICU. [1-3] Experience from large clinical trials also provides incidence data for those select populations of infants studied [4-6]. Many have felt that noninvasive ventilation results in a lower incidence of pneumothorax. However, two very large recent clinical trials did not confirm that expectation [4,5]. In the aggregate these reports provide an indication of the incidence of pneumothorax in smaller infants. However only anecdotal evidence provides a perspective of the impact of pneumothorax on mortality or on the timing of its occurrence.

We previously developed a database documenting the course of treatment and

outcome of every infant requiring respiratory support over a 7-year period in the Warsaw region of Poland [7].

The aim of this analysis was to characterize pneumothorax among infants receiving positive pressure respiratory support. This included not only its incidence and timing in neonates of different maturity, but also its association with invasive and noninvasive ventilation and mortality.

Methods

In collaboration with the Noninvasive Respiratory Support Group of the Polish Neonatal Society, a program was developed to capture the course of treatment and outcomes of all infants requiring respiratory support in the 18 hospitals in the Warsaw region of Poland. It was developed to document changes in morbidity and mortality associated with modes of respiratory support in Poland. Its development and publishing of summary results were approved by the Ethics Committees of the coordinating center for all 18 sites.

The database includes the demographics, respiratory care and neonatal outcomes of all infants who required respiratory support. Our definition of respiratory support did not include supplemental oxygen. It straddles the adoption of new guidelines calling for expanded use of noninvasive ventilation. The median year of this experience is 2004 (range 2001:2007). The data were collected through careful chart review by clinicians at each site. Once submitted to the coordinating center, data were carefully reviewed for completeness and illogical responses. This was accomplished through rule based data flagging and also manual review. Clinical monitors adjudicated apparent problems, and also conducted site visits to clarify and audit the data [7].

The prospectively identified primary endpoints for this analysis were the incidence and timing of pneumothorax as well as the relative risk associated with mortality and the initial mode of respiratory support (invasive or noninvasive). For descriptive purposes, parameters were cross-tabulated into four EGA categories. Pneumothorax was defined as an air leak requiring puncture of the plural space and placement of at chest tube, its severity was otherwise not categorized. Those on noninvasive respiratory support who developed a pneumothorax were also intubated.

The Pearson chi-square test was used to evaluate differences in categorical risk of pneumothorax or mortality. To control for baseline risk factors that might impact the risk of pneumothorax and the risk of mortality two logistic regression models were developed. The following prospectively selected baseline parameters were considered in the two models: (gestational diabetes, antenatal steroids, out-born, multiple births, c-section, gender, birth weight, small for gestational age, Estimated Gestational Age, Apgar 1 minute, Apgar 5 minute, and early surfactant (<2 hours). These were all available for 93.2% of the cases. They were retained, using a backward stepwise approach, if they contributed significantly ($p<0.05$). Only out-born, c-section and gestational diabetes were significantly associated with the risk of pneumothorax. All the baseline factors except birth weight and multiple births were significantly associated to the risk of death. Finally the independent categorical variable of interest was forced into respective model, with the significant baseline risk factors. All these analyses were conducted with PASW software (IBM, version 18, Chicago USA). A p value <0.05 was considered statistically significant.

Results

During the 7-year period there were 5,551 neonates in the Warsaw region that required respiratory support. Forty-three percent were initially supported with mechanical ventilation, and the balance (57%) initially received either nasal continuous positive airway pressure (NCPAP) or biphasic noninvasive support. The overall incidence of pneumothorax was 5.1%. The risk was markedly higher in those receiving invasive respiratory support. (7.2%/3.6% = 2.0, $p<0.001$). Elective invasive ventilation continued to be associated with the increased risk of

Table 1. Study Population and Outcomes by EGA Category

	<28 weeks	28-32 wks	33-36 wks	>36 wks
Number	739	1861	1718	1233
Weight in grams	847 (219)	1456 (441)	2314 (551)	3182 (636)
Antenatal steroids	52.2%	49.9%	24.6%	4.6%
Day of first RS	1 (1-1)	1 (1-1)	1 (1-1)	1 (1-2)
Initial NIV (%)	21.8%	43.5%	26.7%	43.6%
Early surfactant (%)	19.5%	7.3%	1.5%	0.6%
Weeks of RS	6 (1-21)	2 (1-6)	2 (1-4)	1 (0.5-3)
Death %	28.8%	6.6%	4.1%	6.2%
BPD-grade3 (%)	16.2%	2.8%	0.1%	0.2%
% pneumothorax	5.8%	4.0%	5.0%	6.3%
1st RSM MV %				
Pneumothorax (%)	6.6%	5.8%	8.3%	8.0%
Day of pneumothorax	3 (3-5)	4 (2-6)	3 (2-3)	2 (2-3)
Mortality without	3.9%	4.8%	3.4%	6.2%
Mortality with	12.0%	13.0%	9.0%	19.4%
During MV (%)	94.1%	97.6%	74.4%	33.3%
1st RSM NIV %				
Pneumothorax %	3.1%	2.6%	3.8%	5.0%
Day of pneumothorax	2 (2-2)	3 (2-4)	2 (2-3)	2 (2-3)
Mortality without	2.9%	2.6%	0.0%	4.9%
Mortality with	4.8%	4.5%	3.8%	20.0%
% during NIV	66.7%	66.7%	82.5%	84.4%

Data presented as Percent Incidence, Mean (std) or Median (Interquartile range) as appropriate. RS is Respiratory Support, NIV is noninvasive ventilation, MV is invasive mechanical ventilation. BPD-grade3 is the need for >30% FiO2 or respiratory support at 28 days.

pneumothorax after controlling for significant baseline factors (odds ratio 1.61, p<0.001) The incidence of pneumothorax was associated with a markedly higher risk of hospital mortality (11.4%/4.5%= 2.5, p<0.001). Pneumothorax continued to be associated with an increased risk of mortality after controlling baseline factors (odds ratio 3.90, p=0.031).

Descriptive details of the population and outcomes are cross-tabulated into four estimated gestational age [EGA] categories in Table 1. In each of these maturity categories, pneumothorax generally occurred in the first days of treatment. However, the length of respiratory support was generally many weeks. Except for those infants greater than 36 weeks EGA who were invasively ventilated, pneumothorax usually occurred during the initial method of respiratory support. The data reflect small differences in pneumothorax incidence among the EGA categories. There was a trend of higher incidence of pneumothorax in those infants greater than 32 weeks EGA. This difference was more marked in the elective noninvasive infants (4.2%/2.6%, p=0.019) than in the initially intubated infants (8.1%/6.1%, p=0.057).

Discussion

We analyzed a database that included all infants requiring respiratory support in our region. We found an overall incidence of pneumothorax of 5.1%. The incidence was twice as high in infants

treated initially with invasive ventilation than in those initially treated with noninvasive ventilation (7.2%/3.6%). The relative risk of mortality increased with pneumothorax and was more than twice as high (11.4%/4.5%). These increased risks remained highly statistically and clinically relevant after controlling for baseline risk factors. While the course of respiratory support in these infants was generally weeks, we found that the development of pneumothorax typically occurred in the early days of treatment, on the initial respiratory support modality.

We are aware of only one population based report of the incidence of pneumothorax in the neonatal ICU; from the Vermont-Oxford Network for 2004 [2]. Based on over 100,000 NICU admissions, they report a median incidence of 4% (IQR 2%-5%) among 241 centers. We reported an overall incidence of 5.1% just among infants receiving respiratory support. Considering the risk is higher in those receiving respiratory support, we feel our outcomes are comparable. They also reported, consistent with our experience, an increased incidence in the larger infants. We believe these points of comparability support the generalize-ability of our multicenter Polish experience.

There are also helpful reports for very low birth weight infants and select study populations. The Vermont-Oxford Neonatal Network provided another population-based estimate sometime ago [2]. They reported a drop in the incident of pneumothorax in all infants between 500-1500 grams from about 8% in the early 90s to about 6% by the end of the decade. Surfactant trials, in the early 90's, report an incidence of 15% in 3,427 extremely low birth weight infants [6]. In another important more recent report, the incidence of pneumothorax in infants <1500 grams in Europe in 2006 was considerably lower (3.7%, range between centers 0-16%) [3]. These suggest an obvious trend of continuing risk reduction, presumably associated with improved respiratory care. Our data showing a decreased risk associated with noninvasive support, might indicate that its increased use could be one of the factors of improved respiratory care. Surely attention to providing the appropriate level of distending and peak pressures, regardless of mode of respiratory support, is most critical.

Two recent large clinical trials suggested, contrary to the expectations of many, that noninvasive ventilation may not reduced the risk of pneumothorax. The COIN trial, of 610 infants between 24-27 weeks EGA, found elective NCPAP was associated with a higher incidence (9.1% vs. 3.0%) [5]. The SUPPORT trial of 1,316 infants, also between 24-27 weeks EGA, reported a comparable incidence (6.8% vs. 7.4%) [4]. In contrast to these studies, our clinical experience reflects a markedly decreased risk of pneumothorax associated with noninvasive ventilation. In the smallest intubated infants (<28 weeks EGA), we experienced a risk of pneumothorax (6.6%) consistent with that reported in the SUPPORT, but higher than seen in the COIN trial. In those smallest infants noninvasively ventilated, our rate of pneumothorax (3.1%) was markedly lower than experienced in the COIN and SUPPORT trials. We feel that the difference between our population (every infant needing respiratory support) and these two study cohorts (infants eligible for randomization to either intubation of NCPAP) would result in higher risk in our population of intubated infants. We speculate that it is also possible that bedside natural selection of mode of ventilation in our population was perhaps more effective than a strict randomization within the infants who met study enrollment criteria. The identification of the ideal candidates for each mode of support needs to be explored further.

We are unaware of any reports about the timing of pneumothorax or on its association with mortality. We do not believe our related findings are controversial, but rather confirmatory of anecdotal experience. It seems reasonable that during the early stages of respiratory support, when respiratory status is less stable, that inappropriate airway pressures are more likely to be applied. We do feel, however, our work provides a new metric for the increased risk of mortality associated with pneumothorax.

Our report has several limitations. While it reflects the aggregate of our experience, different practices associated with the indications for and use of respiratory support modes and other respiratory care practices might result in different outcomes, perhaps as seen in the COIN and SUPPORT trials. Most importantly, we must highlight that our reported association of pneumothorax with mortality should not be construed as clearly causal. Our definition of pneumothorax only included the need for a chest tube, which we feel was the only reliable definition for a prospective chart review, other reports of the incidence might be more expansive.

We conclude that in routine use significant pneumothorax tends to occur early in the period of respiratory support. Its incidence is associated with a doubling of the risk of mortality. Finally, noninvasive ventilation when applied clinically can be expected to be associated with a lower incidence of pneumothorax.

Abbreviations

EGA- estimated gestational age, IQR- interquartile range, NCPAP- nasal continuous positive airway pressure, NICU- neonatal intensive care unit

Conflict of Interest

The authors declare they have no conflicts of interest and there was no specific funding for this project. ncidence of pneumothorax.

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