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Risk factors associated with extubation failure in preterm infants with very low birth weight

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ABSTRACT

Repeated endotracheal intubation is associated with complications and additional risks for a preterm infant. The aim of this study was to determine the risk factors related to extubation failure (EF) in preterm newborns. **Materials and methods:** Ninety two very preterm infants with respiratory distress syndrome (RDS), birth weight of <1500 g, mechanically ventilated, and extubated before the 7th day of life were enrolled into prospective study. Following extubation, noninvasive respiratory support was provided. Infants who required reintubation within 72 h after primary extubation constituted the main group ($n = 27$) while those, whose primary extubation was successful, were included into the comparison group ($n = 65$). **Results:** Infants from the main group differed by lower antenatal steroid administration rate, higher incidence of intraventricular hemorrhage, severe RDS, arterial hypotension, metabolic acidosis, and pulmonary bleeding, as well as by the need in higher initial mechanical ventilation settings. According to logistic regression analysis the risk of EF was significantly associated with severe RDS (OR – 3.82; 95% CI: 1.21–12.02), arterial hypotension (OR – 24.05; 95% CI: 1.99–290.48) or metabolic acidosis (OR – 4.62; 95% CI: 1.41–15.16) in the first 3 days of life. Antenatal steroid prophylaxis considerably decreased the probability of EF (OR – 0.2; 95% CI: 0.063–0.68). **Conclusions:** The risk of reintubation after primary extubation is determined by severe RDS, arterial hypotension or metabolic acidosis during the first 3 days of life. Antenatal steroid prophylaxis substantially decreases this risk. The method of non-invasive respiratory support following primary extubation does not influence the reintubation risk.

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Mechanical ventilation (MV) is a treatment method that is frequently used in neonatal intensive care units. Even though MV plays a key role in reducing mortality in preterm infants with pulmonary disease, its use is often associated with complications [1].

Respiratory distress syndrome (RDS) is the most common disease in very preterm infants and its incidence increases with gestational age decrease [2–4]. RDS is the most frequent reason for MV application in newborns with gestational age of less than 32 weeks [5]. Immature lungs

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are more sensitive to damage caused by different factors, including MV. Very preterm newborns that have been intubated and mechanically ventilated for prolonged periods of time have increased risk of death, nosocomial infections, bronchopulmonary dysplasia (BPD), and survival with neurologic deficit [1, 6, 7]. That is why it is important to minimize the amount of time this type of respiratory support (RS) is used and to extubate the infants as soon as possible with subsequent application of noninvasive RS. An obligatory requirement for this is the infant's ability to breathe spontaneously supporting adequate gas exchange levels with minimal breathing efforts. However, determining or even foreseeing such ability in preterm infant who is still being mechanically ventilated proves to be problematic [1]. Meanwhile, early or untimely extubation can increase the risk of repeated intubation. One of the main risk factor associated with extubation failure is considered to be extreme prematurity (gestational age of less than 28 weeks) [8, 9]. Probability of extubation failure increases with gestational age decrease and postnatal age increase [6]. This can be related to longer MV in older infants [10]. Mechanical ventilation settings also matter. Infants that were ventilated with higher peak inspiratory pressure and higher oxygen concentration required repeated intubation more frequently [9]. A connection has been described between extubation failure and intraventricular hemorrhage (IVH) or patent ductus arteriosus (PDA) presence [8]. Besides those infants with lower hematocrit and pH levels as well as higher partial CO₂ pressure (PaCO₂) required repeated MV more often [9].

“Ideal” moment for weaning from MV is usually determined on the basis of certain clinical, instrumental and laboratory parameters. But these parameters are seldom objective, oftentimes making the weaning of preterm newborns in NICUs a trial-and-error approach [1]. That is why 15–40% of premature infants require subsequent reintubation. Extubation failure exposes the newborn to “respiratory shock” that in turn causes the need for repeated intubation and higher ventilation settings due to alveoli collapse or atelectasis, as well as brings on additional risk associated with the intubation procedure itself [11].

Hence, knowledge of the risk factors related to extubation failure will diminish the need for repeated intubation that is associated with additional morbidity and mortality [1].

The aim of the study was to determine the risk factors that increase the likelihood of repeated intubation after primary extubation in preterm very low birth weight newborns.

Materials and methods

Ninety two very premature infants with RDS were under observation. The inclusion criteria were birth weight lower than 1500 g, RDS presence, preceding treatment with mechanical ventilation, and extubation not later than on the 7th day of life. After primary extubation, the infants were switched to noninvasive respiratory support, i.e. continuous positive airway pressure (CPAP), high frequency

noninvasive ventilation (HFNV), or standard noninvasive ventilation (NV). The infants, who required repeated intubation within 72 h after the primary extubation, constituted the main study group (27 infants). Newborns, whose primary extubation was successful, comprised the comparison group (65 infants).

The following ventilation settings preceded primary extubation: oxygen concentration in respiratory gas mixture (FiO₂) < 35%, peak inspiratory pressure/positive expiratory pressure (PIP/PEEP) < 20/5 cm H₂O, ventilation frequency (VF) < 30/min, and partial CO₂ pressure in arterial blood (PaCO₂) < 55 mm Hg.

Criteria of the need for repeated intubation were [12]:

1. FiO₂ ≥ 60%; PaCO₂ ≥ 55; pH < 7.25 on noninvasive respiratory support;
2. Considerable and progressive respiratory impairment;
3. Pathologic apnea episodes (more than three episodes in an hour that are accompanied by bradycardia, or 12 documented apnea episodes in 24 h, or one apnea episode that required ventilation with the bag-mask ventilation).

Extubation failure was defined as the need in repeated intubation within 72 h after the primary extubation.

The study groups were compared for the most important perinatal risk factors, morbidity and mortality. Special attention was paid to the factors and conditions that may have been associated with extubation failure [6, 8–10].

Overall illness severity on the first day of hospitalization was standardly assessed with the SNAPPE-II scores [13]. The grade of RDS was determined based on X-ray data and need for exogenous surfactant therapy. PDA was confirmed by Doppler-Echocardiography, IVH and periventricular leukomalacia (PVL) were assessed by head ultrasound and on autopsy when applicable.

Standard protocols of respiratory support were applied to all newborns with arterial blood gas assessment and routine vitals monitoring. During NICU stay, heart rate, arterial blood pressure, hemoglobin oxygen saturation (SpO₂), body temperature, and diuresis were monitored.

The obtained data were analyzed using descriptive statistics methods, categorical, correlational and logistic regression analysis. Differences between continuous parameters were evaluated using Student's criterion or in the Mann-Whitney test, while discrete parameters were estimated by means of the χ^2 criterion. The measurements with normal distribution are presented as mean (standard deviation), and nonparametric data are presented as median [minimal-maximal value]. All values were considered significant if $p < 0.05$.

Results

The study groups were not different in terms of gestational age, birth weight, rates of delivery via Cesarean section, postnatal age, and illness severity at the time of enrollment into the study (Tab. 1). Infants from the comparison group were more often intubated after birth in the course of immediate postnatal care (42 (64.62%) cases versus 11 (40.74%) cases in the main group; $p = 0.03$), and were

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