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COMPLICATIONS OF THE POST-VENTILATION PERIOD IN PRETERM NEWBORN INFANTS

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Abstract: Mechanical ventilation is a life-saving method of respiratory support for preterm newborn infants with severe respiratory failure; however, infants requiring invasive ventilation remain at increased risk of pulmonary and extrapulmonary morbidity. The aim of this study was to assess the frequency of major complications during the post-ventilation period in preterm newborn infants and to compare outcomes between infants who required mechanical ventilation and those managed without invasive ventilation. The study included 90 newborn infants divided into two groups: Group 1 comprised 70 infants who received mechanical ventilation, while Group 2 included 20 infants who did not require mechanical ventilation and served as the comparison group. Bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), echocardiographically confirmed pulmonary hypertension and periventricular leukomalacia (PVL) were evaluated. BPD occurred in 17 infants (24.3 %) in Group 1 and in none of the infants in Group 2; this was the only difference that reached statistical significance ($p = 0.010$; risk difference 24.3 percentage points, 95 % CI 6.1–35.5). ROP was diagnosed in 13 infants (18.6 %) and 1 infant (5.0 %), respectively ($p = 0.179$); pulmonary hypertension was detected in 9 ventilated infants (12.9 %) and was absent in the comparison group ($p = 0.199$); PVL occurred in 5 infants (7.1 %) in Group 1 and in none of Group 2 ($p = 0.583$). All four complications were more frequent among ventilated infants and three occurred exclusively in that group, but with only 20 infants in the comparison group the three latter differences could not be confirmed statistically. The findings support lung-protective respiratory strategies and early transition to non-invasive respiratory support whenever clinically feasible.

Keywords: preterm newborn infants, mechanical ventilation, post-ventilation period, bronchopulmonary dysplasia, retinopathy of prematurity, pulmonary hypertension, periventricular leukomalacia, neonatal intensive care.

Introduction and Literature Review

Respiratory insufficiency is one of the major clinical problems in premature newborn infants and frequently requires respiratory support during the early neonatal period. Mechanical ventilation remains indispensable in severe respiratory failure, but the immature lungs of preterm infants are particularly vulnerable to pressure- and volume-related injury, oxygen toxicity, inflammation and oxidative stress. Consequently, newborns who require invasive respiratory support constitute a high-risk population for subsequent pulmonary and extrapulmonary complications.

Bronchopulmonary dysplasia is among the most important chronic respiratory outcomes in premature infants. In a retrospective



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cohort of 1 980 very-low-birth-weight infants born before 32 weeks of gestation, mechanical ventilation lasting longer than 60.5 hours was independently associated with bronchopulmonary dysplasia (aOR 6.01; 95 % CI 3.63–9.95) and with periventricular leukomalacia (aOR 2.19; 95 % CI 1.24–3.87) [1].

Retinopathy of prematurity represents another important complication in this population. In a case-control study of 276 preterm infants, each additional day of mechanical ventilation increased the odds of requiring treatment for retinopathy by approximately 5 % (OR 1.05; 95 % CI 1.02–1.09) [2]. It should be noted that in the same multivariate model ventilation was the weakest of three predictors: a slow rate of retinal vascularisation carried a considerably larger effect (OR 19.0; 95 % CI 6.5–55.5). Mechanical ventilation is therefore best regarded as one contributing factor among several rather than the dominant one.

Pulmonary hypertension is particularly important in infants who develop bronchopulmonary dysplasia. In a prospective study of 126 infants born before 30 weeks of gestation, pulmonary hypertension was identified in 48 infants (38 %) during hospitalisation; severe bronchopulmonary dysplasia (OR 3.31; 95 % CI 1.12–9.74) and ventilator-associated pneumonia (OR 17.9; 95 % CI 3.9–82.11) remained independent risk factors after adjustment [3]. Ventilator-associated pneumonia, being a direct consequence of invasive respiratory support, provides a plausible mechanism linking ventilation to pulmonary hypertension and underlines the need for echocardiographic surveillance in high-risk neonates.

Neurological complications may also be related to physiological instability during invasive ventilation. An association between hypocarbia and periventricular leukomalacia in mechanically ventilated premature infants has been demonstrated, highlighting the importance of careful control of PaCO₂ and avoidance of excessive ventilation [4].

Current respiratory-care concepts therefore favour minimising invasive ventilation whenever clinically possible. The World Health Organization recommends continuous positive airway pressure for preterm infants with respiratory distress syndrome and notes evidence that early CPAP can reduce both the need for mechanical ventilation and the occurrence of bronchopulmonary dysplasia [5]. A recent review similarly emphasises that avoiding intubation and prolonged invasive ventilation through appropriate non-invasive respiratory support may reduce lung injury and bronchopulmonary dysplasia [6].

The aim of the present study was to compare the frequency of clinically significant complications during the post-ventilation period in preterm newborn infants who required mechanical ventilation with those who did not receive invasive ventilatory support.

Materials and Methods

The comparative clinical study included 90 preterm newborn infants. According to the requirement for mechanical ventilation, the patients were divided into two groups. Group 1 consisted of 70 newborn infants who required mechanical ventilation, whereas Group 2, which served as the comparison group, included 20 infants managed without mechanical ventilation.

The frequency of four major neonatal complications was assessed. Bronchopulmonary dysplasia was defined according to the National Institute of Child Health and Human Development consensus criteria [7]. Retinopathy of prematurity was classified using the International Classification of Retinopathy of Prematurity [8]. Pulmonary hypertension was confirmed echocardiographically in accordance with the joint guidelines of the American Heart Association and the American Thoracic Society [9]. Periventricular leukomalacia was diagnosed by neurosonography.

Results are expressed as absolute numbers and percentages. Because three of the four outcomes produced cells containing no events, intergroup differences were assessed by Fisher's exact test rather than the chi-squared test, which is not valid under these conditions. Risk differences are reported with 95 % confidence intervals calculated by the Newcombe hybrid score method, which remains valid when a cell contains no events. Values of $p < 0.05$ were considered statistically significant.

Because the available dataset does not include complete adjustment for gestational age, birth weight, duration and mode of mechanical ventilation, cumulative oxygen exposure and severity of the primary disease, the observed differences are interpreted as associations rather than proof of a direct causal relationship.

Results

The frequency of each complication in the two groups is presented in Table 1 and Figure 1.

Table 1. Frequency of post-ventilation complications by ventilation status

Complication	Group 1 (n = 70)	Group 2 (n = 20)	p	Risk difference, pp (95 % CI)
Bronchopulmonary dysplasia	17 (24.3 %)	0 (0 %)	0.010	24.3 (6.1 to 35.5)
Retinopathy of prematurity	13 (18.6 %)	1 (5.0 %)	0.179	13.6 (–6.5 to 25.0)
Pulmonary hypertension	9 (12.9 %)	0 (0 %)	0.199	12.9 (–4.3 to 22.7)
Periventricular leukomalacia	5 (7.1 %)	0 (0 %)	0.583	7.1 (–9.5 to 15.7)

Fisher's exact test; pp — percentage points.

Bronchopulmonary dysplasia was the most frequent complication in mechanically ventilated newborns. It was diagnosed in 17 of 70 infants (24.3 %), whereas no cases were recorded in the comparison group. This was the only difference that reached statistical significance ($p = 0.010$).

Retinopathy of prematurity was the second most frequently observed complication, developing in 13 infants (18.6 %) after mechanical ventilation compared with 1 infant (5.0 %) in Group 2 ($p = 0.179$). Echocardiographically confirmed pulmonary hypertension occurred in 9 mechanically ventilated newborns (12.9 %) and was not detected among infants who did not require mechanical ventilation ($p = 0.199$). Periventricular leukomalacia was identified in 5 infants (7.1 %) in Group 1 and in none of the infants in Group 2 ($p = 0.583$).

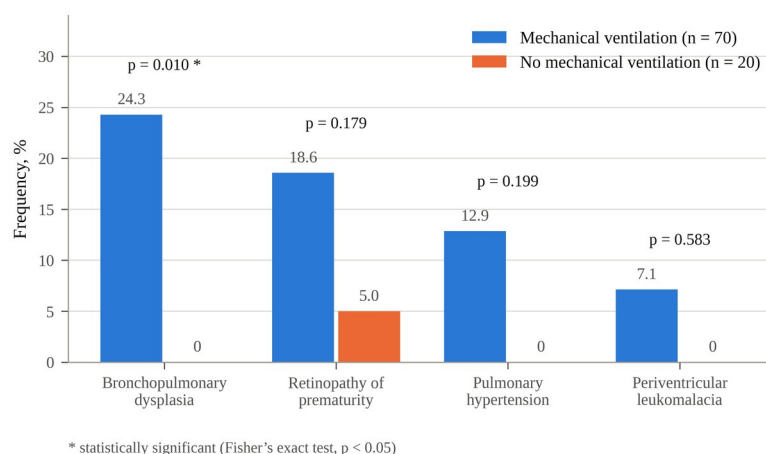


Figure 1. Frequency of complications in preterm newborn infants with and without mechanical ventilation

All four complications were more frequent among ventilated infants, and three of them occurred exclusively in that group. As Figure 2 shows, however, only the confidence interval for bronchopulmonary dysplasia excludes zero. For the three remaining outcomes the intervals are wide and cross zero. This reflects the limited size of the comparison group rather than an absence of effect: with 20 infants in Group 2, the number of events expected under the null hypothesis would be only two to three, so observing none is entirely compatible with chance.

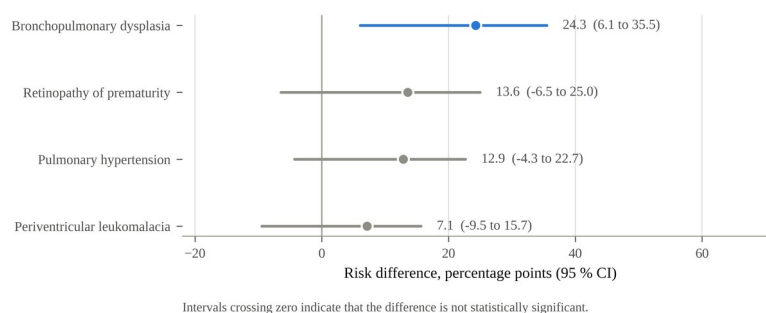


Figure 2. Risk differences with 95 % confidence intervals. Intervals crossing zero indicate that the difference is not statistically significant

The high frequency of bronchopulmonary dysplasia among mechanically ventilated infants is consistent with contemporary neonatal literature demonstrating a relationship between the duration of invasive respiratory support and chronic lung disease [1]. The higher frequency of retinopathy of prematurity in Group 1 is directionally consistent with evidence that longer mechanical ventilation is associated with a greater likelihood of severe retinopathy requiring treatment [2], although the present sample is too small to demonstrate this independently.

The occurrence of pulmonary hypertension exclusively in Group 1 may reflect the interaction between pulmonary immaturity, parenchymal lung injury, impaired pulmonary vascular development, oxygen exposure and chronic respiratory disease. Published prospective data confirm that pulmonary hypertension is a clinically important complication among premature infants with bronchopulmonary dysplasia [3]. Although periventricular leukomalacia did not show a statistically significant intergroup difference, its occurrence exclusively among ventilated infants remains

clinically noteworthy; previous studies suggest that neurological injury may be influenced by disturbances of cerebral perfusion and excessive hypocarbia during mechanical ventilation [4].

Overall, the post-ventilation clinical course of preterm newborn infants in the present study was characterised by a high frequency of pulmonary and extrapulmonary morbidity. The observed pattern is compatible with the contemporary concept that ventilation-induced lung injury, oxygen-related oxidative stress, underlying prematurity and severity of illness interact in determining neonatal outcomes.

Conclusions and Recommendations

Preterm newborn infants requiring mechanical ventilation had a substantially higher frequency of clinically important complications than newborns managed without invasive respiratory support. Bronchopulmonary dysplasia was the most common complication, occurring in 24.3 % of mechanically ventilated infants compared with 0 % in the comparison group ($p = 0.010$). Retinopathy of prematurity (18.6 % versus 5.0 %), pulmonary hypertension (12.9 % versus 0 %) and periventricular leukomalacia (7.1 % versus 0 %) were observed predominantly or exclusively among ventilated infants, but these differences did not reach statistical significance in a comparison group of 20 infants.

The findings support several practical recommendations. Ventilation parameters should be individually selected and continuously reassessed to reduce the risk of ventilator-associated lung injury. Oxygen administration should be titrated carefully to avoid unnecessary hyperoxic exposure, particularly in premature infants at risk of bronchopulmonary dysplasia and retinopathy. Excessive hypocarbia should be prevented through appropriate monitoring of blood gases. Prevention of ventilator-associated pneumonia deserves particular attention, given its strong association with pulmonary hypertension [3]. When the infant's clinical condition permits, invasive mechanical ventilation should be discontinued as early as safely possible and replaced by appropriate non-invasive respiratory support, in line with current World Health Organization guidance [5, 6]. Mechanically ventilated preterm infants should additionally undergo systematic ophthalmological surveillance for retinopathy and echocardiographic evaluation for pulmonary hypertension when clinically indicated.

Two limitations should be emphasised. First, infants selected for ventilation are by definition more severely ill, so the observed associations cannot be attributed to ventilation alone. Second, the unequal group sizes (70 versus 20) markedly limit statistical power for the less frequent outcomes. Further prospective studies with larger and more balanced cohorts should analyse gestational age, birth weight, duration of ventilation, FiO_2 exposure, PaCO_2 levels, ventilatory modes, surfactant therapy and severity of underlying disease in order to distinguish the independent contribution of mechanical ventilation from the effects of prematurity and critical illness.

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