Predictive indices of ventilatory weanning in prematures: Literature review

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ABSTRACT

Objective: To describe the predictive indices for MV weaning in preterm infants. Methodology: This is a descriptive literature review, carried out in a bibliographic survey from July to September 2023, in articles published in the last 10 years, using the databases: National Library of Medicine (Pubmed), Scientific Electronic Library Online (SCIELO), Physiotherapy Evidence Databases (PEDro). RESULTS: Only three articles were selected for this review, showing that 56.5% of the newborns admitted to the NICU were male, with a mean GA of 25 to 36 weeks, birth weight of 754g to 1500g. Conclusion: The correct timing of weaning from mechanical ventilation and extubation is still considered a challenge in NICUs, where the scarcity of literature shows that further studies should be carried out in order to establish the best strategy for a possible success of extubation. Results: Gestational age ranges from 26 to 36 weeks and 6 days, birth weight from 882 g to 1500 g, APGAR score at 1' from 4.9 to 5.4 and at 5' from 6 to 8. In the clinical trials, the underlying diseases found were: In the first group, Respiratory Distress Syndrome (60.4-67.4%), preterm infants used Mechanical Ventilation from 27-29 hours, the number of deaths was 22 (50-53), and the following predictive indices were used: Evaluate: Pulmonary mechanics; Pressure-time index; Minute ventilation test; Clinical trials; and Dynamics of biological signals. In the randomized clinical trial. In group 2: Bronchopulmonary Dysplasia (30%); Intracranial hypertension (7.5%). Deaths in this group were 5.7% and the predictive indices used were: Higher APGAR score at 5 minutes; Higher pH (before extubation); Lowest peak FiO2 (in the first 24 hours of age); Lower PCO2 and FiO2 (before extubation); and Non-PIG status. Subgroup 2: Bronchopulmonary Dysplasia (64%); Intracranial hypertension (23%). Deaths in this group were 28% and the predictive index used was gestational age. And in the third study: Apnea 54.5%; SDR 18.1%; PCA: 5.5%. Days of mechanical ventilation was 2 days. The predictive indices used were: RR = 12 bpm; PIP = 16 cmH 2 0; PEEP = 6 cmH 2 0; FiO 2 ≤ 40%. In group 2 of the third study: Apnea: 16.6%; SDR 33.3%; PCA: 19.4%. Days of ventilation was 1 day and a half. The predictive indices used were: Pressure equal to .6 cmH 2 0; Oxygen Fraction from 2 ≤ 40%.

Keywords: Ventilatory weaning, Prematurity, Mechanical Ventilation, Extubation failure.

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INTRODUCTION

Preterm infants can be considered any child born preterm, i.e., before completing 37 weeks of pregnancy, classified according to gestational age: extreme preterm infant has a gestational age of less than 28 weeks; very preterm from 28 weeks to 31 weeks and 6 days; moderate preterm, 32 weeks to 33 weeks and 6 days, late preterm 34 weeks to 36 weeks and 6 days, and birth weight is also associated with prematurity (VERRESCHI et al., 2020).

The physiological particularities that premature newborns present are characteristics of pulmonary immaturity, reduced alveoli quantity, low surfactant production, absence or underdevelopment of collateral ventilation, and decreased pulmonary compliance, but the rib cage has cartilaginous tissue that results in increased compliance, but many of them are susceptible to requiring mechanical ventilation (SANTOS et al., 2019).

Mechanical Ventilation (MV) is an artificial ventilatory support used to replace spontaneous ventilation in order to maintain normal physiological functions. MV has the function of assisting gas exchange, oxygenation, and the removal of carbon dioxide (CO2) from the body (SANGSARI et al., 2022). Long-term use of MV can cause ventilator-induced lung injury (VILI), ventilator-associated pneumonia (VAP), tracheal lesions, and neurodevelopmental impairment. As a result, weaning premature neonates from mechanical ventilation as early as possible is extremely indicated (SANGSARI et al., 2022).

The Spontaneous Breathing Test (SBT) evaluates the patient's ability to maintain spontaneous breathing through continuous positive airway pressure support (CPAP) ventilation, however, there are still restrictions to predict who will need reintubation after passing an ERT, its implementation in children and neonates can simplify weaning and decrease the duration of ventilatory support (NASCIMENTO et al., 2017). Use SBT before extubation, avoiding ventilation-related failures (THILLE et al., 2015).

After weaning and extubation, the work of breathing is transferred to the patient, who is able to use his own respiratory muscle activity to maintain alveolar ventilation with an ideal tidal volume capable of maintaining adequate lung volume to oxygenate organs and tissues, without exacerbated work of breathing (ROCHA et al., 2018).

Predictive indices establish foundations for examining the physiology of the respiratory system, indicating success or possible failures of ventilatory weaning in preterm infants (MOURA et al., 2021). Extubation failure is considered as reintubation within a specified period from extubation, which can vary from a few hours to several weeks after the procedure, reintubation in the first 48 h post-extubation is shown to be higher (LI et al., 2022). The main causes for extubation failure are respiratory muscle weakness, high oxygen concentrations, electrolyte disturbances, and prolonged use of sedation (HEUBEL et al., 2020).

Weaning from MV in newborns can still be seen as complex and of high literary scarcity, since failures in this process can lead to reintubation, which may be associated with prolonged MV and evolve to fatal complications (SANGSARI et al., 2022).

In view of the above, it is notorious that the long permanence of MV use can cause fatal repercussions in preterm infants, so it is necessary to understand the real protocols that favor a better control of the measurement of the adverse effects of ventilatory weaning in preterm infants, since the acceleration of weaning can increase the length of stay on MV. Therefore, the objective of this study is to describe the predictive indices to predict possible extubation failures and successes in preterm infants using mechanical ventilation.

METHODOLOGY

This is a literature review with a descriptive approach. The survey was carried out between July and September 2023, in articles published in the last 10 years, using the databases: National Library of Medicine (Pubmed), Scientific Electronic Library Online (SCIELO), Physiotherapy Evidence Databases (PEDro).

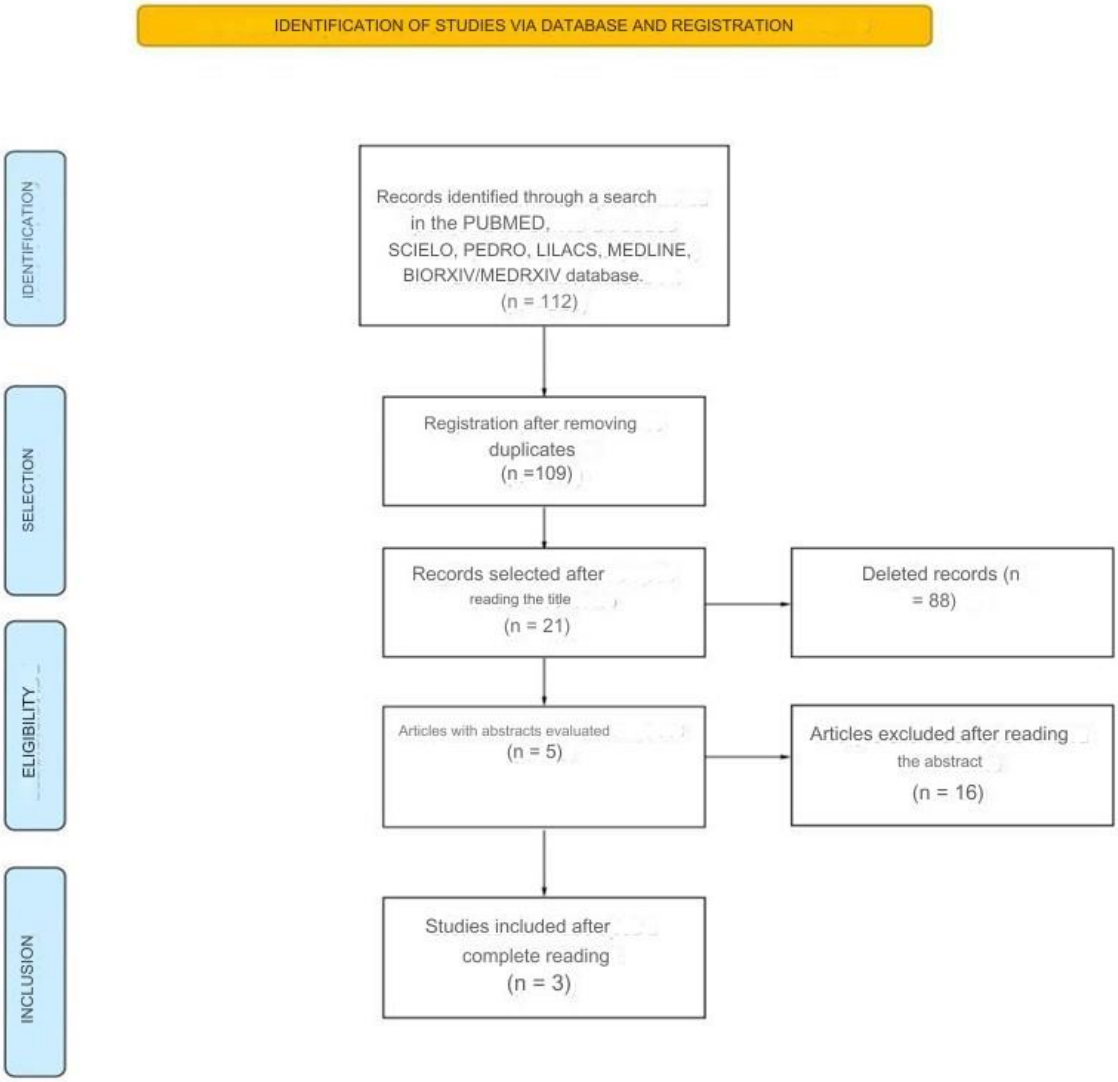
The research was directed by the Health Sciences Descriptors (DeSC) using the following descriptors: "Neonatology", "Mechanical Ventilation", "Ventilatory Weaning", "Prematurity" performed with the Boolean operator technique "AND" to obtain results.

Randomized clinical trials, case reports, and books were used as inclusion criteria, with no language restrictions. Articles that were not related to the research objective, type of literature, letter, commentary, reviews and studies published more than 10 years ago were excluded.

RESULTS

This research totaled 112 articles, and after analytical reading and respecting the aptitude criteria, 3 articles were selected for this review. All the steps involved in the identification, screening and selection of studies are described in the Flowchart.

Flowchart 1 - Steps for study eligibility.



Two articles were available in the database of the National Library of Medicine (Pubmed) and one in the Brazilian Scientific Electronic Library Online (SciELO), all complete, free of charge and in English.

The year of publication ranged from 2016 to 2021, published in Brazil, the United States, and India, with two randomized clinical trials and one secondary analysis of the randomized trial. The studies indicate that the most common factors that led to admission to the intensive care unit were respiratory distress syndrome (RDS), pulmonary immaturity, weak respiratory drive, excessively compliant chest wall, surfactant deficiency, sleep apnea, respiratory failure, and neurological and gastrointestinal complications. The days of mechanical ventilation range from 27 hours to 5 days,

with bradycardia apnea as the main cause of death, because the longer the MV time, the greater the risk of developing respiratory complications and extubation failure.

The predictive indices analyzed were pulmonary mechanical evaluation, pressure-time index, minute ventilation test, clinical tests, higher APGAR score at the fifth minute, higher pH before extubation, lower peak FIO_2 in the first 24 hours of age, lower $PaCO_2$, and FIO_2 before extubation. Other data are described in Table 1.

Table 1 – Characteristics of the studies included in the research

Author Year, Country	**Type of study**	**Sample**	**Underlying Diseases**	**VM Days**	**Hospitalization**	**Deaths**	**Preditive indices**
SETHE, et al, 2021 India	Randomized clinical trial	G1: n= 43 M= 24 F= 19 IG= 26 to 36 weeks and 6 days Weight = 1500 g APGAR 5'= 6 to 8 G2: n= 43 M= 24 F= 19 IG= 26 to 36 weeks and 6 days Weight = 1495 g APGAR 5'= 6 to 8	Respiratory Distress Syndrome (60.4 -67.4%)	27-2 9 hours	Not reported	22 (50-53%)	Evaluate: Pulmonary mechanics; Pressure-time index; Minute ventilation test; Clinical trials; and Dynamics of biological signals.
CHAWLA, et al, 2017 USA	Randomized clinical trial	G1: Weight = 882g N= 538 M= 295 (55%) F= 243 (45%) GI= 26.5 weeks APGAR 5'= 6 to 8 G2: Weight = 764g N= 388	G1: Bronchopulmonary dysplasia (30%); Intracranial hypertension (7.5%). G2: bronchopulmonary dysplasia (64%); Intracranial hypertension (23%).	5 Days	Not reported	G1: 31 (5,7%) G2:109 (28%)	G1: Higher APGAR score at 5 minutes; Higher pH (before extubation); Lowest peak FiO2 (in the first 24 hours of age); Lower PCO2 and

		M= 237 (61%) F= 151 (39%) GI= 25.8 weeks Apgar 5'= 5 to 8					FiO2 (before extubation); and Non-PIG Status G2: IG .
KOMATSU, et al, 2016 Brazil	Randomized Controlled Trial	G1: 38 M= 18 F= 20 Average Weight = 1.271g GI= 30.2 weeks Apgar 1'= 5.4 Apgar 5'=. 7 l7 G2: 38 M= 17 F= 21 Average Weight = 1.425 g GI= 31.3 weeks Apgar 1'= 4.9 Apgar 5'= 8.0	G1: Apnea 54.5%; SDR 18.1%; PCA: 5,5% G2: Apnea: 16.6%; SDR 33.3%; PCA: 19.4%	G1= 2 days G2= 1 day and a half	Not Reported	Not Reported	G1: FR = 12 bpm ; PIP = 16 Cmh 2 0; PEEP = 6 Cmh 2 0; Thread 2 ≤ 40%. G2 = P = 6 Cmh 2 0; Thread 2 ≤ 40%. 36 preterm infants - nIPPV and 36 - nCPAP
Legends: **n:** Sample Number; **GA:** gestational age; **M:** Male; **F:** Female; **RDS:** Respiratory Distress Syndrome; **FiO2:** Fraction of Inspired Oxygen; **PIP:** Peak Inspiratory Pressure; **PEEP:** Positive End-Expiratory Pressure; **pCO2:** Partial Pressure of Carbon Dioxide; **pO2:** Partial Pressure of Oxygen, **pH:** Hydrogen Potential; RR: Respiratory Rate; **MAP:** Mean Arterial Pressure.							

DISCUSSION

It is essential that mechanical ventilation ends as soon as possible, so that the variety of possible complications are avoided, the definition and criteria for the best time for weaning is immensely important to avoid mortality, reduce the length of stay in the ICU and the probability of failures causing reintubation (TARPGAARD et al., 2014).

Our study revealed that the mean gestational age (GA) was 36 weeks, with a mean weight of 750g. According to Chawla et al., (2017) gestational age was associated as a marker to predict possible extubation failures and successes, with adequate infants having a gestational age indicative of success, while lower gestational ages are indicative of extubation failure.

In the cross-sectional study by Oliveira et al., (2015), the mean GA of preterm infants at birth was 31 weeks, which is the period in which surfactant formation by type II pneumocytes occurs,

however, 53% of the preterm newborns analyzed required exogenous surfactant administration, which may be closely related to the interruption at the time of surfactant production. This fact contributes to 93.8% of cases with respiratory complications.

Our review showed that newborns submitted to mechanical ventilation were more prevalent in males than females. This profile is similar to the study by Kaltofen et al., (2015), where there was a predominance of respiratory distress syndrome in males, however, this occurs during lung development, where female fetal alveolar cells have a higher Na+ transport activity compared to those of the opposite sex, in addition, male androgens also decrease the production of surfactants and delay lung maturity.

According to Moura et al., (2021) the evaluation of the Tension-Time Index (ITT) is essential to obtain transdiaphragmatic pressure before extubation, to assess risk factors in case of respiratory muscle weakness. Another considerable index is the APGAR values at the 1st and 5th minute, in the studies by Seth et al., (2021); Chawla et al., (2017); Komatsu, et al., (2016) demonstrated ranges from 5 to 8 and are related to success or failure in extubation. Corroborating the research by Costa, Schettino and Ferreira (2014) in which the lowest APGAR values at the 1st and 5th minutes are associated with extubation failure, the values found were also from 5 to 8.

In the research by Bacci et al., (2020), the most common method of weaning from MV was the gradual decrease in ventilatory assistance, which was employed in 49.7% of the ICUs surveyed, mainly in NICUs and NICUs, with extubation being performed after minimum ventilation parameters have been reached or the patient has a successful spontaneous breathing test (SBT). In addition, the most frequently used criteria to assess readiness for extubation in NICUs were ventilatory parameters (98%), blood gas analysis (92%), and clinical and hemodynamic stability (86%). Corroborating the findings of the study by Komatsu et al., (2016), preterm infants that demonstrated minimal ventilatory parameters were more successful in extubation.

For the authors Chawla et al., (2017) neonates who had higher pH, lower peak FiO2 in the first 24 hours of life, lower pCO2 and FiO2 before extubation, were associated with extubation success, in addition to the pH of blood gases before extubation is an important marker for extubation readiness.

In the study by Glass et al., (2015), it was demonstrated that better measures to delineate the lowest oxygen fraction concentration can increase survival and decrease ocular, pulmonary, and neurocognitive morbidities in preterm infants. Going against the research of Seth et al., (2021) where they found that the pre-extubation mean airway pressure (MAP), FiO2 and tidal volume in volumetric ventilation, play fundamental roles in the success of extubation, and another important point to prevent extubation failure is the effective clearance of pCO2.

In the prospective and observational study by Nascimento et al., (2017), SBT has been increasingly used to determine extubation readiness, but there are still restrictions to predict who will need reintubation after undergoing SBT, however its use in children may make weaning simpler and reduce ventilatory support time.

In the research by Shalish et al., (2020), the approval or failure of SBT is determined from a combination of clinical events, and the test associated with gestational age demonstrated that neonates above the median GA (84% for successful extubation) and below the median GA (61% for successful extubation), however no one was able to define the between success or failure with sufficient precision to justify the use of the test routinely.

In the study by Komatsu et al., (2016) the participants were divided into two groups and the decisive factors of failures were regular episodes of apnea (54.5% vs. 16.6%), frequent decreases in oxygen saturation (27.2% vs. 50%) and clinical signs of respiratory distress (18.1% vs. 33.3%). Data similar to the randomized clinical trial by Chawla et al., (2017) where preterm neonates may be prone to extubation failure due to increased work of breathing, significant apnea and bradycardia, low oxygen saturation, respiratory acidosis, and upper airway narrowing.

CONCLUSION

The correct timing of weaning from mechanical ventilation and extubation is still considered a challenge in ICUs, in the area of pediatrics and neonatology there is still no solid evidence of effective methods and there are no validated tests or criteria that are reliable to determine patient readiness, in the literature there are numerous strategies and criteria for weaning and extubation, However, all of them must be further studied and analyzed in order to know exactly the ideal occasion.

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