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INTUBATION PROTOCOL AND VENTILATORY SUPPORT IN NEONATOLOGY: A SYSTEMATIC REVIEW OF CLINICAL TRIALS

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Abstract: Introduction: Worldwide, 15 million babies are born prematurely each year, and preterm birth is one of the biggest direct causes of neonatal mortality and morbidity. Respiratory distress syndrome is the main cause of respiratory failure in premature newborns. Several non-invasive respiratory support modalities are available in neonatal intensive care to minimize invasive ventilation, such as continuous positive airway pressure and non-invasive positive pressure ventilation. **Goal:** To understand intubation and ventilatory support protocols in neonatology. **Methodology:** This is a systematic review of clinical trials, in the PubMed database, with the descriptors: "protocol" AND "intubation" AND "neonatology", in the last 10 years. 7 scientific articles were selected, with full text and free. **Results:** The continuous positive airway pressure (CPAP) technique is the most used. Furthermore, providing nitric oxide (NO) in addition to oxygen during positive pressure ventilation for extremely preterm infants at birth is associated with a decreased need for supplemental oxygen treatments. In addition, high flow (HF) therapy is yet another non-invasive respiratory support modality for preterm infants. Finally, it was noted that the Intubate Surfactant Extubate (IN-SUR-E) method is not successful in all preterm infants with respiratory distress syndrome, with a failure rate of 19 to 69%. **Conclusion:** The intubation and ventilatory support protocols used in newborns with consolidated scientific evidence are continuous positive airway pressure, nitric oxide delivery and high flow therapy. Other methods such as IN-SUR-E have a failure rate with a relatively high variation, requiring further studies. It is concluded that any intervention in neonatology must be followed up over time for a better assessment of the potential adverse effects in this age group.

Keywords: Intubation, Neonatology,

Interactive Ventilatory Support.

INTRODUCTION

Preterm birth is the leading cause of death for newborns worldwide. Every year, 15 million babies are born premature and >1 million die from complications. Discomfort syndrome (RDS) is one of these complications that occurs in 44% of very low birth weight infants (<1,500 g); Compared with full-term newborns, preterm infants are at higher risk for neurodevelopmental impairments, so identifying the optimal method to provide respiratory support is crucial for this group (ROBERTS, C. T. et al., 2015).

Thus, the proportion of children who develop RDS (due to surfactant deficiency in the lungs) is significantly higher in newborns with a lower gestational age (GA). However, about 80% of preterm infants are born moderately to late preterm (32-36 weeks GA), where RDS is less common. Respiratory symptoms in this population of more mature preterm and full-term neonates may be due to conditions such as transient tachypnea of the neonate or infection. In addition, it is estimated that 2.5% to 5% of all newborns have respiratory difficulty (MANLEY, B. J. et al., 2017).

The survival of extremely premature babies has improved over the past two decades. However, morbidities associated with prematurity such as necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), patent ductus arteriosus (PDA), neurodevelopmental delay, bronchopulmonary dysplasia (BPD) and retinopathy of prematurity (ROP) present a significant burden for surviving preterm infants. Of these comorbidities, the last two are associated with the use of oxygen and mechanical ventilation, and this is because the optimal concentration of inspired oxygen for preterm infants during resuscitation is still uncertain. Current resuscitation guidelines recommend sticking to established oxygen goals while minimizing exposure to oxygen after birth. Administration of high levels of oxygen during resuscitation to maintain target oxygen saturation can be harmful due to the generation of reactive oxygen species (SEKAR, K. et al., 2020).

The transition from fetal to neonatal circulation involves a complex sequence of events during which pulmonary vascular resistance drops dramatically in association with an increase in peripheral vascular resistance. This cardiovascular adaptation at birth is facilitated by the release of cortisol, catecholamines, and vasodilatory mediators such as nitric oxide (NO) and prostaglandin (PG). NO is particularly important as it regulates pulmonary vascular tone at birth. NO is released from the vascular endothelium and plays a critical role in vascular adaptation during the perinatal period. It is a potent vasodilator, regulates pulmonary vascular tone, facilitates the clearance of fluid from the alveoli and ensures the integrity of the endothelial barrier. It activates soluble guanylate cyclase in vascular smooth muscle cells and the cyclic production of guanosine monophosphate, leading to pulmonary smooth muscle relaxation by regulating intracellular calcium levels. The major emphasis of current resuscitation guidelines is ventilation, with the expectation that pulmonary vasodilation will follow. In fact, ventilation of the lungs with air alone promotes a reduction in pulmonary vascular resistance by releasing vasoactive mediators. However, these guidelines do not provide any additional steps to facilitate pulmonary vasodilation beyond oxygen administration and lung expansion (SEKAR, K. et al., 2020).

This way, the complications of prematurity can be minimized in view of the existing intubation and ventilatory support protocols

for the neonate. Continuous positive airway pressure (CPAP) is the most commonly used. In addition, noninvasive positive pressure ventilation (NIPPV) appears to be effective in the early post-extubation phase. A recently introduced alternative is noninvasive high frequency oscillatory ventilation (NHFOV) (SHI, DE LUCA et al., 2019). As other modalities, it is possible to mention high flow therapy (HF), continuous positive nasal airway pressure (NCPAP) (MANLEY et al., 2017), Intubate-Surfactant-Extubate (IN-SUR-E) (VENTO et al., 2016), among others. In addition, it is important to emphasize that preterm newborns can receive these respiratory supports for several weeks upon adequate indication of which type of ventilatory support will be beneficial to that newborn, and it is important to pay attention to possible sequelae of ventilation, such as bronchopulmonary dysplasia (BPD) (VENTO et al., 2016).

In view of the above, the main purpose of this article is to elucidate the current protocols for intubation and ventilatory support in neonates, as well as to discuss their respective indications, risks, benefits, feasibility and other particularities within medical practice.

METHODOLOGY

This is a systematic review of the literature designed according to the criteria of the PICO strategy, an acronym that represents: population, intervention, comparison and outcome, for the elaboration of the research guiding question: "What is the applicability and use of current protocols? of intubation and ventilatory support in neonatology?".

In this sense, according to the parameters mentioned above, the population or problem of this research refers to patients who used Naloxone to reverse the condition of opioid intoxication; the intervention has a prognostic character; the comparison is of non-intervention, due to the design of the work; and the expected outcome is the identification of corollary benefits to the use of Naloxone for the aforementioned circumstance.

From this, a search was carried out in the PubMed (Medline) database, from the Virtual Health Library, with the descriptors MeSH/ DeCS Protocol, Intubation and Neonatology and the Boolean term AND, that is, the search strategy was: " protocol AND intubation AND neonatology". It is worth remembering that the last search was carried out in September 2022.

Furthermore, for the development of the present study, all complete and free indexed articles, of the clinical trial type, written in English, Portuguese and Spanish, related to the evaluation of intubation and ventilatory support protocols in neonatological patients, which were published in the last 10 years, so that incomplete articles or articles that did not fit the objective of the study were excluded and the filters used were, namely: "*free full text*", "*clinical trial*", "*English*", "*Portuguese*", "*Spanish*" and "*10 years*" at PubMed.

From the screening methodology, a total of 84 studies were found in the electronic database search. After applying the filters, 72 were removed from the list, with 12 remaining. After reviewing titles and abstracts, 5 articles were excluded, so that 7 remained for full-text analysis. Of these, all were included in the qualitative analysis synthesis.

Among the reasons for excluding the identified articles are: they do not present the filters indicated in the methodology and do not fit the theme proposed in the objectives.

RESULTS

Worldwide, 15 million babies are born prematurely each year, and preterm birth is one of the biggest direct causes of neonatal mortality and morbidity. Compared with full-term babies, premature babies are at increased

risk of neurodevelopmental impairment. In this sense, the first hours after birth represent a sensitive period for the very low birth weight newborn (LBW), and mothers who see their baby within 3 hours after birth tend to establish a more secure attachment to the baby in compared to those who don't see their baby within 3 hours. Thus, skin-to-skin care immediately after delivery is a common practice for term babies and has been shown to improve cardiorespiratory stability, facilitate early bonding, and promote breastfeeding. Neurodevelopmental complexity and genetic, epigenetic, and environmental factors that can influence development make it less likely that a single, short-term intervention will lead to a change in cognition and/or behavior after 2 years. Thus, any intervention offered to these infants must be followed up over time to learn more about its potential effects or lack thereof (KRISTOFFERSEN et al., 2016).

Thus, it is understood that prematurity is also exposed to several other complications among them, respiratory distress syndrome (RDS) is the main cause of respiratory failure in premature newborns, with an incidence ranging from ≈80% to ≈25%, depending on gestational age. Several non-invasive respiratory support modalities are available in neonatal intensive care to minimize invasive ventilation. Continuous positive airway pressure (CPAP) is the most commonly used, but noninvasive positive pressure ventilation (NIPPV) appears most effective in the early post-extubation phase, although it is unclear whether NIV can influence long-term outcomes. deadline. A recently introduced alternative is noninvasive high-frequency oscillatory ventilation (NHFOV), which may be especially useful in infants who need constant high pressure distention. Premature newborns can receive these respiratory supports for several weeks, upon adequate indication of which type of ventilatory support will be beneficial to that newborn (SHI; DE LUCA, 2019).

High flow (HF) therapy is an increasingly popular modality of non-invasive respiratory support for preterm infants. However, the use of nHF is also being adopted in non-tertiary special care nurseries (SCNs), a setting where there is little evidence of its efficacy and safety (MANLEY et al., 2017). Although they now exist to support the use of HF to reduce extubation failure, there are no adequately designed and powered studies to assess the use of HF as primary respiratory support soon after birth. The hypothesis of the present study is that HF is not inferior to the standard treatment - nasal continuous positive airway pressure (NCPAP) - as primary respiratory support for preterm infants. It is critical that FH therapy is delivered harmlessly, with proper assessment of its use before it becomes widely accepted in neonatal practice. If HF provides comparable support to NCPAP for preterm infants with early respiratory distress, it is likely to be widely adopted in preference to NCPAP in the NICU as it is easier to use, more comfortable for infants, reduces nasal trauma, and is preferred by clinicians. and parents. The use of FH in neonatal practice is already well established, but good quality evidence is needed to determine in which clinical settings this is appropriate. If this study demonstrates that HF is not inferior to NCPAP as a primary support, it is likely that this practice will be widely adopted around the world.

Another successful method in clinical practice is INtubate-SURfactant-Extubate (IN-SUR-E), however its effectiveness is not guaranteed in all preterm neonates with respiratory distress syndrome, with a reported failure rate ranging from 19 to 69%. One of the possible mechanisms responsible for the failure of the IN-SUR-E method, requiring subsequent reintubation and mechanical ventilation, is the inability of the preterm

lung to achieve and maintain an "optimal" functional residual capacity. The importance of pulmonary recruitment prior to surfactant administration has been demonstrated in animal studies showing that recruitment leads to a more homogeneous distribution of surfactant within the lungs. From all the available data, there is no definitive evidence for a positive effect of recruitment prior to surfactant instillation, but there is a rationale for testing the following hypothesis: a pulmonary recruitment maneuver performed with a stepwise increase in Continuous Distending Pressure during a High Frequency Oscillatory Ventilation (and not with a sustained insufflation) could have positive effects in terms of better surfactant distribution and consequently its greater effectiveness in premature newborns with respiratory distress syndrome (VENTO et al., 2016).

Associated with these intervention proposals in the face of this pediatric pulmonary emergency, the adjuvant use of nitrous oxide during neonatal resuscitation was presented, in preclinical studies, NO showed anti-inflammatory properties, stimulated angiogenesis, increased alveolar growth, improved surfactant function and inhibited smooth muscle cell proliferation. In large randomized trials in preterm infants, none of the benefits seen in animal models were seen when NO was given to reduce inflammation and chronic lung disease, although a subset of preterm infants appeared to benefit from this. However, these trials demonstrated that NO is safe and does not increase oxidative stress or lung inflammation. NO has never been evaluated in newborn resuscitation for its vasodilating properties, which is essential for extrauterine adaptation (SEKAR et al., 2020).

Therefore, premature babies are often unable to breathe and establish effective gas exchange at birth, and so most infants receive mask ventilation or are intubated in the delivery room. Knowing that positive pressure ventilation, the quality, corrections made and clinical responses were not influenced by the respiratory function monitor, which points to the fact that the availability of monitor data did not change the caregivers' performance, established whether a last proposal, more conservative among all those previously discussed, which proposes the implementation of monitoring by other devices or even an improvement in the technique used by caregivers could benefit the outcomes of RDS cases (VAN ZANTEN et al., 2021).).

CONCLUSION

The intubation and ventilatory support protocols used in newborns with consolidated scientific evidence are continuous positive airway pressure, nitric oxide delivery and high flow therapy. Other methods such as IN-SUR-E have a failure rate with a relatively high variation, requiring further studies. It is concluded that any intervention in neonatology must be followed up over time for a better assessment of the potential adverse effects in this age group.

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