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Original article

Weaning of infants from non invasive ventilation

C. Gizzi[1], L. Massenzi[1], M.G. Pattumelli[1], C. Moretti[2], R. Agostino[1]

[1] Neonatal Intensive Care Unit, Pediatric and Neonatal Department – "S. Giovanni Calibita" Fatebenefratelli Hospital – Isola Tiberina, Rome, Italy; [2] Pediatric Emergency Medicine and PICU – Sapienza University of Rome, Policlinico Umberto I, Rome, Italy

Abstract. Non invasive ventilation (NIV) is commonly used to treat RDS in preterm infants. Although less risky than invasive ventilation, NIV has some potential side effects and appropriate weaning is therefore desirable. However, criteria for the definition of stability prior to attempting NIV weaning as well as the best weaning strategies need to be more investigated. The aim of this review is to identify criteria and interventions that can facilitate correct weaning from NIV. (www.actabiomedica.it)

Key words: non invasive ventilation, NCPAP, weaning, preterm infant

Introduction

Non invasive ventilation (NIV) is largely used for the management of respiratory distress syndrome (RDS) in preterm infants. Although less risky than mechanical ventilation (MV), NIV has some potential side effects. These mainly include damage to the nose, air leaks syndromes and abdominal distension (1). Moreover, during the recovery phase of RDS, when lung compliance has improved, most of the pressure applied to the airways can be transmitted to the heart and major blood vessels, possibly impeding systemic and pulmonary venous return (2). Finally Infants on NIV require more nursing care and the use of extra equipment than infants not on NIV. Appropriate weaning of premature infants from NIV to unsupported breathing as soon as stable conditions are reached, is therefore highly desirable. Inappropriate weaning, conversely, may result in an increased work of breathing (WOB) and in a deterioration of the respiratory function that prolongs time on ventilatory support, oxygen need and hospital stay. Failure of weaning from NIV is also potentially distressing to staff and family. Nevertheless, the identification of the criteria for the definition of stability prior to attempting to withdraw NIV as well as the best strategies of weaning need to be more deeply investigated. The aim of this review is then to identify criteria and interventions that can facilitate correct weaning from non invasive ventilation.

Predictors of successful weaning

Theoretically, several factors may influence the success of weaning process from NIV in preterm infants. Among these, gestational age (GA) at birth, birth weight (BW), prenatal and postnatal history, ethnicity, gender, postnatal age, indications for nasal continuous positive airway pressure (NCPAP) and associated clinical comorbidities have been studied. Rastogi et al. (3) retrospectively reviewed 454 neonates ≤32 weeks of GA who were placed on NCPAP and successfully weaned to room air. In their study neonates had a mean birth weight (BW) of 1357 ± 392 g with a mean GA of 29.3 ± 2.2 wks. Neonates were weaned off NCPAP at mean weight of 1611 ± 432 g and mean postmenopausal age of 32.9 ± 2.4

wks. Univariate analysis of their data showed that chorioamnionitis, intubation, surfactant therapy, patent ductus arteriosus (PDA), sepsis/ necrotizing enterocolitis (NEC), anemia, apnoea, gastroesophageal reflux (GER) and intraventricular hemorrhage (IVH) were significantly associated with the time to NCPAP wean. On multivariate analysis, among neonates who were intubated, BW was the only significant factor (p<0.001) that was inversely related to time to successful NCPAP wean. Amongst non-intubated neonates, along with BW (p <0.01), chorioamnionitis (p <0.01), anemia (p <0.0001), and GER (p <0.02) played a significant role in weaning from NCPAP, indicating that different factors play different roles if neonates were intubated or not. It is worthy of note that in the Rastogi's study caffeine use was limited to those infants who showed significant apnea (22.3%).

Recently, Pickerd et al. (4), by using electromagnetic inductive plethysmography, measured tidal (VT) and minute volume (MV) normalized to body weight in 29 preterm infants (GA 28 ± 2 weeks) who were in stable clinical condition and intended to be weaned from non invasive respiratory support. Infants were studied weekly while receiving variable-flow NCPAP, bubble NCPAP, nasal bi-level positive airway pressure (BiPAP) and during unsupported breathing. These authors reported that at different pressure settings, on all NCPAP devices the measured MV/kg was similar either through increasing VT/kg and decreasing respiratory rate (variable flow NCPAP and BiPAP) or maintaining both (bubble CPAP). Moreover, serial tidal breathing measurements showed decreasing difference for VT/kg over time on and off NCPAP, indicating an improvement in lung function. They conclude that serial tidal breathing measurements may aid weaning from NCPAP.

Also clinical criteria to discontinue NIV and to replace NIV in case of weaning failure has been poorly defined. Some studies have been conducted to evaluate the methods of NCPAP wean used at several neonatal intensive care units (NICUs) (5, 6). These identified a lack of agreement on the method of NCPAP wean among units, with only 6% having written guidelines regarding NCPAP wean. According to the resulting data, the start of the NCPAP weaning is frequently arbitrarily determined by healthcare providers (physicians, nurses, and respiratory technicians) and many units only wean NCPAP once the infant is breathing air, while some others include parameters such as BW or corrected GA before considering weaning. Even less is standardized about the "failure" criteria of weaning that should indicate when to put the babies back on NCPAP in case of unsupported breathing failure. Todd et al (7) proposed standardized 'stability' and 'failure' criteria formulated on previous studies and literature data, that are reported in Table 1-2. This criteria, if adopted by future studies, would greatly help in any further meta-analysis of studies reporting on weaning from non invasive ventilation. However, whether or not these or other criteria are best, still needs to be established.

Table 1. Stability criteria (must have all 8 criteria for ≥12 hours [From: Todd et al. (7)]

1. CPAP 4-6 cm H_2O
2. Oxygen requirement less than 25% and not increasing
3. Respiratory rate less than 60
4. No significant chest recession (sternal/diaphragmatic)
5. Less than 3 episodes of self reverting apnoeas (<20 seconds) and/or bradycardias (<100 BPM) and/or desaturations (≤86%) in 1 hour for the previous 6 hours
6. Average saturation >86% most of the time or PaO_2/ transcutaneous PaO_2>45 mmHg
7. Not currently treated for patent ductus arteriosus or sepsis
8. Tolerated time off CPAP during cares (up to 15 minutes)

Table 2. Criteria for failed trial off CPAP (at least 2 of the following) (7) [From: Todd et al. (7)]

1. Increase work of breathing (intercostal recession and accessory muscles contributing for respiration) with respiratory rate >75
2. Increased apnoea and/or bradycardia and/or desaturation > 2 in 1 hour for the previous 6 hour period
3. Increased O_2 requirement >25% to maintain the oxygen saturations > 86% and/or PaO_2/transcutaneous PaO_2 > 45 mm Hg
4. pH of <7.2
5. $PaCO_2$/transcutaneous $PaCO_2$ >65 mmHg
6. Major apnoea or bradycardia requiring resuscitation

Strategies of withdrawal from NIV

Most of the available literature on weaning from NIV is related to weaning from NCPAP. However, lack of standardization has been reported over the best method of weaning NCPAP and this issue is often approached in an 'ad hoc' manner depending upon units protocols. Described strategies for withdrawal of NCPAP include (1):

- Stopping NCPAP completely, independent of the level of airway pressure, and remaining off NCPAP unless certain criteria are met that require the infant to go back onto NCPAP;
- Decreasing NCPAP to predefined level of airway pressure, then stopping NCPAP completely;
- Removing NCPAP for a predetermined number of hours each day gradually increasing the amount of time off NCPAP each day until NCPAP is able to be stopped completely (graded time off);
- Stopping NCPAP and starting low flow oxygen or humidified high flow air (and oxygen if required) via nasal cannula;
- Combinations of the above strategies;
- Combinations of the above strategies in addition to co-interventions (e.g. methylxanthines).

The possible benefits of these different methods of NCPAP withdrawal are intuitive. Weaning the distending pressure may gradually increase respiratory muscle strength without the associated risk of atelectasis. Having periods of time off may have a similar effect of respiratory muscle training but for shorter and more intense periods. However, time off NCPAP may be more likely to cause "atelectotrauma" (due to alveolar collapse when off NCPAP and re-recruitment once NCPAP is started again). At the same time, having periods of time off NCPAP may reduce the incidence of nasal trauma and temporarily increase patient's comfort also allowing the parents an opportunity to have unhindered interaction with their infant. A recent Cochrane review (1) and a more recent randomized controlled trial (RCT) (7) compared different methods of NCPAP weaning. Both concluded that using the strategy of taking babies off NCPAP with the intention of discontinuing any nasal ventilatory support, when predefined "stability" criteria are reached, reduces the length of weaning time and time on NCPAP, O_2 duration, the incidence of bronchopulmonary dysplasia (BPD) and the length of NICU stay.

Rastogi et al. (8) recently compared a sudden vs gradual method to wean from NCPAP in 56 infants born at ≤32 weeks who were stable on NCPAP of 5 cmH_2O and on FiO_2 of 0.21. In the sudden weaning group, NCPAP was removed and kept off completely. In the gradual wean group, it was cycled on and off increasing the time off for 96 hours and then discontinued. In contrast with the previous findings, the authors found that there was no difference in the success of weaning between the 2 groups. Also, the weight and postmenstrual age at the time of successful NCPAP wean did not differ between the sudden and the gradual group (33.7 ± 2.8 wks vs 33.8 ± 2.6 wks -1,736 ± 487 g vs 1,736 ± 501 g, respectively). The authors commented that factors other than the method of NCPAP wean, such as pulmonary maturity and comorbidities, may determine the success of weaning in preterm infants.

About combined strategies, Abdel-Hady et al. (9) performed a RCT to determine the better approach for weaning preterm infants from NCPAP with or without transitioning to nasal cannula (NC). Sixty preterm infants born at ≥28 weeks gestation who were clinically stable on NCPAP of 5 cmH_2O with FiO_2<0.30 for at least 24 h were randomly assigned to two weaning groups. Infants in group 1 were kept on NCPAP until they were on FiO_2=0.21 for 24 h, and then were weaned off NCPAP completely without any exposure to NC. Infants in group 2 were weaned off NCPAP when FiO_2 was ≤0.30 to NC (flow set at 2 L/min) followed by gradual weaning from oxygen supply. After randomization, infants in group 1 had fewer days on oxygen [median (interquartile range): 5 (1-8) vs 14 (7.5-19.25) days, p<0.001] and shorter duration of respiratory support [10.5 (4-21) vs 18 (11.5-29) days, p=0.03], indicating that weaning preterm infants from NCPAP to NC is associated with increased exposure to oxygen and longer duration of respiratory support. More recently, Fernandez-Alvarez et al. (10) retrospectively compared the outcome of very premature infants with RDS treated with a combination of NCPAP and heated humidified high-

flow nasal cannula (HHHFNC) versus NCPAP and low-flow nasal cannula (LFNC) during weaning from NCPAP. Between 2004 and 2008, 79 patients with GA ≤28 weeks and BW <1,250 g were treated with one of the two strategies. The total number of NCPAP days was significantly reduced by 50% in the HHHFNC group. Thirteen percent of the patients on NCPAP suffered from nasal bridge lesions compared to none on HHHFNC, while respiratory and non-respiratory outcome was not significantly different otherwise. The authors also outlined that combination of NCPAP and HHHFNC reduced costs by 33%. Combined results from the mentioned studies seem to indicate that during weaning if the respiratory system is still immature and unstable, to reduce the level of positive pressure applied to the airways by using LFNC or taking off and on NCPAP can be detrimental, while, once reached the respiratory stability, cycling ma be not necessary.

Weaning from modes of NIV other than NCPAP, such as nasal intermittent positive pressure ventilation (NIPPV) synchronized or not to the infant's spontaneous breathing or BiPAP, has been poorly studied. Indeed, in common clinical practice, infants who are treated with (S)NIPPV or BiPAP are switched on NCPAP as respiratory conditions improve and then weaned directly from this mode. However, some suggestions on when to wean infants directly from (S)NIPPV to oxyhood/nasal cannula come from Bhandari et al. (11). They suggests to wean infants from (S)NIPPV when they are assisted with minimal settings and have blood gases within normal limits. Minimal setting are: respiratory rate ≤20 per minute, PIP ≤14 cm H_2O, PEEP ≤4 cm H_2O, FiO_2 ≤0.3 and flow 8-10 L/m. No studies are available comparing weaning infants directly from (S)NIPPV or BiPAP or switching them to NCPAP before completely stop nasal ventilatoy support.

In our NICU, we mostly use flow-SNIPPV to support non invasively our preterm infants (12, 13) and directly wean from this mode of ventilation quite often. Our strategy is to progressively reduce PIP, rather than reducing the number of assisted breaths, as this seems to better avert diaphragmatic fatigue and gradually train respiratory muscles (14). Moreover, while using SNIPPV, we minimize the well described effects of asynchrony on blood pressure, cerebral blood flow fluctuations, air-leaks and WOB (15,16) that can be met when using IPPV at high rate. We usually discontinue SNIPPV with the intention to stay off ventilatory support if PIP ≤12 cm H_2O, PEEP <5 cm H_2O and FiO_2 ≤0.25.

Adjunctive respiratory support

Methylxantines facilitates transition to spontaneous, unsupported breathing. Among these Caffeine has a longer half-life, an earlier onset of action and is less toxic than theophylline and is therefore considered the methylxanthine of choice. Caffeine has a diuretic effect, which may explain the improved lung compliance in treated infants, and also enhances diaphragmatic activity and respiratory muscle strength (14). Neonatal caffeine therapy was found to reduce the risks of important short-term morbidities such as bronchopulmonary dysplasia (BPD) and severe retinopathy of prematurity, decrease the incidence of cerebral palsy and cognitive delay at 18 months, and improve gross motor function at 5 years (17). Nearly one-half of the neuroprotective effect of caffeine at 18 months could be explained by the earlier discontinuation of positive airway pressure in infants assigned to caffeine. Moreover, infants who start caffeine before three days of age appeared to experience a greater reduction in the duration of respiratory support, invasive and non invasive, than those commencing treatment between 4 and 10 days of age (18). From this point of view, caffeine must be considered as an helpful co-intervention in weaning infants from NIV.

Conclusions

Findings from the mentioned studies may provide neonatal health care providers clinical information on successful NCPAP weaning that may be used to initiate wean and help in decreasing the number of weaning failures. Most of the available data seems to indicate that infants who have their NCPAP pressure weaned to a predefined level and then stop

NCPAP completely have less total time on NCPAP and shorter durations of oxygen therapy and hospital stay compared with those that have NCPAP removed for a predetermined number of hours each day. Clear criteria need to be established for the definition of stability prior to attempting to withdraw NCPAP. Finally, caffeine is an effective adjunctive respiratory support during weaning from NIV.

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Correspondence:
Camilla Gizzi
Piazza Confienza, 3 - 00185 Rome, Italy
Phone: +39 339 4024709
Fax + 39 06 68300746
E-mail: camillagizzi@tin.it