Management of Extremely Low Birth Weight Infants in Delivery Room

Asma Nosherwan, MBBS[a,b], Po-Yin Cheung, MBBS, PhD[a,b], Georg M. Schmölzer, MD, PhD[a,b,*]

KEYWORDS

• Infants • Newborn • Neonatal resuscitation • Very low birth weight infants

KEY POINTS

- Establishing breathing and improving oxygenation after birth are vital for survival and long-term health of preterm infants.
- Approximately 50% of extremely low birth weight (ELBW) infants are hypothermic after admission to neonatal intensive care units (NICUs).
- Active measures to avoid hypothermia during stabilization in the delivery room (DR) should include the use of plastic wrapping; warming equipment, such as radiant warmers; warmed humidified resuscitation gases; and adequate temperature.
- Respiratory support at birth should aim to facilitate the early establishment of an effective functional residual capacity (FRC), initiate spontaneous breathing, facilitate gas exchange, and deliver an adequate tidal volume, without damaging the lung.
- Current neonatal resuscitation guidelines recommend the use of 21% to 30% oxygen during neonatal resuscitation at birth.

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[a] Centre for the Studies of Asphyxia and Resuscitation, Royal Alexandra Hospital, 10240 Kingsway Avenue Northwest, Edmonton, Alberta T5H 3V9, Canada; [b] Department of Pediatrics, University of Alberta, 116 St & 85 Avenue, Edmonton, AB T6G 2R3, Canada
* Corresponding author. Neonatal Research Unit, Centre for the Studies of Asphyxia and Resuscitation, Royal Alexandra Hospital, 10240 Kingsway Avenue Northwest, Edmonton, Alberta T5H 3V9, Canada
E-mail address: georg.schmoelzer@me.com

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INTRODUCTION

Establishing breathing and improving oxygenation after birth are vital for survival and long-term health of preterm infants. Very preterm infants often have difficulty in establishing effective breathing after birth because their lungs are structurally immature, surfactant deficient, and not supported by a stiff chest wall,[1] which render the lungs of very preterm infants uniquely susceptible to injury.[2,3] A majority of ELBW infants receive respiratory support in the DR. The DR is a stressful environment where decisions are made quickly and resuscitators need to be skilled in clinical assessment, decision making, and mask ventilation.[4] These tasks, however, are often more difficult than is widely appreciated, and it is possible that these infants are not optimally supported because of difficulties in ventilation and perfusion during initial resuscitation.[1,5,6]

CORD CLAMPING

For centuries a physiologic approach to clamping the cord was routinely used. In the middle of the twentieth century, this physiologic approach to cord clamping was changed to immediate cord clamping (ICC). One reason for this practice change was the thought that keeping the cord intact could contaminate the obstetric sterile field. The practice of ICC has recently been questioned as unphysiologic,[7] which is also reflected in the current neonatal resuscitation guidelines, which recommend delayed cord clamping (DCC) for at least 30 seconds.[4] Using DCC (defined by various definitions of time delays [eg, >30 seconds or until pulsation is no longer detected]) allows transfusion of blood to the newborn from the placenta; it can provide an infant with up to an additional 30% blood volume,[8] which may improve pulmonary blood flow and left ventricular preload.[9] In spontaneously breathing ELBW infants, DCC has short-term benefits on neonatal hemodynamic transition physiology.[10–12] A recent meta-analysis of preterm infants receiving DCC compared with ICC reported on 10 studies (199 infants).[13] Compared with ICC, DCC improves short-term outcomes of ELBW infants (mean difference 0.61; 95% CI, −2.52 to −1.92), including higher blood pressure and hemoglobin on admission and less frequent blood transfusions.[13] Although DCC has been shown to reduce overall intraventricular hemorrhage (IVH) (mainly lower grades 1 and 2) by 50%,[14,15] it has not been proved to reduce the incidence of severe (grade 3 or 4) IVH or death.[13] Furthermore, these short-term benefits have failed to translate into improved neurodevelopment outcomes at later age.[13,16]

Umbilical cord milking (UCM) is an alternate to DCC, is a faster technique of promoting placental transfusion, and takes approximately 5 seconds to 10 seconds.[12] The 2 interventions when compared showed no any difference in mean hemoglobin concentration at birth, number of blood transfusions in first 6 weeks of life,[17] or long-term neurodevelopmental follow-up.[17] Katheria and colleagues[12] showed UCM to be a more efficient technique than DCC to improve blood volume in premature infants when delivered by cesarean section. Alternative strategies include UCM[12] and initiation of resuscitation while the newborn remains attached to the cord.[18,19] Additional evidence is awaited, however, from ongoing clinical trials before this can be translated into clinical practice.

Practical Aspects

Currently, the evidence is equivocal; there is minimal advantage to DCC, which has, at minimum, hematologic benefits; it is suggested that ELBW infants not requiring immediate resuscitation should receive DCC for at least 30 seconds.[4] Infants could be either held above or below the level of the placenta.[20]

THERMOREGULATION

Maintenance of thermal homeostasis using a target range of 36.5°C to 37.5°C is one of the most critical supportive therapies during fetal to neonatal transition, in particular for preterm infants. Silverman and colleagues[21] first cited the association between survival and incubator temperature and hypothermia. On review of the data, only the ELBW infants had higher mortality in the cold (incubator temperature of 28.7°C) than the warm (31.7°C) groups. Both hypothermia and hyperthermia should be avoided during stabilization to prevent common morbidities.[22] Hypothermia remains problematic even when recommended routine thermal care guidelines are followed in the DR. ELBW infants are at a high risk of developing hypothermia due to an imbalance between heat loss by conduction (cold surface), radiation (cool walls), evaporation (thin epidermis with increased permeability), and convection (cool ambient room temperatures) to heat production (reduced quantities of subcutaneous brown fat and inadequate vasomotor responses).[18] There is a dose-related effect on mortality with an increased risk of approximately 30% for each degree below 36.5°C body temperature at admission. Therefore, the current neonatal resuscitation guidelines emphasize the importance of maintaining thermal homeostasis throughout neonatal stabilization. Strategies to minimize heat loss include (1) occlusive wrapping, (2) exothermic warming mattress, (3) warmed humidified resuscitation gases, (4) polyethylene caps, and (5) adequate DR temperature.[4]

A Cochrane review examined different barriers to prevent heat loss (eg, plastic wrap or bag, plastic cap, and stockinet cap).[23] Plastic wraps or bags were effective in reducing heat losses in infants less than 28 weeks' gestation (mean difference [95% CI] 0.68°C [0.45°C –0.91°C]). Plastic caps were effective in reducing heat losses in infants less than 29 weeks' gestation (mean difference [95% CI] 0.80°C [0.41°C –1.19°C]). The Cochrane review concluded that there was insufficient evidence to suggest that either plastic wraps or plastic caps reduce the risk of death during hospitalization,[23] and that stockinet caps were not effective in reducing heat loss.[23]

Using an external heat source (eg, skin-to-skin care [SSC] or a transwarmer mattress) can effectively reduce the risk of hypothermia compared with conventional incubator care for infants.[23] Using SSC or a transwarmer mattress reduces the incidence of hypothermia on admission to NICU in ELBW infants (relative risk [RR]: SSC 95% CI, 0.09 [0.01–0.64]; transwarmer mattress 95% CI, 0.30 [0.11–0.83]). Plastic wraps or bags, plastic caps, SSC, and transwarmer mattresses all keep preterm infants warmer, leading to higher temperatures on admission to neonatal units and less hypothermia. Furthermore, there is emerging evidence to use heated humidified gases for initial respiratory support during EBLW infant resuscitation, resulting in more infants with normothermia compared with cold dry gas (mean [SD] rectal temperature 35.9°C [0.6] vs 36.4°C [0.6] for cold and heated cohorts, respectively; $P = .0001$).[24]

It is recommended that DR temperature should be maintained at 23°C to 26°C.[4] Cold stress and incidence of hypothermia were reduced by increasing the DR temperature to that recommended by World Health Organization.[25] Duryea and colleagues[26] found that an increase in operating room temperature from 20°C to 23°C at the time of cesarean reduced the rate of neonatal and maternal hypothermia (without a measurable decrease in neonatal morbidity). Neonatal resuscitation guidelines (2015) recommend prewarming the DR to 26°C for infants with weight less than 1500 g.[4]

On the contrary, infants born to hyperthermic mothers seem to have increased neonatal mortality, seizures, and encephalopathy. Although there is an association between chorioamnionitis at the time of delivery with cerebral palsy, hyperthermia has

many deleterious effects on the perinatal brain, including an increase in cellular metabolic rate and cerebral blood flow alteration; release of excitotoxic products, such as free radicals and glutamate; and hemostatic changes.[27] Therefore, hyperthermia (>38.0°C) should be avoided during stabilization of ELBW infants.[4]

The current evidence is limited by the small number of infants included in randomized trials. No long-term follow-up data are available to recommend any precise method for clinical practice.[23]

Practical Aspects

Active measures should be initiated and performed to avoid hypothermia in ELBW infants during stabilization in DR, including the use of plastic wrapping, warming equipment such as radiant warmer, warmed humidified resuscitation gases, and adequate DR temperature at 26°C. Especially for infants born to mothers with fever, however, vigilance in thermoregulation should be exercised to avoid hyperthermia.

Respiratory support in the delivery room

Although a majority of infants make the fetal-to-neonatal transition without help,[28] ELBW infants often need respiratory support at birth.[28] These infants often have difficulty establishing effective breathing after birth due to structurally immature surfactant-deficient lungs and not supported by a stiff chest wall,[1] which render the lungs of very preterm infants uniquely susceptible to injury. During the transition of spontaneously breathing ELBW infants, to facilitate the early establishment of an effective FRC, reduced atelectotrauma, and improved oxygenation, continuous positive airway pressure (CPAP) has been advocated at the initiation of respiratory support.[29–33] If an infant fails to initiate spontaneous breathing, current neonatal resuscitation guidelines recommend positive pressure ventilation (PPV) via a face mask[4] to establish FRC, facilitate gas exchange, deliver an adequate tidal volume (V_T), and initiate spontaneous breathing, without damaging the lung.[1] Further, using a sustained inflation (SI) may help lung liquid clearance, recruitment of FRC,[34] and positive end-expiratory pressure by preventing repeated collapse and opening of alveoli.[34]

CONTINUOUS POSITIVE AIRWAY PRESSURE

Observational studies in the era before the widespread use of antenatal steroids and the introduction of surfactant and the postsurfactant era have documented an association between lower rates of BPD and increased use of nasal CPAP in the DR.[31] Studies comparing centers predominantly using nasal CPAP in DR to centers using early mechanical ventilation (MV) and surfactant administration reported lower BPD rates in centers with a focus on nasal CPAP.[35–37] Van Marter and colleagues[37] reported higher rates of BPD in centers with more MV (75% vs 29%) and increased surfactant use (45% vs 10%) compared with centers with predominantly use of early nasal CPAP. These reports stimulated large randomized control trials comparing nasal CPAP or early endotracheal intubation at birth. A pooled analysis of a total of 2782 preterm infants less than 29 weeks' gestation (1296 infants in the nasal CPAP group and 1486 in the intubation group) showed a significant benefit for the combined outcome of death or BPD, or both, at 36 weeks' corrected gestation for babies treated with nasal CPAP (RR [95% CI] 0.91 [0.84–0.99]; risk difference −0.04, −0.07 to 0.00; number needed to treat 25). This suggests that 1 additional infant could survive to 36 weeks without BPD for every 25 babies treated with nasal CPAP in the DR rather than being intubated.[31]

SUSTAINED INFLATION

Animal studies have reported that SI (1) improves lung compliance without adverse circulatory effects,[38] (2) achieves lung aeration more uniformly,[39] (3) has an increased inspiratory volume and greater FRC compared with PPV alone,[34] and (4) does not cause overdistension of the lungs.[40]

Observational studies using SI during stabilization in the DR have reported a significant reduction in rates of intubation and MV, BPD, and use of oxygen,[41] which led to the design of several randomized controlled trials to compare SI with PPV alone. te Pas and colleagues[42] compared 2 different DR approaches —SI delivered via a T-piece and followed by early nasal CPAP compared with PPV with a self-inflating bag. They reported a significant reduction in intubation in the DR and BPD with SI and early nasal CPAP compared with traditional ventilator support in the DR. The studies comparing SI with nasal CPAP to CPAP alone did not find any difference in BPD in the 2 groups despite reduction in need of MV in first 72 hours.[43,44]

A recent meta-analysis of SI in DR reported a significant reduction in need for MV within the first 72 hours after birth in the SI group (RR [95% CI] 0.87 [0.77–0.97]; number needed to treat 10).[45] Neonatal mortality and BPD were similar, however, between the 2 groups. More concerning was the increase in patent ductus arteriosus treatment in infants receiving SI (RR [95% CI] 1.27 [1.05–1.54], number needed to harm 10).[45] The investigators speculated that early FRC establishment associated with reduction of pulmonary vascular resistance might induce rapid development of left-to-right shunting through the ductus.[45] A recent Cochrane review,[46] which was limited to infants who received a 15-second pressure-controlled SI versus standard inflations, reported no differences in mortality, intubation in the first 3 days of life, or BPD. In addition, there are several factors that may considerably influence the effectiveness of any SI intervention, including (1) skill of the clinical team, (2) interface by which an SI is delivered,[47] (3) an infant's intrinsic respiratory effort,[48] and (4) mask leak.[48] This suggests that an SI might not be the optimal approach in all apneic infants. These data suggest that more studies are needed before SI can be routinely used in the DR. Currently studies comparing SI to PPV alone are ongoing[49] and their results might help to inform the next cycle of the neonatal resuscitation guidelines in 2020. Until new results become available, SI should be limited to clinical trials.

OXYGEN USE IN THE DELIVERY ROOM

In 2010, neonatal resuscitation guidelines recommended use of blended air and oxygen to babies born at less than 32 weeks' gestation, and that F_{IO_2} should be guided by pulse oximetry.[50] These guidelines stated that resuscitation should be started with air in infants who were at least 32 weeks of gestation.[51] In 2015, the guidelines made a strong recommendation to initiate stabilization of preterm infants less than 35 weeks gestation with lower initial fraction of inspired oxygen (F_{IO_2}) (0.21–0.3) and not higher F_{IO_2} (>0.65).[4] This approach is supported by a few small studies comparing different oxygen concentrations during neonatal resuscitation at birth. Wang and colleagues[52] reported that preterm infants ventilated in air required oxygen to achieve target oxygen saturation as measured by pulse oximetry (Spo_2) and to overcome bradycardia. Although ELBW infants resuscitated with an initial F_{IO_2} of 0.3 compared with 0.9 had reduced oxidative stress and risk of BPD.[53] There was no difference in the overall risk of death or other common preterm morbidities when resuscitation is initiated at delivery with lower ($\leq$0.30) or higher ($\geq$0.6) F_{IO_2} in infants less than or equal to 28^{+6} weeks' gestation.[52–54] The opposing results for masked and unmasked trials may represent a type I error, emphasizing the need for larger, well-designed studies.[55]

A recent meta-analysis in 677 preterm infants less than or equal to 32 weeks' gestation showed no differences in morbidity, with a trend toward lower mortality in the lower (0.21–0.3 F_{IO_2}) oxygen group compared with the higher (0.6–1.0 F_{IO_2}) oxygen group.[56] These data support the current neonatal resuscitation recommendations to initiate stabilization of preterm infants less than 35 weeks' gestation with lower initial F_{IO_2} (0.21–0.3) and not higher F_{IO_2} (>0.65).[4]

There is recent evidence, however, from several studies that initiating stabilization of ELBW infants with lower initial F_{IO_2} (0.21–0.3) might increase morbidities and mortality in these infants. The Targeted Oxygenation in the Resuscitation of Premature Infants and Their Developmental Outcome (TO2RPIDO) trial compared F_{IO_2} of 1.0 versus 0.21 during DR resuscitation of preterm infants less than 32 weeks' gestation targeting for Sp_{O_2} 65% to 95% up to 5 minutes and 85% to 95% until admission. The study endpoints were mortality and neurodevelopmental outcome at 2 years of corrected age; however, the trail was closed prematurely due to slow enrollment. In 2015, Oei and colleagues reported that mortality was 16.2% versus 6% in the 0.21 versus the 1.0 F_{IO_2} group ($P = .013$), but only in a subgroup of babies less than 29 weeks' gestation.[57] In 2006 the Canadian Neonatal Resuscitation Program recommended use of either room air or an intermediate concentration of oxygen (eg, 0.3–0.4 F_{IO_2}) in preterm infants and to adjust F_{IO_2} according to Sp_{O_2} values. Rabi and colleagues[58] compared pre-epochs (use of 1.0 F_{IO_2}) and post-epochs (titration of F_{IO_2}) epochs on the effects on neonatal outcomes. The adjusted odds ratio (AOR) for the primary outcome of severe neurologic injury or death was higher in the lower oxygen group (AOR 1.36; 95% CI, 1.11–1.66) than those resuscitated in 100% oxygen (AOR 1.33; 95% CI, 1.04–1.69). These studies[57,58] (published after the current neonatal resuscitation guidelines) suggest that the current recommendations do not reflect the present state of uncertainty regarding best initial F_{IO_2} for ELBW infants and certainly not how to optimally titrate F_{IO_2}.[55]

Practical Aspects

Since the 2010 resuscitation guidelines recommendations, there has been a change in practice in centers using 100% oxygen to initiate resuscitation. Overall, the number of units starting at 100% oxygen decreased from 56.3% (36/64) to 6.3% (4/64) and the rate of those using greater than 40% oxygen decreased from 76.6% (49/64) to 9.4% (6/64).[59] For the resuscitation and stabilization ELBW infants at birth, while waiting for the results from larger, well-designed studies on the comparison of low versus high oxygen concentrations, it seems appropriate to start with 21% to 30% oxygen.

MONITORING DURING NEONATAL TRANSITION

In the NICU, preterm infants are continuously monitored using an array of devices to assess arterial blood gases, heart rate (HR), oxygen saturation, end-tidal carbon dioxide, and respiratory functions to guide effectiveness of respiratory support. Although these methods are not commonly applied in the DR, there is an increasing interest in monitoring physiologic changes during neonatal transition.[60–64]

Heart Rate and Oxygen Saturation

The oxygen saturation and HR reflect adequate transition of newborn infants in the DR.[4] The pulse oximeter should be placed on the right hand or wrist of the infant to obtain both oxygen saturation and HR measurement.[4] Fetal life occurs in a hypoxic environment and it is well established that preterm preductal oxygen saturation reaches 80% to 90% between 5 minutes and 10 minutes of life.[65] Recently, oxygen

percentiles have been established and are recommended to be used when ELBWs are supported in the DR.[65,66] The targeted oxygen saturation reference ranges for first 10 minutes of neonatal life are encouraged to be incorporated in neonatal resuscitation to titrate the inspired oxygen in the DR. During neonatal resuscitation, an increase in HR is an indicator for effective ventilation.[4,67] The neonatal HR dictates interventions in the DR and quick and reliable detection of HR improves the timeliness of critical interventions.[66] Traditional assessment techniques (eg, palpation of the umbilical cord or auscultation) have been demonstrated to be inaccurate.[68–71] Furthermore, newborn HR increases more slowly in (1) preterm vs term infants,[72] (2) after cesarean vs vaginal birth,[72] and (3) in newborns after maternal analgesia administration and DCC.[65,73] Recently there has been a trend to either use pulse oximetry or ECG to continuously display HR during resuscitation.[74,75] Potential limitations of ECG includes difficult ECG lead placement on the wet skin of ELBW infants, epidermal loss at the site of leads placement, and overestimation of HR in the setting of potential pulseless electric activity, thus delaying needed resuscitation efforts.

Respiratory Function Monitor

Effective mask PPV, however, can be compromised by mask leak, airway obstruction,[76,77] poor technique,[78,79] placing a hat, or drying the infant.[78] In addition, current neonatal resuscitation guidelines recommend a set peak inflation pressure with the assumption this delivers an adequate V_T; however, the V_T has rarely been measured.[80,81] Observational studies in the DR reported a delivered V_T between 0 mL/kg and 30 mL/kg when a set pressure was used.[80,81] This is concerning because animal studies have reported that only 6 inflations with a V_T of 35 mL/kg damage the lungs and alter the response to surfactant.[82]

Using a respiratory function monitor (RFM) can provide real-time assessment of airway pressures, gas flow, V_T, and leak[83] during neonatal training[84] and neonatal resuscitation.[48,83,85–88] Using an RFM in addition to clinical assessment compared with clinical assessment alone has the potential to lower the rate of excessive V_T delivery and reduce DR intubation.[85] Caregivers using an RFM during mask PPV, however, need to be familiar with their device and the waveforms displayed.[83] Further research is needed to determine whether the routine use of an RFM during neonatal training or neonatal resuscitation improves clinical outcomes.

Exhaled Carbon Dioxide

Spo_2 and HR in the DR guide oxygen delivery and respiratory support; these are further supplemented by using an RFM to measure gas flows and V_T. These parameters provide little information, however, on ventilation efficiency and the degree of gas exchange and provide limited feedback to guide clinical care when cardiorespiratory indicators fail to improve. CO_2 is produced in tissues as a byproduct of oxidative metabolism, enters the blood, and is eliminated from the body by diffusion across the alveolar epithelium before it is exhaled in the expired gas. Because CO_2 can only be present in expired gas if gas exchange has commenced, expired CO_2 (ECO_2) levels may indicate the degree and success of lung aeration and gas exchange.[89] Currently, colorimetric CO_2 detectors are commonly used in the DR to assess mask ventilation and to confirm correct endotracheal tube placement.[76,88,90–92] In addition, several observational studies have described the value of using ECO_2 to assess lung aeration and guide respiratory support in the DR.[64,93–95] Recent small trials using ECO_2 to guide respiratory support at birth reported no difference in admission blood gases[96] but a trend to lower rates of BPD.[45]

Near-infrared Spectroscopy

Near-infrared spectroscopy (NIRS) allows noninvasive continuous real-time measurement of the regional tissue oxygen saturation.[97] NIRS can also be used in conjunction with arterial pulse oximetry to calculate the fractional tissue oxygen extraction: the ratio of cerebral oxygen consumption to cerebral oxygen delivery. Pichler and colleagues[98] found spontaneously breathing premature infants (mean gestation 32 weeks) who received DCC had a lower initial (first 3 minutes of life) cerebral saturation whereas Baenziger and colleagues[99] found infants who received DCC had higher cerebral oxygenation levels at 4 hours and 24 hours of life compared with ICC. Similarly, infants who received UCM compared with DCC had a trend toward higher cerebral saturations between 3 hours and 24 hours after birth.[12] Low cerebral tissue oxygen saturation, as measured by NIRS in the first few days of life, has been shown associated with adverse neurologic outcome and IVH.[100] To prevent brain injury, the brain must have adequate tissue oxygen delivery.

Practical Aspects

Currently, Spo_2 monitoring should be used to titrate oxygen delivery during initial stabilization at birth.[4] Furthermore, ECG is the most accurate technique to assess HR at birth.[75] There is some evidence that during PPV an RFM can improve mask ventilation performance,[85] and ECO_2 can assess lung aeration.[89,93,96] In addition, using NIRS has the potential to monitor cerebral oxygen delivery.[101] Further evidence is needed before these techniques can be translated into routine care in the DR.

SURFACTANT DEFICIENCY

ELBW infants are born with structurally immature and surfactant-deficient lungs, which can be translated in difficult to maintain FRC and upper airway patency. Early administration of surfactant treatment, that is, within 2 hours after birth, has been shown to significantly decrease rates of death, air leak, and BPD, but comparing early surfactant in the DR against CPAP at birth, early surfactant does not show any benefit in the outcome with death or BPD.[30] The use of CPAP at birth can counteract the preterm RDS with reduced need of surfactant, ventilator dependence and BPD.[29,102]

Alternative surfactant administration methods (eg, intubation, surfactant, and extubation [INSURE] and minimal invasive surfactant therapy [MIST]) have been advocated to avoid MV after surfactant administration.[103–105] Verder and colleagues[106] first described INSURE in 1992 and reported that the need for subsequent MV after INSURE was significantly reduced to 43% compared with 85% in infants treated with CPAP alone ($P = .003$). A meta-analysis (n = 1551 preterm infant) comparing INSURE + CPAP vs CPAP alone, however, did not show any significant difference in either death or BPD. Side effects of INSURE include (1) CPAP failure rates of 10% to 50%, (2) sedation and analgesia, and (3) need for intubation and MV/PPV until extubation.

More recently, other strategies to administer surfactant by avoiding intubation and MV and/or analgesia/sedation have been described.[103–105] The Kribs technique[103] uses a thin feeding tube placed into the trachea using a Magill forceps during direct laryngoscopy. The procedure is performed without pharmacologic sedation and well tolerated.[103,107,108] Overall, the need for MV was reduced; however, no differences in BPD or death were observed.[103] The MIST technique uses a narrow-bore tracheal catheter during direct laryngoscopy without analgesia while receiving CPAP.[104,105] Observational studies using MIST reported a reduction for the need of MV in 25 weeks' to 28 weeks' gestation compared with controls (32% vs 68%; OR

[95% CI] 0.21, 0.083–0.55), with a similar trend at 29 weeks' gestation to 32 weeks' gestation (22% vs 45%; OR [95% CI] 0.34, 0.11–1.1).[104] Although MIST is feasible and potentially effective, further investigation in clinical trials are needed, particularly in the periviable period.

Practical Aspects

Currently, surfactant administration could be performed either after routine intubation or using the INSURE technique. MIST techniques are currently being investigated in multicenter randomized controlled trials and should only be used in the research environment.

EARLY USE OF CAFFEINE

Methylxanthines as treatment of apnea of prematurity have been demonstrated to reduce rates of BPD,[109] and caffeine improves survival without neurologic impairment or developmental delay at 18 months to 21 months of age.[110] Furthermore, early (prophylactic) use of caffeine is associated with less BPD and patent ductus arteriosus. Katheria and colleagues,[111] in a small feasibility study, randomized preterm infants to receive caffeine in the first 2 hours or 12 hours after birth. Administration of earlier caffeine administration was associated with improved blood pressure and superior vena cava flow without any differences in need for intubation or vasopressors. Currently, there is insufficient evidence to suggest routine caffeine administration in the DR, and larger studies are needed to determine the benefits of prophylactic caffeine.

Practical Aspects

Caffeine should be given to ELBW infants to reduce apnea of prematurity and BPD.[109] The timing of caffeine administration (DR or NICU), however, has not being determined.

SUMMARY

Extremely preterm infants face major challenges at birth due to their immature physiology leading to complicated transition. Multifactorial morbidities and lack of robust long-term neurodevelopmental outcome remain the main barriers in establishing clear well-defined guidelines for neonatal resuscitation for this vulnerable population.

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