

Year in Review 2015: Neonatal Respiratory Care

Sherry E Courtney MD MSc

Introduction

American Heart Association Neonatal Resuscitation Guidelines

Assessment of Heart Rate

Delayed Cord Clamping

Temperature Control

Respiratory Management

Discontinuing or Not Initiating Care

Apgar Score

Off-Label Use of Inhaled Nitric Oxide

Surfactant Administration

Hypo- and Hypercarbia

Automated Control of Oxygen Saturation

Summary

Neonatal respiratory care practices have changed with breathtaking speed in the past few years. It is critical for the respiratory therapist and others caring for neonates to be up to date with current recommendations and evolving care practices. The purpose of this article is to review papers of particular note that were published in 2015 and address important aspects of newborn respiratory care. Key words: neonatal respiratory care, Apgar score, inhaled nitric oxide, surfactant, resuscitation, oxygen saturation [Respir Care 0;0(0):1–•. © 0 Daedalus Enterprises]

Introduction

Many practitioners of neonatal care may remember, not so very long ago, when all babies received 100% oxygen at birth, when all infants with meconium-stained fluid were intubated and suctioned, when all preterm infants were intubated at birth and given surfactant,

when initial CPAP in the delivery room was rarely used, and when all mechanical ventilation for the neonate was pressure-controlled and not volume-targeted. Neonatal respiratory care is changing rapidly, based on new clinical trials and better understanding of physiology. This paper highlights important current changes and some developments on the horizon in respiratory care of the neonate.

Dr Courtney is affiliated with the Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, Arkansas.

Dr Courtney has disclosed relationships with Salter Labs, Pfizer Labs, Radiometer, Discovery Labs, Draeger, Infant Bacterial Therapeutics, United Therapeutics, and Maquet.

Correspondence: Sherry E Courtney MD MSc, Arkansas Children's Hospital, Section of Neonatology, One Children's Way Slot 512-5, Little Rock, AR 72202. E-mail: scourtney@uams.edu.

DOI: 10.4187/respcare.04787

American Heart Association 2015 Consensus on Neonatal Resuscitation

The following are major changes that will affect newborn resuscitation. The full text of these and other changes, as well as a summary of the evidence, is available through the American Heart Association (AHA) and published in *Circulation*,^{1,2} and has been reprinted in several other journals.

Assessment of Heart Rate

Practitioners should be aware that palpation of the umbilical cord as well as auscultation are often inaccurate and underestimate the heart rate. The most accurate measurement of heart rate appears to be by electrocardiography. This does not replace the need for pulse oximetry to assess oxygenation.

Delayed Cord Clamping

Delayed cord clamping for >30 s is reasonable for infants, both term and preterm, who do not require immediate resuscitation at birth. An alternative approach, routine milking of the cord, is not recommended for infants <29 weeks gestation due to lack of evidence at this time. Given that delayed cord clamping may provide benefits for the newborn and is now suggested for preterm infants not requiring immediate resuscitation, delivery services should develop protocols for this intervention and should utilize a multidisciplinary approach.

Temperature Control

Admission temperature of nonasphyxiated infants strongly predicts mortality, and hypothermia is still a problem in many cases. Preterm infants are at especially high risk of morbidity and mortality. The AHA strongly recommends maintenance of infant temperature between 36.5 and 37.5°C.

There are many ways to improve infant temperature control, including increased room temperature, plastic wraps, caps, and thermal mattresses. *For respiratory support, however, one thing that can be done is the use of warmed, humidified gas in the delivery room.* The AHA mentions this in the current guidelines as an intervention that is effective in reducing hypothermia. Articles by te Pas et al³ and Meyer et al⁴ provide data to support this recommendation.

Respiratory Management

Oxygen Administration. The AHA now recommends that for preterm infants of <35 weeks gestation, resuscitation be initiated with oxygen of 21–30%. Oxygen level can then be titrated as needed. Starting resuscitation with a high level of oxygen is not recommended, because there is no benefit. Unnecessary exposure to high levels of oxygen may be detrimental in both term and preterm infants.

Use of CPAP. Nasal CPAP rather than immediate intubation is now recommended for preterm infants who are breathing spontaneously. Practitioners need to remember that a self-inflating bag cannot deliver CPAP, and reliable

end-expiratory pressure may not be achieved even with a PEEP valve. A policy statement on the use of CPAP has recently been issued by the American Academy of Pediatrics (AAP) Committee on Fetus and Newborn.⁵

Since the AAP and the AHA now recommend early use of CPAP, it is my recommendation that all hospitals where deliveries may occur provide a mechanism for nasal CPAP administration.

Sustained Inflations. Sustained inflations have been advocated to establish functional residual capacity in preterm infants. Several trials have evaluated the use of sustained inflation, but length of inflations and peak inspiratory pressures employed vary widely among studies. The AHA does not recommend a sustained inflation of >5 s, but shorter sustained inflations may be considered in individual circumstances. Readers may wish to review the meta-analysis of the randomized trials done to date.⁶ This meta-analysis found that preterm infants treated with sustained inflation required less mechanical ventilation but concluded that further study is needed.

Laryngeal Mask. For infants of ≥34 weeks gestation, a laryngeal mask airway is an alternative to intubation. If intubation is not feasible or is unsuccessful, use of a laryngeal mask airway can be lifesaving and is recommended by the AHA. In my opinion, any institution where deliveries may occur should have laryngeal masks in the delivery room, and their proper use should be regularly reviewed.

Intubation and Tracheal Suctioning in Nonvigorous Infants Born Through Meconium. This is perhaps the biggest change in the Neonatal Resuscitation Program (NRP) recommendations. For years, we have intubated and suctioned infants born with meconium-stained amniotic fluid. In the past, all such babies were intubated; in more recent times, only depressed, nonvigorous infants were intubated and suctioned. Given the total lack of data on the effectiveness of this intervention plus the potential harm of repeated attempts at intubation and possible continued bradycardia and hypoxia, this recommendation has been dropped.

Practitioners must remember that the mouth and nose should still be suctioned as with any resuscitation and that intubation may be appropriate in some circumstances, such as possible plug in the airway. Intubation should be done when appropriate as with any other newborn resuscitation.

Discontinuing or Not Initiating Care

Preterm Infants of <25 Weeks Gestation. This remains a difficult area, with no major changes from the last guideline. However, it is important to point out that not

initiating care and discontinuing care are ethically equivalent; once initiated, care can be withdrawn. Region-specific guidelines and parental involvement are both very important.

Apgar Score of 0 for 10 Minutes. Resuscitation of an infant with no detectable heart rate can sometimes continue for very long periods. An Apgar score of 0 at 10 min strongly predicts death or very poor outcome. The AHA suggests it is reasonable to stop resuscitation at this point. However, it is important to individualize this decision based on available information, such as timing of the insult if known, adequacy of the resuscitation efforts, and family wishes.

Apgar Score

This past year, the AAP published an interesting and informative policy statement on the Apgar score, including a recommendation on use of an expanded Apgar score.⁷

The Apgar score has often been used inappropriately. Clearly, it is not useful to determine the need for resuscitation, because resuscitation must be initiated immediately, during the first “golden minute” of life and before assignment of the 1-min Apgar score. The outcome of a particular infant cannot be predicted by a 5-min Apgar score, and most infants with an Apgar score of <5 at 5 min will develop normally. There is, however, an increased risk of adverse neurologic outcome, as noted in large population studies.^{8–11} A low Apgar score should not be used to diagnose asphyxia, because this diagnosis depends on the documented presence of hypoxia, hypercarbia, and severe metabolic acidosis. Preterm infants may have low Apgar scores because of immaturity. An Apgar of 0 at 10 min, as previously noted, may be useful in deciding whether to continue resuscitation.

A major problem with the Apgar score is that the score assigned to an infant who is not requiring active resuscitation is not the same as the score assigned to an infant who may be requiring oxygen, positive-pressure ventilation, or even chest compressions. The AAP and American Congress of Obstetricians and Gynecologists now recommend the use of an expanded Apgar score, which records the standard Apgar score but in addition reports any resuscitative efforts occurring simultaneously with provision of the Apgar score at 1, 5, 10, 15, and 20 min.

The authors⁷ comment that this expanded score may also be useful for delayed cord clamping, which is now suggested by the AHA, as noted above. The expanded Apgar score sheet provides a comment box to record time of cord clamping or other important events.

Off-Label Use of Inhaled Nitric Oxide

Inhaled nitric oxide (INO) is an important therapy for term and near-term infants with persistent pulmonary hypertension of the neonate. However, its use in infants at <34 weeks gestation is off-label and has not been shown to be effective. In an article published this year by Ellsworth et al,¹² off-label use of INO was shown to be increasing rather than decreasing.

In 2011, the National Institutes of Health released a consensus statement that discouraged the use of INO in preterm infants.¹³ Evidence from most controlled trials as well as from an individual subject data meta-analysis of these trials¹⁴ shows no benefit in reducing morbidity and mortality in these subjects. Ellsworth et al¹² queried data from $>420,000$ subjects and found a 23% increase in use of INO between 2009 and 2013. The authors estimated that the cost to United States health care, if these data apply to all similar infants similarly treated, is about \$153 million.

In an accompanying editorial Finer and Evans¹⁴ point out that INO is not benign and may result in adverse outcomes in infants $<1,000$ g. Since it is true that some infants may have persistent pulmonary hypertension of the neonate even if premature, they recommend limiting INO use to infants whose pulmonary arterial pressure is at or above systemic pressure. They stress that trials focusing on preterm infants with specific conditions associated with pulmonary hypertension are needed.

Current evidence does not support the use of INO in preterm infants in most cases. This therapy is extremely expensive, harmful in some cases, and not helpful in most other circumstances. Respiratory therapists should establish guidelines for their units that are consistent with the current guidelines and recommendations.

Surfactant Administration

Although nasal CPAP is now a cornerstone of respiratory distress syndrome early management, surfactant use is still often needed and can be lifesaving. When and how to give surfactant is still controversial given the current use of early nasal CPAP.

Two recent articles in JAMA Pediatrics explore some current controversies. Isayama et al¹⁶ report a review and meta-analysis of nasal CPAP versus early INSURE (intubate, surfactant, extubate). There were no statistically significant differences in any outcomes, although trends were noted favoring INSURE in chronic lung disease and/or death, chronic lung disease alone, and air leak.

Kribs et al,¹⁷ in the same issue of JAMA Pediatrics, report a randomized trial of nonintubated versus intubated surfactant administration. In this multi-center trial conducted in Germany, >200 infants were randomized to

either conventional intubation and administration of surfactant or less invasive surfactant application. During the less invasive surfactant application, a small catheter was passed between the vocal cords, and the infant was supported on nasal CPAP. Surfactant was administered over about 1–2 min. In this study, infants who received less invasive surfactant application were less frequently intubated and had fewer pneumothoraces, fewer days of ventilation, and less severe intraventricular hemorrhage. Survival without severe adverse events was increased in the group with less invasive surfactant application.

In an editorial accompanying these articles, Dargaville¹⁸ points out some of the difficulties in drawing conclusions about the best timing and method for surfactant administration, pending further data. Less invasive surfactant application is one of several alternatives to intubation being currently evaluated, others being surfactant administration by less invasive application and by aerosol.

Perhaps the best approach at present is the one currently stated by the AAP: Early nasal CPAP with subsequent surfactant treatment results in lower rates of bronchopulmonary dysplasia/death than immediate intubation and surfactant. However, if surfactant is needed, early rescue at <2 h of age will decrease mortality, air leak, and chronic lung disease. If intubation is needed, the endotracheal tube should be removed as soon as possible to minimize lung damage.^{5,19}

Hypo- and Hypercarbia

Hypocarbica, hypercarbia, and wide fluctuations in P_{CO_2} levels have been associated in multiple studies^{20–24} with an increased risk of intraventricular hemorrhage, periventricular leukomalacia, and poor neurodevelopmental outcome. Yet another article published in 2015 found this association. Ambalavanan et al,²⁵ in a secondary data analysis of the large SUPPORT trial, found that higher P_{CO_2} was an independent predictor of severe intraventricular hemorrhage or death, bronchopulmonary dysplasia or death, and neurodevelopmental impairment or death.

There is little doubt today that significant variations in P_{CO_2} are associated with significant adverse outcomes. This is due to the effect of P_{CO_2} on cerebral blood flow, with hypocarbica causing cerebral vasoconstriction and hypercarbia causing cerebral vasodilation.

Careful attention to P_{CO_2} is of utmost importance in the critically ill ventilated neonate. Because intermittent arterial or capillary blood gas monitoring is not sufficient to monitor changes in P_{CO_2} levels, I recommend that all such infants receive transcutaneous CO_2 monitoring to help prevent these severe adverse outcomes.

Automated Control of Oxygen Saturations

Computerized control of various respiratory parameters is a reality today, with new innovations constantly being developed. Volume-targeted ventilation is now standard of care. Automated control of oxygen saturations, although still proprietary, is moving into the clinical care arena. van Kaam et al²⁶ randomized 80 preterm infants to saturation target ranges and then, in random sequence, treated the infants with manual or automated oxygen control. The percentage of time in target range was significantly higher when oxygen control was automated. Hypoxemia was consistently reduced, and the number of manual adjustments needed was reduced almost 100%. Other recent studies have reported very similar findings.²⁷

Summary

This review highlights important updates in neonatal respiratory care reported in 2015. Changes in this arena are occurring at breakneck speed. New data are overturning old ways of thinking and old ways of respiratory interventions. Things we thought impossible or futuristic a few years ago are now happening or are on the horizon. Even an artificial placenta is now in animal trials with plans to move into clinical trials within 2–3 years.²⁸

Now, more than ever, it is crucial to stay abreast of changes within our field, for without question changes will happen. It is an exciting time to be involved in the respiratory care of the newborn.

REFERENCES

1. Perlman JM, Wyllie J, Kattwinkel J, Wyckoff MH, Aziz K, Guinsburg R, et al. Part 7: neonatal resuscitation: 2015 international consensus of cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. *Circulation* 2015; 132(16 Suppl 1):S204-S241.
2. Wyckoff MH, Aziz K, Escobedo MB, Kapadia VS, Kattwinkel J, Perlman JM, et al. Part 13: neonatal resuscitation: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2015;132(18 Suppl 2):S543-S560.
3. te Pas AB, Lopriore E, Dito I, Morley CJ, Walther FJ. Humidified and heated air during stabilization at birth improves temperature in preterm infants. *Pediatrics* 2010;125(6):e1427-e1432.
4. Meyer MP, Hou D, Ishrar NN, Dito I, te Pas AB. Initial respiratory support with cold, dry gas versus heated humidified gas and admission temperature of preterm infants. *J Pediatr* 2015;166(2):245-250.e1.
5. Committee on Fetus and Newborn. Respiratory support in preterm infants at birth. *Pediatrics* 2014;133(1):171-174.
6. Schmölzer GM, Kumar M, Aziz K, Pichler G, O'Reilly M, Lista G, Cheung PY. Sustained inflation versus positive pressure ventilation at birth: a systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal* Ed 2015;100(4):F361-F368.

7. American Academy of Pediatrics Committee on Fetus and Newborn, American College of Obstetricians and Gynecologists Committee on Obstetric Practice. The Apgar Score. *Pediatrics* 2015;136(4):819-822.
8. Ehrenstein V. Association of Apgar scores with death and neurologic disability. *Clin Epidemiol* 2009;1:45-53.
9. Moster D, Lie RT, Irgens LM, Bjerkedal T, Markestad T. The association of Apgar score with subsequent death and cerebral palsy: a population-based study in term infants. *J Pediatr* 2001;138(6):798-803.
10. Nelson KB, Ellenberg JH. Apgar scores as predictors of chronic neurologic disability. *Pediatrics* 1981;68(1):36-44.
11. Lie KK, Groholt EK, Eskild A. Association of cerebral palsy with Apgar score in low and normal birthweight infants: population based cohort study. *BMJ* 2010;341:c4990.
12. Ellsworth MA, Harris MN, Carey WA, Spitzer AR, Clark RH. Off-label use of inhaled nitric oxide after release of NIH consensus statement. *Pediatrics* 2015;135(4):643-648.
13. Cole FS, Alleyne C, Barks JD, Boyle RJ, Carroll JL, Dokken D, et al. NIH Consensus Development Conference statement: inhaled nitric oxide therapy for premature infants. *Pediatrics* 2011;127(2):363-369.
14. Askie LM, Ballard RA, Cutter GR, Dani C, Elbourne D, Field D et al. Meta-analysis of preterm patients on inhaled nitric oxide collaboration: inhaled nitric oxide in preterm infants: an individual-patient data meta-analysis of randomized trials. *Pediatrics* 2011;128(4):729-739.
15. Finer NN, Evans N. Inhaled nitric oxide for the preterm infant: evidence versus practice. *Pediatrics* 2015;135(4):754-756.
16. Isayama T, Chai-Adisaksotha C, McDonald SD. Noninvasive ventilation with vs without early surfactant to prevent chronic lung disease in preterm infants: a systematic review and meta-analysis. *JAMA Pediatr* 2015;169(8):731-739.
17. Kribs A, Roll C, Göpel W, Wieg C, Groneck P, Laux R, et al. Nonintubated surfactant application vs conventional therapy in extremely preterm infants. *JAMA Pediatr* 2015;169(8):723-730.
18. Dargaville PA. CPAP, surfactant, or both for the preterm infant: resolving the dilemma. *JAMA Pediatr* 2015;169(8):715-717.
19. Polin RA, Carlo WA, Committee on the Fetus and Newborn, American Academy of Pediatrics. Surfactant replacement therapy for preterm and term neonates with respiratory distress. *Pediatrics* 2014;133(1):156-163.
20. Fabres J, Carlo WA, Phillips V, Howard G, Ambalavanan N. Both extremes of arterial carbon dioxide pressure and the magnitude of fluctuations in arterial carbon dioxide pressure are associated with severe intraventricular hemorrhage in preterm infants. *Pediatrics* 2007;119(2):299-305.
21. Kaiser JR, Gauss CH, Pont MM, Williams DK. Hypercapnia during the first 3 days of life is associated with severe intraventricular hemorrhage in very low birth weight infants. *J Perinatol* 2006;26(5):279-285.
22. Shankaran S, Langer JC, Kazzi SN, Laptook AR, Walsh M, National Institute of Child Health and Human Development Neonatal Research Network. Cumulative index of exposure to hypoxia and hyperoxia as risk factors for periventricular leukomalacia in low birth weight infants. *Pediatrics* 2006;118(4):1654-1659.
23. McKee LA, Fabres J, Howard G, Peralta-Carcelen M, Carlo WA, Ambalavanan N. PaCO₂ and neurodevelopment in extremely low birth weight infants. *J Pediatr* 2009;155(2):217-221.
24. Pappas A, Shankaran S, Laptook AR, Langer JC, Bara R, Ehrenkranz RA, et al. Hypoxia and adverse outcome in neonatal hypoxic-ischemic encephalopathy. *J Pediatr* 2011;158(5):752-758.
25. Ambalavanan N, Carlo WA, Wragg LA, Das A, Laughon M, Cotten CM, et al. P_aCO₂ in surfactant, positive pressure, and oxygenation randomized trial (SUPPORT). *Arch Dis Child Fetal Neonatal Ed* 2015;100(2):F145-F149.
26. van Kaam AH, Hummler HD, Wilinska M, Swietlinski J, Lal MK, te Pas AB, et al. Automated versus manual oxygen control with different saturation targets and modes of respiratory support in preterm infants. *J Pediatr* 2015;167(3):545-550.e1-2.
27. Waitz M, Schmid MB, Fuchs H, Mendler MR, Dreyhaupt J, Hummler HD. Effects of automated adjustment of the inspired oxygen on fluctuations of arterial and regional cerebral tissue oxygenation in preterm infants with frequent desaturations. *J Pediatr* 2015;166(2):240-244.e1.
28. Flake AW. Extracorporeal support of the premature infant: the artificial placenta/uterus. Presentation at: Hot Topics in Neonatology, Washington DC, December 6-9, 2015.