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The Institute for Johns Hopkins Nursing

eNeonatal Review

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Post-Test

In this issue... Volume 1, Number 10

Our focus this issue is on neonatal resuscitation, and it begins with some sobering facts:

- Of the approximately 100 million babies born annually worldwide, about ten million need some type of resuscitation.
- Worldwide there are 5 million neonatal deaths a year, with 19% due to birth asphyxia.

The aim of resuscitation is to reduce not only neonatal death but also the adverse long term neurodevelopmental sequelae associated with birth asphyxia. The International Liaison Committee on resuscitation and the Neonatal Resuscitation Program have made recommendations based on the best levels of evidence available. These recommendations set the basis for the new NRP Neonatal Resuscitation Textbook published in 2000.

In this month's issue, we address three areas of current interest in neonatal resuscitation:

- Ventilation as the most important feature of neonatal resuscitation;
- The role of resuscitating with room air; and
- Resuscitation of infants born through meconium stained amniotic fluid.

Reviews & Commentary:
Rune Toms, M.D.&
Wally Carlo, M.D.

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COMMENTARY

Effective ventilation is the key to neonatal resuscitation. Ventilation alone will usually result in improvement even in the most depressed neonates. Inflation pressures generated by bag and mask may stimulate Head's paradoxical reflex, which results in inspiratory effort in response to lung inflation. The study by Perlman et al explores the frequency and process of ventilating infants in the delivery room.

Concerns have been raised regarding potential adverse effects of the use of excessive oxygen, in that high concentrations of oxygen may lead to the generation of excess free radicals. These destructive molecules may overwhelm the newborn's natural defense mechanism, increasing the risk for the development of retinopathy of prematurity (ROP) and bronchopulmonary dysplasia (BPD). It is known from animal studies that cerebral perfusion is decreased with hyperoxia, potentially leading to ischemic injury and free radical production. Further, the purine metabolite hypoxanthine - a potential oxygen radical generator and a product of the stimulation of the hypoxanthine-xanthine oxidase system - has been shown to accumulate in body fluids during hypoxia.

Many textbooks as well as the Advisory Statement from the International Liaison Committee on Resuscitation (ILCOR) recommend that resuscitation of the newborn infant be performed with 100% oxygen. However, as some experts in the field have challenged, there is little actual scientific evidence to support this practice. Furthermore, evidence from both animal studies and human trials suggests that room air is as effective as 100% oxygen for neonatal resuscitation. With birth asphyxia and the need for neonatal resuscitation more common in the developing world, where the difficulty of providing 100% oxygen is very often a limiting factor, evidence showing air as effective as oxygen would make it the preferred gas for neonatal resuscitation and likely improve outcomes. The studies by Sauestad et al and Vento et al shed new light on this possibility.

Approximately 10-15% of infants are born through meconium stained amniotic fluids (MSAF). Of these, 5-12% develop meconium aspiration syndrome (MAS). The previous observational studies

that suggested that intratracheal suctioning of meconium stained infants could prevent the development of MAS formed the basis of the current practice of routine intratracheal suctioning of all infants born through thick MSAF. However, these infants are by no means a homogeneous group: many are vigorous and initiate a good respiratory response, whereas others are notably depressed. The studies by Wiswell et al and Vain et al challenge the current recommendations, showing that vigorous infants with MSAF may not need to routinely undergo intratracheal suctioning, as this therapy may not be universally beneficial.

VENTILATION

Perlman JM, Risser R. Cardiopulmonary Resuscitation in the Delivery Room. Archives of Pediatrics and Adolescent Medicine 1995; 149: 20-25

An observational study to determine what percentage of infants received chest compressions and medications as part of resuscitation in the delivery room.

In a large urban hospital in Dallas with 15,000 births annually, the protocol for the treatment of depressed infants was as follows:

- After initial stabilization and evaluation, bag-and-mask ventilation was begun with a flow-inflating bag, using inflating pressures of 25-30 cm H2O with a frequency of 40 to 60 breaths per minute, and was continued for approximately 15 to 30 seconds.
- If the heart rate was at least 100/min and spontaneous respirations were present, positive-pressure ventilation was discontinued.
- If the initial heart rate was less than 80/min and not responding to bag-and-mask ventilation, chest compressions were initiated, with the same or an increase in the inflating pressures.
- If the heart rate remained below 80/min for additional 30 seconds, endotracheal intubation and further positive pressure ventilation with the same or increased pressures was initiated.
- If after 30 seconds of increasing positive pressure ventilation the heart rate remained below 80/min, epinephrine was given (preferably intravenously) at 0.01 to 0.03 mg/Kg and repeated every 3 to 5 minutes if required.
- Resuscitation was stopped when the heart rate increased above 100/min.

Important exceptions to these guidelines were: 1) extremely-low-birth-weight infants with low heart rate, who failed to respond to bag-and-mask ventilation, were intubated before the initiation of chest compressions; and 2) infants with thick meconium, who were flaccid and bradycardic, were immediately intubated and suctioned before bag-and-mask ventilation was initiated.

Of 30,839 infants delivered, only 39 (0.12%) required chest compression and/or epinephrine as part of their resuscitation. However, within this group, 62% were found to have improper initial ventilatory support, and the opening pressures required to expand the lungs at birth varied greatly.

The fear of causing a pneumothorax often prevents clinicians from using higher inflating pressures, even when strongly indicated. The authors conclude that an incremental increase in peak inflating pressures - in conjunction with making a good seal, opening the airway, and proper neck positioning - should be thought of as the initial appropriate therapeutic responses to an infant with persistently low heart rate despite bag and mask ventilation, before initiating chest compressions.

Perlman JM, Risser R. Cardiopulmonary Resuscitation in the Delivery Room. Archives of Pediatrics and Adolescent Medicine 1995; 149: 20-25

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RESUSCITATION WITH ROOM AIR

Saugstad OD, Rootwelt T, Aalen O. Resuscitation of asphyxiated newborn infants with room air or oxygen: An International Controlled Trial: The Resair 2 Study. Pediatrics 1998;102: e1.

Saugstad OD, Ramji S, El-Meneza S, Vento M, Talvik T, Solberg, Rootwelt T, Aalen O. Resuscitation of newborn infants with 21% or 100% oxygen: Follow-up at 18 to 24 months. Pediatrics 2003;112: 296-300

Vento M, Asensi M, Sastre J, Lloret A, Garcia-Sala F, Vina J. Oxidative stress in asphyxiated term infants resuscitated with 100% oxygen. J Pediatr;2003;142:240-246

Three studies address concerns regarding the potential adverse effects of 100% oxygen by evaluating the efficacy of resuscitation with room air.

In the "Resair 2" study, ten centers, most located in developing countries, enrolled 609 newborn infants with asphyxia who weighed 1,000 g or more. Patients were allocated to receive resuscitation with either 100% oxygen or room air. Mortality rates during the first 7 days (12.5% vs. 15.0%) and the presence of hypoxic ischemic encephalopathy grade II or III (16.3% vs. 17.1%) did not differ in the room air versus the 100% oxygen groups. In addition, heart rate, acid base status and oxygen saturations did not differ between the groups. The Room air group had significantly lower PaO2 at 30 minutes after resuscitation (vs. 74 ± 29 vs. 89 ± 42 mm Hg). Apgar scores at one minute were higher in the room air group (5 vs.4). The 100% oxygen group had a significantly higher frequency of very low Apgar (<4)scores: at 1 minute, 44% vs. 32%; at 5 minutes, 32% vs. 25%). However, median Apgar scores at 5 minutes were comparable in the two groups (8 vs. 7). In addition, the room air group had a significantly shorter time to first breath (1.1 vs. 1.5 minutes) and time to first cry (1.6 vs. 2.0 minutes).

Treatment was considered ineffective if the infant developed bradycardia or central cyanosis, (or both) after 90 seconds. Failure rates in the two groups were similar (29.8% vs. 25.7%). As failure to respond to the originally assigned resuscitation gas was common, oxygen was given to all infants who were unresponsive regardless of original treatment assignment. This is important as oxygen was added in 25% of infants randomized to the room air group.

Sixty-six percent of the Resair 2 infants were followed at 18 to 24 months after birth. There was no significant difference in the rates of cerebral palsy, not walking, not talking and "abnormal development" as assigned by the examining pediatrician between groups.

The Vento 2003 trial was a single center randomized controlled trial. In this trial, 151 term neonates with clinical and blood gas changes consistent with asphyxia - apneic, hypotonic, unresponsive to stimuli and bradycardic (heart rate < 80/min) and acidotic (pH ≤ 7.05) - were enrolled. Unlike the trial by Saugstad et al., the intervention was masked with a nurse not involved in the resuscitation, who switched the inhaled gas between 21% and 100% oxygen for resuscitation. Similar to the Resair 2 trial, a shorter time to onset of spontaneous respiration was found in infants resuscitated with room air ($p<.01$). No significant difference in median 5 and 10 minute Apgar scores were found.

The combined results from these trials suggest that infants resuscitated with room air have comparable outcomes to those resuscitated with oxygen. However, there appears to be evidence that room air may actually be superior in resuscitation of the newborn, as pooled analysis of all room air resuscitation trials showed a trend towards lower mortality in the room air group [6% vs. 11%, $p<0.01$, OR 0.57 (95%CI 0.4-0.8)].

Saugstad OD, Rootwelt T, Aalen O. Resuscitation of asphyxiated newborn infants with room air or oxygen: An International Controlled Trial: The Resair 2 Study. Pediatrics 1998;102: e1.

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RESUSCITATION OF MECONIUM STAINED INFANTS

Wiswell TE, Gannon CM, Jacob J, et al. Delivery Room Management of the Apparently Vigorous Meconium-stained Neonate: Results of the Multicenter, International Collaborative Trial. Pediatrics 2000; 105: 1-7

Vain NE, Szyld EG, Prudent LM, Wiswell TE, Aguilar AM, Vivas NI. Oro-and Nasopharyngeal suctioning of Meconium-stained neonates Before Delivery of Their Shoulders Does Not Prevent Meconium Aspiration Syndrome: Results of the international, Multicenter, Randomized Controlled Trial. Pediatric Research 2002; 51: 379A

Two large trials shed new light on the value of intubation and suctioning in preventing MAS.

The objective of the Wiswell et al. trial was to determine whether intubation and suctioning of the apparently vigorous meconium-stained neonate would reduce the incidence of meconium aspiration syndrome (MAS). Meconium-stained infants who were vigorous and spontaneously breathing with heart rate >100 bpm were randomized to tracheal suctioning (1051 infants) or to expectant management (1043 infants) - which consisted of no initial endotracheal suction but with endotracheal suctioning performed if respiratory distress developed to the degree that the clinician found it advisable to intubate and suction. MAS was diagnosed in 62 (3%) of the infants and other respiratory disorders in 87 (4.2%).

The authors concluded that intratracheal suctioning was no better than expectant management for preventing respiratory disease, and that intubation and endotracheal suctioning of vigorous infants should not be performed routinely, as it did not decrease the incidence of MAS.

Intrapartum oro- and naso-pharyngeal suctioning of MSAF has been widely recommended for the prevention of MAS. Vain et al. performed a multicenter trial, randomizing 2514 newborns with MSAF to intrapartum oro- and nasopharyngeal suctioning or to no suction, to assess the effectiveness in the prevention of MAS. Infants in the suction group received intrapartum oro-pharyngeal suction with a catheter followed by bilateral nasopharyngeal suctioning. Thereafter, care was administered following the NRP guidelines. No difference was found in the incidence of MAS (3.8% vs. 4.1%) or the use of mechanical ventilation (1.4% vs. 1.9%) in the non-suction vs. the suction group.

This trial suggests that intrapartum oro- and nasopharyngeal suctioning did not decrease the incidence of MAS or its severity. Outcomes - including mortality, air leaks, and duration of mechanical ventilation, oxygen therapy, or length of hospital stay - were unaffected by intrapartum oro- and nasopharyngeal suctioning. In addition, potential complications such as apnea, cardiac arrhythmias, worsening hypoxia, and delay in resuscitation can occur secondary to oro- and nasopharyngeal suctioning.

Note, however, that the results of this trial have not been published in peer review form and the current NRP recommendations have not been changed.

Wiswell TE, Gannon CM, Jacob J, et al. Delivery Room Management of the Apparently Vigorous Meconium-stained Neonate: Results of the Multicenter, International Collaborative Trial. Pediatrics 2000; 105: 1-7

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REFERENCES AND ADDITIONAL SOURCES OF INFORMATION

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Saugstad OD, Ramjii S, Vento M. Neonatal Mortality is Lower in Depressed Newly Born Infants if Resuscitation is Performed with Ambient Air Instead of Pure Oxygen. A Meta-Analysis Pediatric Research 2003; 53: 376A

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- Evaluate the information presented to develop a more complete understanding of the current research in ventilation, neonatal resuscitation, and the prevention of MAS.
- Demonstrate a more complete understanding of the advantages/disadvantages of oxygen versus room AIR in infant-resuscitation outcomes.
- Use the information presented herein as a basis for decision making in determining resuscitation methods in your clinical practice.

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- Dr. Nogee has indicated a financial relationship of grant/research support with Forest Laboratories and has received an honorarium from Forest Laboratories.
- Dr. Lawson has indicated a financial relationship of grant/research support from the NIH. He also receives financial/ material support from Nature Publishing Group as the Editor of the Journal of Perinatology.

All other faculty have indicated that they have not received financial support for consultation, research, or evaluation, nor have financial interests relevant to this e-Newsletter.

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