

Point of View

NRP 2020: Changes, implications for practice and concerns for developing countries

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Very recently, the American Heart Association updated the guidelines for neonatal resuscitation^{1,2}. The GRADE process was followed for the formulation of recommendations, with updated evidence from recently published studies. In this article, we are discussing the changes made, their implications and concerns when applied to developing countries. The first and important change noted is anticipating the need for resuscitation. While Neonatal Resuscitation Programme (NRP) 2015 recommended team briefing as an optional need, the current guideline gives a strong recommendation favouring it. This recommendation is based on data indicating decreased role of confusion during simulation training, better communication and clinical outcomes, with team briefing.

In umbilical cord management, the previous guidelines had class 2a recommendation for delayed cord clamping (DCC) for preterm and term neonates. NRP 2020 provided stronger evidence (B-R) for DCC in preterm neonates as it has been shown to decrease mortality, need for blood transfusions, and use of medications for hypotension, without increasing postpartum haemorrhage rates. The strength of evidence remained the same. However, the latest Cochrane review published in 2019 was not included in the evidence review. For term neonates, the strength of recommendation was downgraded (2a to 2b), while level of evidence remained the same. An important

caution was made against the use of cord milking in preterm neonates <28 weeks gestational age, as there was no benefit. This was based on *post hoc* analysis of data from a randomised controlled trial (RCT), which found increased rates of severe intraventricular haemorrhage (IVH), but no change in the composite outcome of death or severe IVH³.

The measures to maintain temperature of the neonate has two notable changes. While the recommendation for avoiding hyperthermia (>38°C) was based on expert opinion in NRP 2015, it is now backed up with evidence showing increased mortality and morbidity in very preterm⁴ and very low-birth-weight neonates⁵ (LOE: B-NR). Similarly, while the use of skin-to-skin contact for maintaining normothermia was a measure recommended in resource limited settings in NRP 2015, current guidelines generalize its use in all settings, as additional benefits of increased breastfeeding rates and more stable blood glucose levels were noted with early skin to skin contact. In the section on positive pressure ventilation (PPV), a recommendation was made to limit inspiratory time to 1 second, on observations that inspiratory time in spontaneously breathing neonates was about 0.3 seconds. The guidelines however do not specify the approaches to be adopted to achieve this inspiratory time. A strong recommendation is made against the use of sustained inflations during PPV, as it resulted in significant increase in mortality in the first 2 days of life. This recommendation is based on a meta-analysis⁶ and a large RCT which was prematurely terminated due to adverse neonatal outcomes⁷. It is interesting to note the strength of recommendation and level of evidence is downgraded for using 21-30% oxygen to initiate resuscitation in the preterm neonates. The studies that evaluated the role of oxygen showed most preterm neonates needing resuscitation eventually needed supplemental oxygen and there were no differences in the important outcomes of mortality, neurodevelopmental outcomes and other key neonatal morbidities by using lower oxygen concentration⁸.

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The insertion of umbilical venous catheter is included in the algorithm and this is the only change from NRP 2015 algorithm. In post-resuscitation care, the strength of recommendation for use of therapeutic hypothermia is increased from moderate to strong. This is surprising given the fact that therapeutic hypothermia in low-and-middle income countries is not found to reduce mortality and there was insufficient evidence on the long-term neurological outcomes.

Prolonging the time frame for discontinuation of resuscitative efforts from 10 minutes to 20 minutes is a major modification to NRP 2015. This recommendation is based on limited data from observational and randomized trials, in settings where therapeutic hypothermia is available, where 11% of neonates who attained return of spontaneous circulation (ROSC) after 10 minutes of resuscitation survived without moderate to severe disability². Another important modification is strengthening the recommendation to provide individual or team booster training more frequently than 2 years to individuals who have been trained in neonatal resuscitation (Class 2b to 1). More frequent training was shown to improve procedural skills (especially endotracheal intubation), decrease the use of bag-and-mask ventilation and decrease neonatal mortality at 24 hours of age. Other minor changes that are made to the strength of recommendations and levels of evidence are summarized in Table 1.

Neonatal resuscitation in resource limited settings has various concerns including lack of manpower, inadequate training, high delivery burden and inadequate equipment/material for providing supportive care. The various challenges in implementation of NRP2020 are listed in Table 2.

Need for further research and future directions for NRP

- Use of ECG during neonatal resuscitation is shown to be feasible and beneficial in various research settings. It is time to explore the use of wireless recording methods, so that these wirings do not hinder the process of resuscitation.
- Further research is required on the utility of positive end expiratory pressure (PEEP) use during neonatal resuscitation.
- Further studies are needed on intact cord resuscitation using space efficient resuscitation trolleys. Several studies are ongoing to answer this question¹⁰.
- Models need to be developed to improve cost-effective implementation of blenders, humidifiers, T piece resuscitation and ECG leads in the delivery room.

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Table 1: Summary of changes made to NRP 2015, justification for change and implications for practice

Topic	NRP 2015 guideline	NRP 2020 guideline	Reason/ Justification	Implications for practice
Anticipation of resuscitation need	No recommendation was made. It stated, "As time permits, the leader should conduct a pre resuscitation briefing, identify interventions that may be required, and assign roles and responsibilities to the team members."	When anticipating a high-risk birth, a pre resuscitation team briefing should be completed to identify potential interventions and assign roles and responsibilities Class 1; LOE C-LD	Emerging evidence that briefing before and debriefing after clinical events may lead to improvement in practice and outcomes. The advantages noted were decreased role confusion during simulated neonatal resuscitation and improved teamwork skills by conducting a team briefing and better team communication and clinical outcomes.	Team briefing must be done pre resuscitation for high-risk births.
Umbilical cord management	Delayed cord clamping (DCC) for longer than 30 seconds is reasonable for both term and preterm infants who do not require resuscitation at birth Class 2a, LOE C-LD	Preterm neonate: DCC for longer than 30 seconds is reasonable for preterm infants who do not require resuscitation at birth Class 2a, LOE B-R Term neonate: DCC for longer than 30 seconds is reasonable for term infants who do not require resuscitation at birth Class 2b, LOE: C-LD	The advantages noted were 1. Compared with preterm infants receiving early cord clamping, those receiving DCC were less likely to receive medications for hypotension 2. Among preterm infants not requiring resuscitation, DCC may be associated with higher survival. 3. There was no difference in postpartum haemorrhage rates.	Attempts to delay cord clamping should be done in both preterm and term neonates not needing resuscitation.
Umbilical cord management	We suggest against the routine use of cord milking for infants born at less than 29 weeks of gestation outside of a research setting	For infants <28 weeks, cord milking is not recommended Class 3 NB, LOE B-R	A large multicentre RCT found higher rates of intraventricular haemorrhage with cord milking in preterm babies born at less than 28 weeks' gestational age ³ .	Umbilical cord milking has to be avoided in extremely preterm neonates.
Temperature at Birth	Hyperthermia (>38°C) should be avoided due to the potential associated risks Class 3: Harm, LOE C-EO	Prevention of hyperthermia (>38°C) is reasonable due to an increased risk of adverse outcomes Class 2a, LOE B-NR	Two observational studies ^{4,5} found association between hyperthermia & increased morbidity & mortality in very preterm (moderate quality) and VLBW neonates (very low quality).	Measures to prevent hyperthermia have to be actively employed.
Skin-to-skin care	In resource limited settings, it may be reasonable to nurse such newborns with skin-to-skin contact or kangaroo mother care Class 2b, LOE C-LD	Placing healthy newborn who do not require resuscitation skin-to-skin after birth can be effective in improving breast feeding, temperature control and blood glucose stability Class 2a, LOE B-R	Benefits with early skin-to-skin contact after initial resuscitation: Maintained normothermia in healthy neonates, reduced mortality, improved breastfeeding, shortened length of stay, improved weight gain in preterm and LBW babies and better blood glucose levels	Skin-to-skin care should be strongly encouraged in all settings.
Positive pressure ventilation (PPV) Inspiratory time (Ti)	No recommendation on Ti.	In term and preterm newborns, it is reasonable to initiate PPV with a Ti of 1 second or less Class 2a, LOE C-LD	Term and preterm newly born infants were noted to have an inspiratory time of around 0.3 seconds.	Employ measures to shorten Ti during PPV
Positive pressure ventilation- Sustained lung inflation	No recommendation on sustained inflations	In preterm newborn infants, routine use of sustained inflations to initiate resuscitation is potentially harmful and should not be performed Class 3 H, LOE B-R	Two systematic reviews ^{2,6} in preterm newborns found no significant benefit from sustained lung inflation over PPV. Harm noted with sustained lung inflation was increased mortality in the first 48 hours	Sustained inflation should not be used in preterm neonates needing resuscitation.
Continuous positive airway pressure (CPAP)	Spontaneously breathing preterm infants with respiratory distress may be supported with CPAP initially rather than routine intubation for administering PPV Class 2b, LOE B-R	For spontaneously breathing preterm infants requiring respiratory support immediately after delivery, it is reasonable to use CPAP rather than intubation Class 2a, LOE A	The advantage noted with early CPAP was reduction in the combined outcome of death and bronchopulmonary dysplasia	
Oxygen (O₂) administration	Resuscitation of preterm newborns <35 weeks of gestation should be initiated with low O ₂ (21- 30%), and O ₂ concentration should be titrated to achieve pre-ductal O ₂ saturation approximating interquartile range in healthy term infants after vaginal birth at sea level. Class 1, LOE B-R Initiating resuscitation of preterm newborns with high O ₂ (65% or greater) is not recommended Class 3: No Benefit, LOE B-R	In preterm neonates <35 weeks of gestation receiving respiratory support at birth, it may be reasonable to begin with 21-30% oxygen with subsequent oxygen titration based on pulse oximetry Class 2b, LOE C-LD	A meta-analysis enrolling preterm newborns(8), showed no difference in short-term mortality when respiratory support was started with low compared with high oxygen. In the included studies, low oxygen was generally 21% to 30% and high oxygen was always 60% to 100%. It was also noted that all preterm babies in whom respiratory support was initiated with 21% oxygen (air) required supplemental oxygen to achieve the predetermined oxygen saturation target.	Blended air with 21-30% FiO ₂ may be preferred to higher oxygen concentrations and room air.
Chest compressions	The Neonatal Guidelines Writing Group endorses increasing the O ₂ concentration to 100% whenever chest compressions are provided Class 2a, LOE C-EO	Benefit of 100% O ₂ compared with 21% O ₂ for ventilation during chest compressions uncertain. Reasonable to use higher O ₂ concentrations during chest compressions Class 2b, LOE C-EO	In animals, it was noted that using 100% oxygen compared to air during chest compressions, there was no difference in brain or lung inflammatory markers.	Use oxygen when chest compressions are initiated.
Intravascular access	No mention on vascular access in algorithm	For babies requiring vascular access at the time of delivery, umbilical vein is recommended route. Class 1, LOE C-EO Consider emergency UVC is mentioned in algorithm If umbilical vein not accessible reasonable to use intra-osseous route Class 2b, LOE C-EO	There are no human neonatal studies to support one route over others	
Post-resuscitation care- therapeutic hypothermia	Infants born at >36 weeks of gestation with evolving moderate-to-severe HIE should be offered therapeutic hypothermia under clearly defined protocols Class 2a, LOE A	Infants born at >36 weeks of gestation with evolving moderate-to-severe HIE should be offered therapeutic hypothermia under clearly defined protocols Class 1, LOE A		Therapeutic hypothermia should be provided for neonates >36 weeks with moderate to severe HIE
Withholding and discontinuing resuscitation	We suggest that, in infants with an Apgar score of 0 after 10 minutes of resuscitation, if heart rate remains undetectable, it is reasonable to stop assisted ventilation but decision to continue or discontinue resuscitative efforts must be individualized. Class 2b, LOE C-LD	In newborn babies receiving resuscitation, if there is no heart rate and all the steps of resuscitation have been performed, cessation of resuscitation efforts should be discussed with team and family. A reasonable time frame for change in goals of care is around 20 minutes after birth. Class 2a, LOE C-LD	Evidence from RCTs and observational studies done in settings with therapeutic hypothermia described variable rates of survival without moderate-to-severe disability in babies who achieved ROSC after 10 minutes or more despite continued resuscitation. There was no data on outcomes of resuscitation that extended beyond 20 minutes of age.	Continue neonatal resuscitation till 20 minutes.

Class 1- Strong recommendation, Class 2a- Moderate recommendation, Class 2c- Weak recommendation, Class 3: No benefit- Moderate recommendation, Class 3: Harm- Strong recommendation, Level A- High quality evidence, Level B-R- Moderate quality evidence from randomized trials, Level B-NR- Moderate quality evidence from non-randomized trials, Level C-LD- Limited data, Level C-EO- Expert opinion.

Table 2: Concerns while applying NRP 2020 guidelines to the developing countries

S No	Topic	Potential concerns
1	Oxygen administration	A blender and compressed air source are required for administering 21-30% fraction of inhaled oxygen (FiO ₂). Hence, a blender is recommended for resuscitation of preterm neonates to titrate FiO ₂ for targeting the saturations measured by pulse oximetry (SpO ₂). Procuring blender and air compressor is still a challenge in several parts of the world.
2	Oxygen administration	The NRP recommendation for pulse oximetry with signal extraction technology (SET) is costly and is available only in resource rich settings. This may limit its generalizability to resource limited settings.
3	Positive pressure ventilation	The T-piece resuscitator is not widely available, and most in most settings self-inflatable bag (SIB) is the standard equipment used for PPV during neonatal resuscitation. A recommendation to limit inspiration time (Ti) to less than 1 second may be difficult to measure with either of these, even if it is achieved.
4	Positive pressure ventilation	Laryngeal mask airway (LMA) is an emerging alternative to endotracheal intubation, especially when the personnel are not skilled in intubation. In fact, its use in neonatal resuscitation has been shown to reduce rates of endotracheal intubation, need for NICU admission and duration of ventilation(9). It is prudent to highlight its role for use in resource limited settings.
5	Medications	With limited personnel and resources, direct injection of medications (adrenaline) into the umbilical vein may be explored as an alternate option to administer medications during resuscitation. This can potentially save time required for preparing and inserting umbilical venous catheter.
6	Post-resuscitation care	Use of therapeutic hypothermia (TH) may not be feasible in several units of the developing world, because of resource constraints. A context specific recommendation has to be made for these settings understanding the previous evidence that showed increased mortality when TH is used in resource poor settings.
7	Withholding and discontinuing resuscitation	Prolonging resuscitation to 20 minutes may save some babies, but the later mortality, neurodevelopmental impairments, resource utilization and their impact on the family members (both in short-term and long-term) is to be considered before generalizing this recommendation.