The 2010 Guidelines on Neonatal Resuscitation (AHA, ERC, ILCOR): Similarities and Differences – What Progress Has Been Made since 2005?

Kommentar zu den Reanimationsrichtlinien 2010 für Neugeborene (AHA, ERC und ILCOR)

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Abstract

In 2010, the American Heart Association (AHA), the European Resuscitation Council (ERC) and the International Liaison Committee on Resuscitation (ILCOR) issued new guidelines on newborn resuscitation. The new recommendations include: (1) pulse-oximetry for patient assessment during newborn resuscitation; (2) to start resuscitation of term infants with an FiO_2 of 0.21; (3) cardio-respiratory resuscitation with a 3:1 chest compression/inflation ratio for a heart rate <60 beats/min; (4) regarding infants born from meconium stained amniotic fluid: no recommendation is given to suction the upper airways at the perineum (when the head is born), but it is recommended to inspect the oropharynx and trachea for obstruction and suction the lower airway before inflations are given when the infant is depressed; (5) for birth asphyxia in term or near term infants, to induce hypothermia (33.5–34.5 °C) within 6 h after birth. AHA, ERC and ILCOR used nearly identical literature for their evidence evaluation process. While the AHA and ILCOR guidelines are almost identical, the ERC guidelines differ slightly from the latter with regards to (i) promoting sustained inflations at birth, (ii) promoting a wider range in applied inflations during resuscitation, and (iii) to suction the airways in infants born from meconium stained amniotic fluid, before inflations are given.

Zusammenfassung

Die American Heart Association (AHA), die European Resuscitation Council (ERC) und das International Liaison Committee on Resuscitation (ILCOR) veröffentlichten im Oktober 2010 die aktualisierten Fassungen ihrer jeweiligen Richtlinien für die Reanimation von Neugeborenen. Die neuen Richtlinien beinhalten den Einsatz von (1) Pulsoxymetrie zur Beurteilung des deprimierten Neugeborenen während der Erstversorgung; (2) einem initialen Atemgas ohne O_2-Zumischung (FiO_2 0,21) bei Reifgeborenen; (3) einem kardialen Kompressions- zu Ventilationsverhältnis von 3:1 bei persistierend niedriger Herzfrequenz <60/min; (4) bez. mekoniumhaltigen Fruchtwassers: keine Empfehlung für oder wider das intratracheale Absaugen bei Geburt des Kopfes (am Perineum) und beim deprimierten Kind die Inspektion zum Ausschluss von Verlegung des Orophyarynx und der tieferen Atemwege durch Mekonium sowie ggf. Absaugen dessen, bevor Atemunterstützung gegeben wird; (5) die Abkühlung der Körperkerntemperatur auf 33,5–34,5 °C innerhalb der ersten 6 h bei Geburtsasphyxie reifer oder annähernd reifer Neugeborener. Die AHA, ERC und ILCOR geben annähernd identische Textquellen zur Begründung ihrer Empfehlungen an. Die Empfehlungen der AHA und ILCOR sind annähernd identisch, die ERC-Empfehlungen weichen allerdings geringfügig von diesen beiden ab: Der ERC empfiehlt (i) prolongierte Inspirationszeiten während der ersten Atemhübe, (ii) einen breiteren Zielbereich an Atemfrequenzen in der Wiederbelebung und (iii) das konsequente Absaugen der Atemwege im Falle von mekoniumhaltigem Fruchtwasser.

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Abbreviations

AHA	American Heart Association
CO_2	carbon dioxide
CPAP	continuous positive airway pressure
DR	delivery room
ERC	European Resuscitation Council
ET	endotracheal tube
FIB	flow-inflating bag
FiO_2	fraction of inspired oxygen
GA	gestational age
HIE	hypoxic-ischemic encephalopathy
ILCOR	International Liaison Committee on Resuscitation
IV	intravenous
LOE	level of evidence
NICU	neonatal intensive care unit
O_2	oxygen
SIB	self-inflating bag
SpO_2	oxygen saturation by pulse oximetry
VLBWI	very low birth weight infant (birth weight less than 1 500 g)

"*Expert clinicians and organizations offering recommendations to the clinical community have often erred as a result of not taking sufficient account of the quality of evidence" (G. Guyatt, 2008)* [19].

Background

The American Heart Association (AHA) as well as the European Resuscitation Council (ERC) and the International Liaison Committee on Resuscitation (ILCOR) regularly issue guidelines on resuscitation of newly born infants. In October 2010, 5 years after the last release, the AHA [26], ERC [49] and ILCOR [40,69] have published their latest, updated guidelines on neonatal resuscitation (i.e., resuscitation of preterm and term infants at birth).

With respect to recent evidence on several issues of resuscitation, such as oxygen administration and induced hypothermia following resuscitation, this new version has been eagerly awaited. However, numerous publications from the AHA, the American Academy of Pediatrics (identical to the AHA guidelines), the ERC, and ILCOR differ in certain details.

In this article, we analyze similarities and differences between these guidelines, we discuss the evidence upon which the recommendations are based upon and comment on the most relevant changes from the previous 2005 guidelines. Wherever possible, and following the format of our review on the 2005 resuscitation guidelines [21], we formulate practical suggestions on the implementation of these new guidelines in daily clinical care. We emphasize that the clinical evidence and the authors' recommendations given in this paper only refer to the situation of a depressed newly born infant immediately after birth.

Methods

A concise, internet-based literature search on recommendations on resuscitation, and relevant, up-to-date original research articles on neonatal resuscitation was performed (last completed on 24 Feb. 2011). Search terms for retrieving the resuscitation guidelines included "resuscitation, guideline, and neonate", with a restriction to English language articles in Medline, accessed through PubMed (U.S. National Library of Medicine, National Institutes of Health, USA). The searches for relevant evidence on the various topics of this review were conducted by the authors via PubMed without language restriction. Retrieved studies were classified regarding to their levels of evidence (LOE) (**Table 1**), as described by Hazinski et al. [22].

We analyzed for similarities and differences between the recommendations (**Table 2**) and for the most relevant changes from the 2005 guidelines. When considered necessary and feasible, we comment on the 2010 resuscitation guidelines and cite the corresponding literature, as appropriate.

Results

Four guidelines on newborn resuscitation were issued in October 2010. The guideline publications included in this study are: Kattwinkel et al. for the AHA [26], Richmond et al. for the ERC [49], Perlman et al. [40] and Wyllie et al. for ILCOR [69]. A 4th paper, published by Kattwinkel and Perlman on behalf of the Neonatal Resuscitation Program, was omitted from the review as its content was found to be identical to the AHA guidelines [27].

Authors' summary and comments on particular chapters of the 2010 AHA, ERC and ILCOR recommendations

1. Patient assessment

According to AHA, three characteristics denote the newly born infant likely to need resuscitation at birth: preterm gestation, absence of crying or breathing and poor muscle tone [26]. AHA and ILCOR consider heart rate (HR), as determined by precordial auscultation, the most sensitive parameter to assess vitality [26,40]. Once positive-pressure ventilation (PPV) is started and/or supplementary oxygen (O_2) given, the patient should be continuously monitored regarding the progression of HR, respiratory rate (RR), and the state of oxygenation (optimally determined by peripheral pulse oximetry, SpO_2) [26]. Similarly, the ERC recommends the repeated assessment of heart rate (and breathing to a lesser extent), particularly as indicators of the response to resuscitative efforts, or the need for further actions [49]. The AHA and ILCOR have omitted the assessment of color, while the ERC recognizes that color could be used, for instance, as a clue to diagnose hypovolemia [49] (**Table 2**).

Table 1 Levels of evidence (LOE) for therapeutic interventions.

Level of evidence (LOE)	Type of study
1	Randomized controlled trials (RCTs) (or meta-analyses of RCTs).
2	Studies using concurrent controls without true randomization (e.g., "pseudo"-randomized).
3	Studies using retrospective controls.
4	Studies without a control group (e.g., case series).
5	Studies not directly related to the specific patient/population (e.g., different patient/population, animal models, mechanical models, etc.).

From Hazinski et al. 2010 [22]

Scientific basis of changes/differences and levels of evidence

Bradycardia is a reliable indicator for perinatal stress. Heart rate can be assessed by precordial auscultation, palpation of the umbilical pulse, ECG or pulse oximetry. Several studies prove that the evaluation of HR via a pulse oximetry is superior over palpation of the umbilical pulse or precordial auscultation [64]. Visual assessment of color is a poor indicator of the infant's arterial oxygenation (LOE 3) [38]. Hence, the evaluation of color had been omitted in 2005 from the initial assessment by the AHA and ILCOR guidelines [1].

Authors' suggestions

The authors suggest to fully evaluate the newly born infant, starting by determining HR via auscultation, then measuring HR by pulse oximetry obtained from the right hand/wrist. Pulse oximetry has been proven to be a simple, non-invasive and hands free tool for monitoring the progression of both heart rate and oxygenation. Reliable measurements can be expected approximately 1 min after the sensor has been applied [11] (LOE 4). Newly born infants with signs of cardio-respiratory distress should be monitored with pulse oximetry. The decision to intervene, as well as the intensity of the intervention should be guided by the increase in HR and the peripheral oxygenation measurements.

2. Respiratory support

Sufficient airway management to facilitate lung aeration is pivotal to successful resuscitation. The AHA, ERC and ILCOR statements discuss different resuscitation devices for giving

Table 2 Similarities and differences in AHA, ERC and ILCOR 2010.

Procedure	ILCOR Perlman et al. Circulation, 2010 Wyllie et al. Resuscitation 2010	AHA Kattwinkel et al. Circulation, 2010	ERC Richmond & Wyllie Resuscitation, 2010
Delayed cord clamping	Delay cord clamping for at least 1 min for all babies who need no resuscitation.	Delay cord clamping by 1 min in term and preterm infants.	Delay cord clamping for >1 min for both term and preterm infants.
Initial inflations to establish FRC	Do not give sustained inflations. Use pressures between 20–30(40)cmH_2O, inflate at a rate between 40–60/min.	Do not give sustained inflations. Use pressures between 20–30(40)cmH_2O, inflate at a rate between 40–60/min.	5 initial inflations of 2–3 s duration, followed by 1 s lasting inflations (Ti = 1 s), ventilate at 30–60 inflations/min.
Meconium at birth	The available evidence does not support or refute the routine endotracheal suctioning of depressed infants born through meconium-stained amniotic fluid.	The available evidence does not support or refute the routine endotracheal suctioning of depressed infants born through meconium-stained amniotic fluid.	Do not aspirate meconium from nose or mouth during birth. Inspect and clear airway when baby floppy, clear meconium by suctioning.
Epinephrine (Adrenaline)	First line: 10–30 µg/kg IV for HR ≤60 bpm Higher intravenous doses cannot be recommended and may be harmful. If no IV access→50–100 µg/kg ET.	First line: 10–30 µg/kg IV, 1:10 000 solution (0.1–0.3 mg/ml), for HR ≤60 bpm. If no IV access→50–100 µg/kg ET For ET and IV access: specifies to use 1:10 000 solution (0.1 mg/ml).	First line: 10–30 µg/kg IV for HR ≤60 bpm. Higher intravenous doses cannot be recommended and may be harmful If no IV access→50–100 µg/kg ET.
Sodium bicarbonate (4.2% solution)	Not mentioned	Not mentioned	Use is discouraged during brief CPR. If it is used during prolonged arrests unresponsive to other therapy, it should be given only after adequate ventilation and circulation is established with CPR.
Naloxone	Not recommended	Not recommended	Not mentioned
Volume expansion	Early volume replacement with crystalloid or red cells is indicated for babies with blood loss who are not responding to resuscitation. When blood loss could be occult, a trial of volume administration may be considered in babies who do not respond to resuscitation.	Isotonic crystalloid solution or blood is recommended for volume expansion in the delivery room.	If significant blood loss is suspected or the infant appears to be in shock (pale, poor perfusion, weak pulse) and has not responded adequately to other resuscitative measures, consider giving fluid. In the absence of suitable blood (i. e. irradiated and leucocyte-depleted group O Rh-negative blood), isotonic crystalloid rather than albumin, as a bolus of 10 ml/kg, should be given volume IV may need to be repeated.
Intravenous (IV) glucose	IV glucose infusion should be considered as soon as practical after resuscitation, with the goal of avoiding hypoglycemia. Due to the paucity of data, no specific target glucose concentration range can be identified at present.	IV glucose infusion should be considered as soon as practical after resuscitation, with the goal of avoiding hypoglycemia. Due to the paucity of data, no specific target glucose concentration range can be identified at present.	The range of blood glucose concentration that is associated with the least brain injury following asphyxia and resuscitation cannot be defined based on available evidence. Infants requiring significant resuscitation should be monitored and treated to maintain glucose in the normal range.
Temperature control	Room temperature 26 °C for infants <28 weeks gestation. Head and body should be covered with plastic wrapping in addition to heated mattresses and radiant warmers.	Room temperature 26 °C for VLBWI. Head and body should be covered with plastic wrapping in addition to heated mattresses and radiant warmers.	Room temperature 26 °C for infants <28 weeks gestation. Head and body should be covered with plastic wrapping in addition to heated mattresses and radiant warmers.
Therapeutic hypothermia (HT) (33.5–34.5 °C)	Should be offered to newly born infants >36 weeks with evolving moderate to severe HIE.	Should be offered to newly born infants >36 weeks with evolving moderate to severe HIE.	Should be offered to newly born infants >36 weeks with evolving moderate to severe HIE.

respiratory support: All organizations regard a flow-inflating bag, a self-inflating bag (SIB) (ideally with an attached pressure manometer) or a pressure-limited device (so called T-piece resuscitation devices) as equally suitable [26,40,49,69]. Respiratory support should be started by mask ventilation; endotracheal intubation should be reserved for severely depressed infants. Alternatively, use of a laryngeal mask airway is discussed for infants >2000 g or ≥34 weeks gestation [26,40,49,69]. The AHA comments on the limited reliability of PEEP valves [26]. The goal respiratory rate re-commended by the AHA and ILCOR is 40–60/min [26,40,69], whereas the ERC recommends 30–60 breaths/min [49]. While the AHA and ILCOR do not suggest prolonged inflations [26,40,69], the ERC recommends the provision of 5 inflational breaths of 2–3 s, followed by inflations of 1 s duration [49]. The recommended PIPs are between 20 and 40 cmH_2O, according to the AHA, ERC and ILCOR [26,40,49,69] (**Table 2**).

Scientific basis of changes/differences and levels of evidence

T-piece resuscitation devices, as opposed to FIB and SIB deliver defined positive inspiratory pressures (PIP) and positive end expiratory pressure (PEEP) more accurately than self-inflating bags [7,51] (LOE 5). A T-piece resuscitator, however, requires a continuous flow of gas and therefore offers only limited flexibility. Ongoing studies are comparing clinically relevant outcomes between the different devices. Recently, Dawson et al. found no significant differences in oxygenation by 5 min of life in infants <29 weeks gestation when supported by either a T-piece resuscitator (Neopuff®) or SIB [13]. The PEEP valves' limited reliability were highlighted by various investigators [28,36] (LOE 5). With regards to the length of the initial inflations, there is currently only limited evidence available on prolonged (sustained) inflations [30,31,59]. A study by Lindner compared the use of sustained inflations (15 s) in the delivery room (DR) to intermittent pressure ventilation (60/min) via nasopharyngeal tube as means to avoid endotracheal intubation and ventilation of VLBWI [30]. The study showed no statistically significant difference between the groups [30] (LOE 1). In a retrospective study from 1999, Lindner et al. showed a reduction in BPD rate when sustained inflations were applied in the DR (LOE 3) [31]. A prospective trial by tePas et al. compared sustained inflations to mask ventilation followed by CPAP (standard group). The main outcome was endotracheal intubation rate [59]. The authors found a reduction in intubation rate in the intervention group, but it was a semi-randomized trial as the standard group only received rescue CPAP [59] (LOE 2). The ERC, but not the AHA and ILCOR, advocates five, 2–3 s lasting sustained inflations [49]. However, suggestions for or against such a maneuver or even specific inspiratory times currently lack convincing evidence.

Authors' suggestions

Positive pressure ventilation (PPV) in the DR is best administered by a pressure limited T-piece resuscitator as such devices allow more control of the delivered pressure and tidal volumes [7,51]. In the absence of continuous gas flow in the DR, a SIB must be used, ideally together with a manometer. Until further evidence becomes available, we do not recommend sustained inflations. While applying a PIP range of 20–40 mbar (cm H_2O) seems reasonable for patients born at term, this should be adjusted according to the patients GA and weight by assessing the extent of chest rise and the overall clinical status.

3. Use of O_2 in the delivery room

The most progressive alteration in all the discussed guidelines is their definite statement on preferring air (FiO_2 0.21) over pure O_2 (FiO_2 1.0) as primary gas in the resuscitation of term and near term infants at birth [26,40,49,69]. This is a major change to the 2005 guidelines. Furthermore, pulse oximetry and FiO_2 titration based on SpO_2-normograms, and stratified by GA, mark a turning point in newborn resuscitation at birth [12,34] (LOE 3). For infants <32 weeks GA oxygen blenders should be used, but no recommendations on a specific FiO_2 is given by AHA and ILCOR. The ERC has a slightly different perspective and suggests that "if a blend of oxygen and air is not available" whatever available should be given [49] (**Table 2**).

Scientific basis of changes/differences and levels of evidence

The recommendations for term infants are based on two meta-analyses (LOE 1) [52,58], (see also [20]), proving that a FiO_2 of 0.21 increases the chances of survival after resuscitation while the use of 100% O_2 significantly delays the time to first breath and increases mortality of depressed term or near-term infants [52,58]. The subgroup of preterm infants from the Saugstad meta-analysis suggests improved survival in the preterm infants resuscitated with an FiO_2 of 0.21 [52]. Two randomized, controlled studies of preterm infants <32 weeks GA have addressed the question of respiratory adaptation at birth using different initial concentrations of O_2. Wang et al. investigated a starting FiO_2 of 0.21, but premature infants did not reach the targeted SpO_2 of 85% by 5 min [66]. Vento and colleagues studied a group of patients comparable to those of Wang and succeeded in reaching an SpO_2 of 85% by 10 min of age when starting with an FiO_2 of 0.30 [62] (LOE 1). Both studies had small sample sizes and neither study provided but no neurological longitudinal outcome data was provided. While Wang et al. caution against using a low starting FiO_2 of 0.21, the authors report no negative outcomes from their trial, making it difficult to assess whether a lower starting FiO_2 would indeed be harmful. Vento et al. report that during resuscitation even a short episode of high FiO_2 can lead to an unwanted, persistent increase in SpO_2, which was coupled with raised markers of oxidative stress [62] (LOE 1). The recently published SUPPORT trial [9, 16] investigated two different SpO_2-target levels (85–89% vs. 91–95%) from birth to 36 weeks corrected gestation in VLBWI born between 24^{+0}–27^{+6} weeks gestation [9]. There was a slight increase in mortality amongst individuals from the lower SpO_2 target range group (19.9% vs. 16.2%), just reaching statistical significance ($p=0.04$) [9]. Severe retinopathy occurred less frequently amongst survivors from this group (8.6% vs. 17.9%; $p<0.001$) [9]. In a recent meta-analysis, Saugstad and Aune concluded that a low oxygen saturation approach during the 1st week of life reduces severe retinopathy of prematurity by 50%, and BPD/pulmonary problems by 25% (LOE 1) [52].

Authors' suggestions

Resuscitation of term and near term infants should be started with an FiO_2 of 0.21 (LOE 1); the FiO_2 should be carefully titrated according to the patient's need, as assessed by the progression of the SpO_2 and heart rate. Both are ideally measured by pulse oximetry. Until further data are available for preterm infants, an FiO_2 ≥0.21 may be acceptable. The need for additional oxygen over the course of the first 10 min of life is best judged according to the GA specific SpO_2 centiles [13,34].

4. CO_2 Detectors

The AHA and ILCOR advise to use CO_2-detectors to confirm or refute correct tracheal tube placement [26,40,69]. Likewise, ERC suggest their use during resuscitation [49].

Scientific basis of changes/differences and levels of evidence

CO_2 detectors have only been studied in small trials, and in heterogeneous groups of infants [3,48,50,55]. Garey et al. proved their reliability under low tidal volume conditions (LOE 5) [17]. None of the clinical trials of colorimetric CO_2 detectors were randomized [3] (LOE 3), and were only in part blinded [50] (LOE 2). However, they have shown that the use of CO_2 detectors allows prompt recognition of incorrect tube placement (100% predictive value) [3]. Recently, Schmölzer et al. have compared CO_2 detectors (PediCap®) to respiratory function monitors for assessing correct tube placement. The authors found that during 35 intubation attempts the CO_2 detector failed to change color in 11 (31%), despite the respiratory monitor's flow wave indicated the correct tube position [54].

Authors' suggestions

The number of studies on CO_2 detectors in neonates remains very small and most reports come from retrospective studies. Until more solid evidence proves that their use improves patient outcome, we refrain from recommending CO_2 detectors as part of the routine DR management.

5. Meconium aspiration

According to AHA and ILCOR there is insufficient evidence to recommend a change in the current practice of performing endotracheal suctioning of non-vigorous (depressed) babies with meconium-stained amniotic fluid (MSAF). However, if attempted intubation is prolonged and unsuccessful, bag-mask ventilation needs to be performed, particularly if there is persistent bradycardia [26,40,69]. The ERC has taken a more practical approach, and advises to clear the airway of a floppy infant from meconium before ventilation is attempted [49] (▶ **Table 2**).

Scientific basis of changes/differences and levels of evidence

To date there has only been one large RCT investigating the risk of meconium aspiration syndrome (MAS) and death in non-suctioned infants who are born out of thick, meconium stained amniotic fluid (MSAF) [61] (LOE 1). This trial showed no reduction (but also no increase) in the frequency of MAS or perinatal death after intrapartum suctioning, and hence intrapartum suctioning is no longer recommended [26,40,49,69]. Methodologically, this trial was criticized for its retrospective consent process, and the fact that omitting the intrapartum suctioning was not superior over intrapartum suctioning at the perineum, when the newborn's head was born.

Authors' suggestions

We suggest to continue with the current practice of clearing the airway before PPV is started in any infant, in particular those born from thick, MSAF, until further evidence becomes available, this procedure should be performed. The evidence for or against intrapartum suctioning of infants born out of MSAF remains controversial, and hence, we currently cannot give definite recommendations.

6. Temperature control

AHA, ERC and ILCOR suggest that all infants should be dried immediately after delivery, then head and body should be covered with a warm towel to be protected from excessive temperature loss [26,40,49,69]. A small but important difference is being made with regards to the target groups for additional temperature control: While ILCOR and the ERC define infants <28 weeks GA as candidates for additional warming technique, the AHA broadly defines VLBWI as the target group which should, for instance be cared for in ambient temperature of 26 °C in the DR [29], isolating plastic wrapping/plastic bags, and positioning on an exothermic mattress and under radiant heat [56]. Body temperature needs to be closely monitored due to the risk of hyperthermia [26,40,49,69].

Scientific basis of changes/differences and levels of evidence

The recommendations for wrapping the newborn infant in isolating plastic material, in addition to conventional measures (radiant warmer, heated mattress), refers to solid clinical data [10,63] (LOE 1). Compared to 2005, the newly adopted advice is to prevent inadvertent hyperthermia and hypothermia by combining conventional measures and plastic cover.

Authors' suggestions

We recommend the use of plastic cover only for infants with a GA <28 weeks. In any circumstances, close monitoring of the infant's temperature is mandatory, because both hypothermia and hyperthermia negatively affects neonatal outcome.

7. Induced hypothermia

The guidelines from the AHA, ERC and ILCOR unequivocally advise to offer induced hypothermia to newly born infants born at or near term (AHA ≥36 weeks GA) with evolving moderate to severe hypoxic-ischemic encephalopathy (HIE). Whole body cooling and selective head cooling are both appropriate strategies. Treatment should be consistent with the protocols used in the randomized clinical trials (i.e., begin within 6 h of birth, continue for 72 h after birth at a temperature of 33.5–34.5 °C, and rewarm at a maximum of 0.5 °C per hour, over a minimum of 4 h). Carefully monitor for known adverse effects of cooling, e.g., thrombocytopenia, bradycardic arrhythmia and hypotension [26,40,49,69] (▶ **Table 2**).

Scientific basis of changes/differences and levels of evidence

Cumulative evidence from at least 5 randomized controlled trials shows that for newborn infants ≥36 gestational weeks with evolving moderate to severe hypoxic-ischemic encephalopathy, therapeutic hypothermia (33.5 °–34.5 °C), started within 6 h after birth and given for 72 h, reduces neonatal mortality and neurodevelopmental disability at the age of 18 months (LOE 1) [4,15,18,29,57]. According to Edwards et al., the number needed to treat to achieve an improved combined outcome is nine [14]. Trials have not shown an apparent difference in effect between systemic body cooling or selective head cooling, however, more trial data is available on whole body cooling.

Authors' suggestions

Induced hypothermia should be offered to all term or near term infants with evolving HIE. Inclusion should follow the strict criteria used in published trials. A multidisciplinary approach and longitudinal follow-up is mandatory. Establishing hypothermia networks is considered helpful to collect further data and perform future randomized controlled trials.

8. Drugs and fluids

8.1 Epinephrine

If adequate ventilation and chest compression have failed to increase the heart rate >60 beats/min (bpm), all AHA, ERC and ILCOR recommend to use epinephrine at a dose of 10–30 µg/kg intravenously (IV, route of first choice), i.e. epinephrine 1:10 000 solution (0.1 mg/ml)→0.1 ml/kg IV. If no IV access is established yet and the heart remains <60 bpm, it is reasonable to give epinephrine (adrenaline) at a dose of 50–100 µg/kg via the endotracheal (ET) tube [67, 68] (LOE 4–5) (**Table 2**).

Scientific basis of changes/differences and levels of evidence

No controlled studies have directly compared ET and intravenous administration of epinephrine (adrenaline) in infants at birth with a heart rate <60 bpm. Limited evidence from case series indicates that epinephrine given down the ET tube may restore spontaneous circulation [67] (LOE 4) but that probably higher doses are needed. The AHA, but not ERC and ILCOR guidelines, specifies that the epinephrine solution to be used for ET epinephrine should also be 1:10 000 (0.1 mg/ml). No new data was provided which would explain the omission of these previous ERC and ILCOR recommendations, but admittedly the evidence for these 2005 recommendations was poor.

Authors' suggestions

When faced with persistent bradycardia (heart rate <60 bpm) despite adequate ventilation and chest compressions, use epinephrine (adrenaline) at a dose of 10–30 µg/kg IV (route of first choice, epinephrine 1:10 000 solution (0.1 mg/ml) 0.1–0.3 ml/kg IV). It is reasonable to give epinephrine (adrenaline) at a dose of 50–100 µg/kg ET (LOE 4) when IV access is not available [68]. In the absence of a sufficient IV access, an intra-osseous access may also be used.

8.2 Sodium bicarbonate

The ERC, but not the AHA or ILCOR, mentions sodium bicarbonate for the resuscitation of depressed newborn infants at birth. Its use is discouraged during brief CPR. If sodium bicarbonate is used during prolonged cardiac arrests unresponsive to other therapy, the ERC suggests sodium bicarbonate to be given at a dose of 1–2 mmol/kg (1–2 mEq/kg) by slow IV injection after adequate ventilation and circulation has been established with CPR [49].

Scientific basis of changes/differences and levels of evidence

Administration of sodium bicarbonate during neonatal resuscitation in a randomized controlled trial did not help to improve survival or immediate neurological outcome [32]. There is insufficient evidence to recommend the routine use sodium bicarbonate in the resuscitation of newborn infants at birth [5, 8, 68] (LOE 4).

Authors' suggestions

Due to lack of evidence, sodium bicarbonate may only be considered during prolonged cardiac arrests unresponsive to other therapy and on a compassionate use basis [68], and on a case-by-case basis in the post-resuscitation care of newly born infants [33]. The hyperosmolarity and carbon-dioxide generating properties of sodium bicarbonate may in fact impair myocardial and cerebral function. When sodium bicarbonate is used in the prolonged resuscitation of depressed newborn infants (4.2 % solution; 2–4 ml/kg = 1–2 mmol/kg slowly IV), the health care provider needs to keep in mind that rapid infusions of large volume (and hyperosmolar) solutions have been associated with intraventricular hemorrhage – particularly in premature infants (LOE C ≈ LOE 5) [26].

8.3 Naloxone

AHA and ILCOR do not recommend the use of naloxone for the resuscitation of depressed newborn infants at birth. Naloxone is not mentioned in the 2010 ERC guidelines (**Table 2**).

Scientific basis of changes/differences and levels of evidence

No changes. Naloxone is not recommended due to lack of evidence.

Authors' suggestions

Naloxone should not be used during resuscitation or the post-resuscitation care of depressed newly born infants.

8.4 Volume expansion

The three guidelines (AHA, ERC, ILCOR) differ marginally in the details of their recommendations on volume expansion in the resuscitation of depressed neonates at birth (**Table 2**). ILCOR states: "Early volume replacement with crystalloid or red cells is indicated for babies with blood loss who are not responding to resuscitation. There is insufficient evidence to support the routine use of volume administration in the infant with no blood loss who is refractory to ventilation, chest compressions, and epinephrine. Because blood loss may be occult, a trial of volume administration may be considered in babies who do not respond to resuscitation" [40].

Scientific basis of changes/differences and levels of evidence

An isotonic crystalloid solution or blood is recommended for volume expansion in the DR (LOE C ≈ LOE 5) [26]. The recommended initial dose is 10 mL/kg, which may need to be repeated several times.

Authors' suggestions

Isotonic crystalloid solution or blood (10 mL/kg IV) should be used for the initial IV volume expansion in a depressed newborn infant in the DR with a history or clinical signs of significant hypovolemia, but rarely on an empiric basis. Particularly in premature infants, rapid infusion of large IV volume should be avoided, because rapid infusions of large volumes have been associated with intraventricular hemorrhage (LOE 4) [57].

8.5 Glucose IV infusion

AHA and ILCOR recommend that intravenous glucose infusion should be considered as soon as practical after resuscitation, with the goal of avoiding hypoglycemia (LOE 2) [26, 40]. The ERC states 'Infants who require significant resuscitation should be monitored and treated to maintain glucose in the normal range", which implies that IV glucose should be started as soon as possible, i.e. during resuscitation [49].

Scientific basis of changes/differences and levels of evidence

None. Due to the paucity of data, no specific target glucose concentration range is given in either of the guidelines

[26,40,49,69]. Newborns with lower blood glucose levels have a higher incidence of brain injury and adverse outcomes after a hypoxic-ischemic insult (LOE 4) [69]. Increased glucose levels after hypoxia-ischemia does not appear to have adverse effects in studies of pediatric patients (LOE 5) or in animal studies (LOE 5) and may be protective [26].

Authors' suggestions

We suggest to start by giving a 10% glucose (dextrose) IV solution in the DR as early as possible, and independently from resuscitation status (i.e. start infusion during resuscitation). We recommend to start intravenous glucose at an infusion rate of 5–8 mg/kg/min (=glucose 10% at 3–5 ml/kg/h) in order to avoid hypoglycemia (LOE 5), targeting a blood glucose concentration of 50–120 mg/dl (approximately 3–7 mmol/l). There are, however, no evidence-based normal values for newly born infants [53,65]. For treating severe hypoglycemia in the DR, an IV glucose bolus (glucose 10–20%, 1–2 ml/kg IV), followed by an increased infusion rate and titration according to blood glucose concentration, may be needed. However, we caution to monitor the total daily fluid volume and avoid overhydration.

9. Delayed cord clamping

The AHA and the ERC recommend the use of delayed cord clamping for preterm and term infants ([26,49]. The advice is to delay the clamping of the umbilical cord for at least 1 min [26].

Scientific basis of changes/differences and levels of evidence

For full-term neonates, a recent meta-analysis of delayed cord clamping has shown that delayed clamping of the umbilical cord for a minimum of 2 min following birth yields clinical benefit for the newborn, at the expense of an increased risk of polycythemia [25]. For preterm infants, meta-analyses on the effects of delayed cord clamping (delay between birth and clamping 30–120 s) found a significantly higher hematocrit 4 h after birth, fewer blood transfusions for neonatal anemia or low arterial blood pressure, and less intraventricular hemorrhage compared to infants whose umbilical cords were clamped at birth [45,46]. Alternatively, the umbilical cord of preterm infants can be milked 4 times: This increases neonatal blood volume and blood pressure, as described by Rabe et al. and Hosono et al. [23,45,46].

Authors' suggestions

For term infants, cord clamping may be delayed for 1–2 min. Delayed cord clamping may be of benefit to term infants born in countries with poor maternal nutritional state and/or insufficient postnatal follow-up. However, while delayed cord clamping has been shown to increase hematocrit, it may also be associated with hyperviscosity syndrome and hyperbilirubinemia.

In preterm infants, umbilical cord clamping should be delayed for at least 30 s. From a practical point of view, a time of approx. 45 s may be chosen, however, the recent evidence would support even longer delays of cord clamping [45,46].

10. Ethical considerations

AHA and ERC both recommend withholding resuscitation when GA <23 weeks, birth weight <400 g, anencephaly, trisomy 13 or 18 are present. A GA of 25 weeks or above universally warrants resuscitation. This defines a grey zone where parental desires regarding resuscitation should be supported. ILCOR suggests withholding or discontinuing resuscitative efforts when gestation, birth weight, or congenital anomalies are very likely associated with postnatal death and/or an unacceptably severe disability among the rare survivors [40,69]. In the 2010 edition, the ERC definition of the borderline of viability now follows that of AHA (≥25 weeks GA; unchanged from 2005 to 2010). This is noteworthy because recommendations issued by a number of national European societies define the grey zone either below (22–23 weeks: Austria, Germany) [39,44] or above the ERC range (24–25 weeks: Switzerland, the Netherlands, France) [2,36]. The Italian government has issued guidelines mandating resuscitation for all premature babies regardless of GA and parental consent [41–43], and there are similar provisions in Poland. AHA and ERC have, as many national guidelines [37], based their recommendations on GA. Data from more than 4000 extremely low birth weight infants, however, cared for in hospitals of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network suggest that estimating the chances of survival and intact survival can be substantially improved by taking into account birth weight, sex, multiple pregnancy, and fetal lung maturation, in addition to GA [60]. The better chances for survival and intact survival of extremely preterm girls, as opposed to boys, have been documented in other studies as well [6,35].

Authors' suggestions

When extremely preterm delivery or resuscitation is anticipated, the parental wishes should be obtained after unbiased counseling and their opinions should be respected. Before counseling the parents, it is helpful to estimate the infant's chances of survival and survival without major impairment, based on GA, birth weight, sex, multiple pregnancy, and fetal lung maturation, using both local and published outcome data [60], which may be accessed online [24].

Conclusions

The AHA, ERC and ILCOR 2010 guidelines on neonatal resuscitation sought to incorporate the most recent evidence on issues related to patient assessment, oxygen therapy, non-invasive ventilation, induced hypothermia, and drug therapy. This aim was widely achieved. The AHA, ERC and ILCOR recommendation to start term newborn resuscitation without additional O_2 marks a significant and progressive change, finally acknowledging evidence from 2 comprehensive meta-analyses. Conversely, as no good evidence on the optimal initial O_2-concentration for preterm infants is available at present, the only sound advice given is to start with an FiO_2 greater than 0.21, to measure the preductal SpO_2, and to titrate the FiO_2 according to GA matched normograms, as given in the AHA resuscitation algorithm.

When comparing the AHA, ERC and ILCOR recommendations, we noted differences between these guidelines: The most obvious being the ERC's recommendation for including skin color for the initial assessment of a newly born infant, the use of sustained inflations, and a slower respiratory rate (30–60/min, as opposed to 40–60/min as recommended by the AHA and ILCOR). Because all 2010 guidelines claim to be based on the ILCOR statement, the above named differences may be explained by regional preference. Raupp and McCutcheon have previously addressed trans-atlantic differences in the between the US-American and British interpretation of data and had called for more an intensi-

fied dialogue to settle such differences [47]. For the future, we would welcome a single statement, which should be ratified and endorsed by all three organizations (AHA, ERC, ILCOR), and preferably be published internationally for free online access.

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