Resuscitation in resource-limited settings

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Keywords:
Medical education
Newborn resuscitation
Perinatal mortality
Resource-limited settings
Stillbirth

SUMMARY

Intrapartum-related hypoxia leading to deaths and disabilities continues to be a global challenge, especially in resource-limited settings. Primary prevention during labour is likely to have a significant impact, but secondary prevention with focus on immediate basic stabilization at birth can effectively reduce a large proportion of these adverse outcomes as demonstrated in the resource-rich settings. Infants who fail to initiate and establish spontaneous respirations at birth often respond to early interventions such as drying, stimulation, clearing the airways, as well as bag mask ventilation applied within the first minute after birth. Simple resuscitation education such as ‘Helping Babies Breathe’, which focuses on the very basic steps and pays attention to comprehensive program development with local ownership and accountability, can help transfer competency into clinical practice and lead to sustainable programs impacting neonatal mortality and morbidity.

1. Introduction

In 1994 the International Conference on Population and Development set a number of goals and objectives to be attained by 2015 including universal access to comprehensive reproductive health services with reduction in maternal and perinatal mortality and morbidity [1]. The United Nations Millennium Declaration from 2000 emphasizes many agenda items from the above programme in the eight Millennium Developmental Goals (MDG) [2]. The MDG 4 target of reducing the <5-year-old child mortality by two-thirds from 13.2 million in 1990 to 5 million in 2015 still requires a substantial reduction in neonatal mortality, now accounting for >40% of the total deaths [3–5]. Additionally 1.2 million intrapartum-related stillbirths (uncertainty range: 0.8–2.0 million) are not included in the MDG 4 goals [6]. Many of these may be non-breathing infants with heart activity rather than true stillbirths.

Each year ~136 million babies are born globally. It is estimated that about 90% make the transition from intrauterine to extrauterine life without any intervention [7]. This successful transition is dependent on several factors (e.g. the health of the mother, the pregnancy, and the labor process), and healthy fetuses are likely to tolerate some intrapartum hypoxia remarkably well. However, with severe or sustained lack of oxygen during labor, progression to hypoxic–ischemic injury will result in the birth of a non-breathing baby. Approximately 10% or 13.6 million newborns are delivered with absent or poor respiratory effort and need some degree of support to achieve cardiopulmonary stability [8,9]. It is estimated that 3–6% need assisted positive pressure ventilation, and that <1% require advanced resuscitation including intubation, chest compressions, and medications [8]. However, these estimates are based on five reports [8–12], none of which reflect Sub-Saharan Africa where the burden of perinatal deaths and morbidity is considered to be highest [4,7].

2. Neonatal mortality

Neonatal mortality is defined as death before one month of age (per 1000 live births), and recent global estimates range from 2.9 to 3.6 million deaths per year [4,13–15]. Of these, 50–70% occur within the first day of life [4,16–18], and almost 99% take place in resource-poor settings [4]. The presumed causes of neonatal deaths have remained unchanged over the past decade and include infections (~30%), preterm birth (~30%), and birth asphyxia (~25%) [13,18,19]. Uncertainty surrounds all these estimates due to a paucity of data from low-and middle-income countries and almost a complete lack of reliable vital registration systems from settings where mortality is highest, and lack of data from rural community-based settings. In addition, intrapartum-related deaths are likely underreported or misclassified as fresh stillbirths [7,15,20].

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http://dx.doi.org/10.1016/j.siny.2013.07.001
3. Perinatal mortality

Perinatal mortality is defined as intrapartum-related deaths (fresh stillbirths) and early (one week) neonatal deaths per 1000 live births. We find it irrational not to look at these deaths together, because the causes are usually similar whether the baby dies immediately before delivery (fresh stillbirth) or immediately after delivery (early neonatal death). Each year, intrapartum-related hypoxia (equated with birth asphyxia) is estimated to account for about two million perinatal deaths worldwide including intrapartum (fresh) stillbirths and early neonatal deaths [13,20]. The intrapartum stillbirth rate is estimated to be around 10 per 1000 births [20]. The vast majority of intrapartum-related early neonatal deaths occur within the first week of life and the risk for intrapartum-related death on the first day of life is estimated to be about 11 per 1000 births [20]. An additional one million of the surviving infants develop neurocognitive problems such as cerebral palsy and learning difficulties [21]. The psychological and sociological burdens are difficult to measure.

There are several causes contributing to perinatal mortality and morbidity. Adverse perinatal outcome secondary to intrapartum fetal organ damage due to poor oxygenation may be difficult to distinguish from other conditions including infections and trauma. However, these states often co-occur. The intrapartum fetal hypoxia and ischemia is probably the final common pathway for many intrapartum-related fresh stillbirths and early neonatal deaths, whether the event is obstructed labor, hemorrhage, cord prolapse, pre-/ eclampsia, or maternal infection/sepsis. Depending on the severity and duration of intrapartum hypoxia the baby may die during labor and present as a fresh stillbirth, or be delivered with variable degree of hypoxic–ischemic injury.

Strategies for prevention of adverse perinatal outcome can be divided into three phases: (i) primary prevention of the insult by adequate fetal monitoring and correct use of the partogram coupled with timely obstetric interventions; (ii) secondary prevention after the insult by immediate basic stabilization/resuscitation of the non-breathing baby; (iii) tertiary prevention of complications in the baby by adequate postnatal treatment.

Of the three possible approaches outlined above — primary prevention of the insult — is likely to have the greatest impact on intrapartum-related adverse outcome. The ability to detect the fetus at risk of hypoxia during labor is a key catalyst for subsequent interventions to reduce deaths and improve child health. In a recent series on stillbirths in the Lancet, the presence of skilled care at birth linked with emergency obstetric care were identified as two major components to reduce the number of stillbirths. Interestingly, the necessity or importance of fetal heart rate monitoring to detect the babies at highest risk for either intrapartum stillbirths or intrapartum-related neonatal death was not addressed [6,22]. New evidence from a rural African hospital indicates that abnormal fetal heart rate (<120 or >160 beats/min), routinely detected using a fetal stethoscope, is strongly associated with fresh stillbirths, birth asphyxia, increased need for neonatal bag mask ventilation (BMV), and early neonatal death [23].

Primary prevention is likely to have the greatest impact on intrapartum-related adverse outcome, but is probably the most complex, time-consuming and expensive concern to address. However, secondary prevention with focus on immediate basic stabilization/resuscitation at birth can effectively reduce a large proportion of these deaths [24–28]. Failure to initiate spontaneous respirations at birth in most cases is secondary to intrapartum hypoxia and the state of ‘primary apnea’ (heart rate >60 beats/min with compensated blood pressure). These infants invariably respond fairly promptly to early interventions such as drying, stimulation, clearing the airways as indicated, as well as BMV applied within the first minute after birth (Fig. 1) [24–28].

4. Current resuscitation guidelines and new science

In 2011, the World Health Organization (WHO) published new clinical recommendations on basic newborn stabilization and resuscitation to guide birth attendants in settings with poor human and/or technological resources [29]. The WHO guidelines build on the International Liaison Committee on Resuscitation (ILCOR) evidence-based guidelines on neonatal resuscitation [30]. The 2010 ILCOR guideline for resuscitation of newborns is based on limited research with few human cases and has several knowledge gaps [31]. The current 2010 Consensus on Science and Treatment Recommendations (CoSTR) suggests that about 30–60 s of time following delivery should be allocated to assess spontaneous respiratory and heart activity before starting intermittent positive-pressure ventilation if the baby is not breathing regularly. These assumptions were based on the experimental cardiorespiratory responses described in asphyxiated newborn monkeys in the 1960s [32]. Moreover, there has been a lack of evidence related to simple actions at birth (i.e. drying, stimulation, and suction) that could possibly save many newborn lives in resource-limited settings. Therefore, the WHO recommendations on basic newborn resuscitation have many ‘strong’ recommendations on how to handle a non-breathing baby at birth linked to best evidence [32]. Failure to initiate spontaneous respirations and/or technological resources [29]. The psychological and sociological burdens are difficult to measure.

First, observational data on 5845 human newborn infants from a rural hospital in Tanzania are consistent with the experimental findings in monkeys by Dawes in the 1960s. Of the liveborn babies, 84% initiated spontaneous respirations and did not require any basic stabilization at birth; the majority (93%) started breathing within 30 s, and 99.3% were breathing spontaneously within 1 min after birth [25]. The mean time to spontaneous respirations was 10.2 s (median: 5.0 s). In the same study, observed basic stabilization (i.e. specific stimulation of the back and/or suction) was attempted in 8% of infants who eventually initiated breathing. Another 8% did not respond to stimulation and/or suctioning only, but required BMV before initiating breathing [25]. Thus, the majority of babies with birth asphyxia (i.e. failure to initiate spontaneous respirations and/or 5 min Apgar score <7) were in primary apnea and did respond to early basic stabilization/resuscitation within 4–5 min. More than 90% of the babies accomplished the transition from intrauterine to extraterine environment spontaneously or with the basic steps of stabilization including drying and stimulation to initiate breathing (Figure 1). The data also document a significant relationship between a delay in initiation of BMV and early neonatal death and morbidity. Specifically the risk for early death and morbidity increases 16% for every 30 s delay in initiation of BMV up to 6 min when adjusted for birth weight, gestational age, pregnancy, and labor complications [25]. If intervention is delayed there will be progression to ‘secondary apnea’ (bradycardia <60 beats/min and hypotension with final gasping), and with no intervention there will be progression to death or an ‘apparent fresh stillbirth’ (Figure 1).

Second, studies from Zambia, Tanzania, and Bangladesh suggest that the proportion of neonates in need of immediate basic stabilization (stimulation and/or suction) at birth, in these most vulnerable settings, are higher than estimated global numbers [24–27]. In a cluster randomized controlled trial in Zambia, involving traditional birth attendants and rural home deliveries, 16–21% of babies were stimulated [24]. Data from an unpublished study in Bangladesh, including community settings and district hospitals, reveal that 26–44% of babies cried immediately following birth [27]. An additional 50% of babies, that did not cry immediately,
cried after drying; of those remaining, 30–44% cried after stimulation. The number of babies given BMV did not increase after simple HBB resuscitation training [27]. In Tanzania after HBB training in referral and regional hospitals, an increase in babies being stimulated from 44% to 88% resulted in a decrease in babies being subjected to BMV [26]. These studies demonstrate that simple drying and early stimulation will assist the majority of babies and reduce neonatal deaths [24–27].

Third, the recent publications suggest that the proportion of birth asphyxia-related deaths, in these settings, is much higher than hitherto described. Birth asphyxia has for a long time been estimated to account for ~25% of neonatal mortality worldwide [13,19], but data from Tanzania reveal up to 80% of early deaths related to birth asphyxia [26,33]. This huge discrepancy may be due to the imprecise definitions related to the use of Apgar scores, often used retrospectively as the indicator to identify birth asphyxia [33].

Fourth, delayed cord clamping may be the first step of neonatal resuscitation [34]. Evolving data indicate that cord clamping beyond 30–60 s after birth is of benefit for all infants (i.e. decreased iron deficiency anemia) and especially for preterm infants (i.e. increased hemoglobin concentration and systemic blood pressure, reduction in blood transfusion and intraventricular hemorrhage) [34]. A recent experimental study on term lambs demonstrated that ventilation prior to cord clamp markedly improved cardiovascular stability by increasing pulmonary blood flow before cord clamping [35]. In resource-limited settings delay in cord clamping is all the more important to provide the baby with placental transfusion, and it has been suggested that infants with respiratory difficulty may do better with delay in cord clamping for ≥60 s.

Some of the existing gaps related to newborn resuscitation in resource-limited settings are summarized in Box 1.

5. ‘Utstein formula of survival’[36]

The most up-to-date evidence-based guidelines will not help a single baby, either in resource-limited or high-resourced settings, unless they are translated into clinical practice. The Utstein formula of survival states that patient outcome is a product of medical science, educational efficiency, and implementation (Fig. 2). It is predicted that all factors in the formula contribute equally to patient outcome. Hypothetically, if all the factors are optimal, patient survival would be 100%; \( \frac{1}{1} \times \frac{1}{1} \times \frac{1}{1} = 1 \) [36]. It has been suggested that the best that can be achieved is closer to 67% efficiency. The ILCOR guidelines present current medical evidence, but it is more difficult to educate health care staff to utilize this best available knowledge in patient encounters. Another major factor contributing to the high perinatal mortality is a global lack of providers trained and adequately equipped for immediate neonatal stabilization and/or resuscitation, especially in settings where the burden is highest. A program designed for knowledge translation, ability to implement the knowledge and ongoing attention to quality and monitoring with resources for improvement will start to address the gap.
The educational kit includes an action plan, a culturally adopted stillbirth rates, neonatal mortality, and improve intact survival. The Golden Minute

Box 1
Summary of some existing gaps related to newborn resuscitation in resource-limited settings

<table>
<thead>
<tr>
<th>Cord clamping</th>
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<tbody>
<tr>
<td>Timing of cord clamping</td>
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<tr>
<td>Resuscitation with intact cord</td>
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<tr>
<td>Hyperbilirubinemia with delayed cord clamping</td>
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</tbody>
</table>

Stimulation
- Effect of stimulation
- Best way to stimulate
- Additional stimulation before positive pressure ventilation

Suction
- Suction before positive pressure ventilation
- Meconium management
- Suctioning when chest not rising
- Devices for suctioning

Positive-pressure ventilation
- Best interface for positive pressure ventilation
- Optimal ventilation parameters
- Outcome of non-breathing infants

Education
- Frequency of training
- Retention of skills when used frequently and infrequently
- Training of different levels of health workers
- Role of video recording for training

Operational research
- Effects of guidelines
- How to scale up

Others
- Simple ways to administer blended oxygen
- Thermal management of asphyxiated infant
- Burden of resuscitation

6. Educational programs

HBB is a simulation-based educational program, developed to train large numbers of birth attendants in low-income countries in basic neonatal stabilization/resuscitation [37]. The scientific basis of the HBB curriculum stems from the neonatal evidence evaluation of ILCOR. HBB was developed under the leadership of the American Academy of Pediatrics with input from world experts from multiple countries. HBB attempts to ensure that even a single provider can care for the baby and mother in a timely manner. It focuses on immediate assessment of the baby, temperature support, stimulation to breathe, and BMV, all within ‘The Golden Minute’ [38] after birth. These tenets of neonatal resuscitation coupled with appropriate available equipment should reduce ‘apparent’ fresh stillbirth rates, neonatal mortality, and improve intact survival. The educational kit includes an action plan, a culturally adopted flip-over facilitator guide, and a student workbook. The course material is largely pictorial with simple text. Though aimed at midwives, the curriculum can also be adapted for community health workers and even traditional birth attendants with limited literacy. Supplemental oxygen, intubation, chest compressions, and medications do not enter the algorithm — these interventions or actions are not relevant for most of the babies requiring assistance.

To augment the HBB program, a low-tech, low-cost neonatal simulator (NeoNatalie, Laerdal Medical) for resource-limited settings and an affordable manual resuscitator and a bulb suction (that can be easily cleaned for re-use) have been developed to meet the training and clinical equipment needs. Skills training and simulations using the simulator form the foundation of the course, and participants work in pairs or teams to help one another learn the skills. A formative evaluation of the course, conducted in Pakistan and Kenya, indicates significantly better theoretical knowledge after the course, but no significant improvement in mastery of a technical skill such as BMV [38]. The HBB program was modified based on the formative evaluation before being released. Prior to the evolution of HBB, partners strived to develop different local newborn resuscitation programs. Now, HBB is being implemented in more than 50 countries, and the WHO Essential Newborn Care Course has included HBB as its newborn resuscitation tool [39].

7. Kirkpatrick model for evaluation of educational programs

If we have adequate medical evidence and good educational courses to train health providers, what does it take to translate the acquired knowledge and skills into clinical practice for the benefit of the patient? How can we ensure and sustain necessary changes in the clinical setting over time? There is a universal lack of implementation research — the last factor in the Utstein formula of survival (Fig. 2). Most studies/reviews focus on the evidence of ‘what to do’ — not on ‘what is actually done’ — to understand more about how to close the clinical performance gap.

The Kirkpatrick model for evaluation of training courses was first developed by Donald Kirkpatrick in 1959 and later updated several times, most recently in 2006 [40]. It describes four levels of evaluation (Box 2) that provide a thorough understanding of the effectiveness of a training program and potential needs for improvement. Relevant/practical learning will hopefully transfer into clinical practice (Kirkpatrick level 3) and improve patient outcome (Kirkpatrick level 4). It is very rare that educational programs are evaluated through investigation of levels 3 and 4. Does the teaching/training really change behavior of the staff, and is it beneficial for the patients?

HBB is a practical simulation-based course, and simulation-based training engages providers to synthesize and apply knowledge and tasks according to a scenario, thereby combining theoretical, cognitive, technical, and behavioral skills in a dynamic situation. Sub-studies from Tanzania suggest that a one-day HBB training course is sufficient to improve overall resuscitation performance by providers when tested in simulated scenarios seven months later (Kirkpatrick Level 2), but this improvement was not translated into delivery room management (Kirkpatrick Level 3)

Fig. 2. The Utstein formula of survival [36].

Please cite this article in press as: Ersdal H.L, Singhal N, Resuscitation in resource-limited settings, Seminars in Fetal & Neonatal Medicine (2013), http://dx.doi.org/10.1016/j.siny.2013.07.001
[41] before systematic HBB re-trainings and local mentoring were established, which subsequently resulted in a corresponding decline in perinatal mortality [42].

8. Program for newborn stabilization and resuscitation

These studies point to the need for a consistent program (opposed to a single course) targeting ongoing training and local mentoring to impact clinical management and patient outcome. Fig. 3 presents an overview of factors thought to influence newborn resuscitation at birth. Program-developers may need to be aware of, understand and take into account all these factors if they want to develop a successful program that will improve patient outcome over time. For newborn resuscitation in a resource-limited setting, the single practitioner can make the difference between life and death, and it is important to make the program simple and flexible enough to encounter the great variability in knowledge and skills among practitioners, whether it is an untrained birth attendant, a midwife or a doctor. To be able to learn, the education tool(s) must be tailored to meet the providers’ needs at their current level of competency. Once providers have achieved the desired level of competency, they need the resources and support to be able to utilize their skills whenever and wherever the need arises.

**Box 2**

Kirkpatrick model for evaluating effects of educational courses

- Level 1: Reaction. Participants’ perception of the course.
- Level 2: Learning. Acquired knowledge, improved skills, or changes in self-confidence and attitudes because of the training.
- Level 3: Behavior. Translation of the newly acquired knowledge and skills into daily practice.
- Level 4: Results. The ultimate goal; patient outcome.

**Box 3**

Components of the successful Helping Babies Breathe® (HBB) program for newborn resuscitation in Tanzania [26]

- Implementation body: political/resources
  - Commitment by the Ministry of Health and Social Welfare to the prevention of birth asphyxia and reducing early neonatal mortality nationally
  - Appointment of a paediatrician within the Ministry to oversee the implementation and follow-up when required
  - Steady supply of basic equipment
  - Evidence
  - Optimistic that the HBB program would address the needs
- Educational environment: community/practitioner
  - HBB training was conducted at the sites — in the facilities
  - HBB training was targeted at the midwife, most likely the single provider to stabilize and/or resuscitate a newly born infant
  - Use of the cascade model to continually train new providers and re-train all providers
- Clinical practice environment: social/cultural/team
  - HBB materials, resuscitator and bulb suction left behind for ongoing practice
  - Selection of dedicated HBB midwives given the responsibility of short regular refresher trainings to ensure quality of care and local mentoring
  - Placement of the simulator in the labour room where every provider had to document practice of basic skills including bag mask ventilation regularly
- Monitoring and quality improvement
  - Ongoing data collection and reporting of outcome variables
  - Biannual data overview meetings with midwives from all sites to discuss the process and specific needs

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The importance of the addressed factors for program development is confirmed by the clinical roll-out of the HBB program over two years in Tanzania resulting in a 47% reduction in neonatal mortality and 24% reduction in fresh stillbirths [26]. Several implementation strategies are highlighted in the paper, thought to be important for the success. These strategies are summarized in Box 3 linked with the factors outlined in Fig. 3. We believe all these approaches are important for establishment of local ownership and accountability, transfer of acquired novel competency into clinical practice, and sustainability. In addition, the stepwise method of national HBB implementation in Tanzania was critical to demonstrate that the program worked in the major institutions, and to delineate gaps and pitfalls before moving to a full national roll-out. The Tanzanian model, guided by the Ministry of Health and Social Welfare with great focus on implementation, can serve as a template for other resource-limited countries.

9. Summary

Globally perinatal mortality accounts for an increasing proportion of mortality in children aged <5 years. Current guidelines for resuscitation of newborns are based on limited research with few cases and have several knowledge gaps. Nonetheless, some recent studies from resource-limited settings where the burden of deaths is highest document the importance of fetal heart rate monitoring coupled with immediate basic actions at birth. ‘The three delays model’ described for maternal ill-health is applicable to adverse perinatal outcomes: (i) delay in recognizing fetal hypoxia, (ii) delay in actions to accelerate delivery, and (iii) delay in basic stabilization at birth. Each one of these delays should be systematically addressed to give the most recent citizens of the world a chance of morbidity-free survival. The third delay can be addressed by simple steps at birth such as drying, keeping baby warm, immediate stimulation, suction and/or BMV. These actions are proven effective and, if implemented properly as a resuscitation program where births take place, will prevent a large proportion of perinatal deaths worldwide and likely reduce the huge burden of ill-health.

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Please cite this article in press as: Ersdal HL, Singhal N, Resuscitation in resource-limited settings, Seminars in Fetal & Neonatal Medicine (2013), 1–6.