Clinical paper

Early initiation of basic resuscitation interventions including face mask ventilation may reduce birth asphyxia related mortality in low-income countries: A prospective descriptive observational study

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Aim of the study: Early initiation of basic resuscitation interventions within 60 s in apneic newborn infants is thought to be essential in preventing progression to circulatory collapse based on experimental cardiorespiratory responses to asphyxia. The objectives were to describe normal transitional respiratory adaption at birth and to assess the importance of initiating basic resuscitation within the first minutes after birth as it relates to neonatal outcome.

Methods: This is an observational study of neonatal respiratory adaptation at birth in a rural hospital in Tanzania. Research assistants (n = 14) monitored every newborn infant delivery and the response of birth attendants to a depressed baby. Time to initiation of spontaneous respirations or time to onset of breathing following stimulation/suctioning, or face mask ventilation (FMV) in apneic infants, and duration of FMV were recorded.

Results: 5845 infants were born; 5689 were liveborn, among these 4769(84%) initiated spontaneous respirations; 93% in ≤30 s and 99% in ≤60 s. Basic resuscitation (stimulation, suction, and/or FMV) was attempted in 920/5689(16.0%); of these 459(49.9%) received FMV. Outcomes included normal n = 5613(96.0%), neonatal deaths n = 56(1.0%), admitted neonatal area n = 20(0.3%), and stillbirths n = 156(2.7%). The risk for death or prolonged admission increases 16% for every 30 s delay in initiating FMV up to six minutes (p = 0.045) and 6% for every minute of applied FMV (p = 0.001).

Conclusions: The majority of lifeless babies were in primary apnea and responded to stimulation/suctioning and/or FMV. Infants who required FMV were more likely to die particularly when ventilation was delayed or prolonged.

Abbreviations: BPM, beats per minute; BW, birth weight; CS, cesarean section; FHR, fetal heart rate; FMV, face mask ventilation; GA, gestational age; HLH, Haydom Lutheran Hospital.

1 A Spanish translated version of the summary of this article appears as Appendix in the final online version at doi:10.1016/j.resuscitation.2011.12.011.

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1. Introduction

Each year approximately 136 million babies are born globally. It is estimated that about 90% make the transition from intraterine to extraterine life without any intervention.1–3 The remaining ten per cent or 13.6 million newborns are delivered with absent or poor respiratory effort and need some degree of support to achieve cardiopulmonary stability. Between three to six per cent need assisted positive pressure ventilation, and less than one per cent require advanced resuscitation including intubation, chest compressions, and medications.2 However, these estimates are based on five reports,2–6 none of which reflect Sub-Sahara Africa where the burden of perinatal deaths and morbidity is considered to be highest.7

Current International Guidelines on Newborn Resuscitation suggest about 30–60 s of time following delivery should be
allocated to assess spontaneous respiratory and heart activity before initiating intermittent positive-pressure ventilation if indicated. Failure to initiate spontaneous respirations at birth in most cases is thought to be secondary to primary apnea, and the infant should respond fairly promptly to early intervention, i.e. drying, stimulation, clearing the airways as indicated, as well as face mask ventilation (FMV) applied within the first minute. Delaying basic resuscitation in apneic infants is thought to result in a progressive decrease in heart rate and blood pressure and eventual death and/or brain injury in those who may eventually start gasping and/or breathing (frequently called “birth asphyxia”), based on the cardio-respiratory responses described in asphyxiated newborn monkeys (Fig. 1). However, the definition of “birth asphyxia” is imprecise. In low-income countries it has been defined as a failure to initiate spontaneous regular respirations after birth and/or a 5 min Apgar score ≤7. This is distinct from the definition in high-income countries which is more comprehensive and includes biochemical evidence of interruption of placental blood flow with a cord arterial pH < 7.00; a distinctive marker of severe acidemia and the need for resuscitation in the delivery room as well as a low 10 min Apgar score. The use of more precise terms to describe “birth asphyxia” is advocated in several recent papers. Irrespective of definition, defining transitional changes at birth is critical towards understanding the problem of intrapartum-related hypoxia and the importance of basic interventions in the first minutes after birth.

Global estimates on immediate postpartum neonatal needs and interventions are uncertain due to a paucity of data from low- and middle-income countries and almost a complete lack of data from rural community-based settings. Haydom Lutheran Hospital (HLH) is located in rural Northern Tanzania, 300 km from the nearest urban centre, with a poor rural population in the catchment area. It is the referral hospital for approximately 500,000 people, while the greater reference area covers over two million people. HLH provides comprehensive emergency obstetric and basic emergency newborn care. Midwives are the primary providers at most deliveries as well as the initiators of neonatal resuscitation when indicated, with doctors on 24 h backup call. The midwives are trained in basic resuscitative actions (stimulation, mouth suctioning, and providing face mask ventilation when indicated) during nursing school and sporadically re-trained by doctors at HLH. Following birth, infants requiring more than routine care are triaged to a neonatal area; a ten square meter room located within the labour ward, with the capability of administering oxygen, use of wall suction, and providing intravenous fluids and antibiotics. No mechanical ventilation support device is available, thus if required, respiratory support is provided with a self-inflating bag. The infants who are admitted to this area are cared for by family members and labour staff.

The objectives of this study were to define the normal transitional respiratory adaption at birth, to describe interventions performed by birth attendants in the delivery room with ensuing short-term outcomes of the newborns at 24 h, and to assess the importance of the “Golden Minute” after birth as it relates to early neonatal outcome.

2. Methods

This is an ongoing descriptive observational study initiated in August of 2009 at HLH; a rural referral hospital in Northern Tanzania. Research assistants (observers) are continuously present in the labour ward to observe the routine practice of health care providers in the delivery room as well as in the neonatal area through the initial 24 postnatal hours. The observers work in three shifts over 24 h. Three observers cover each shift; two are always located in the labour ward or in the theatre; one in the adjacent neonatal area. Altogether 14 local women have been trained. Observations are timed using a stop watch, and the findings are recorded on a data collection form immediately following the delivery. The research assistants also review the partograms that are filled out by the midwives.

The following information was recorded:

1. antenatal information: antenatal care, pregnancy complications, and maternal infections (i.e. non, uterine, malaria, HIV, sepsis, or other);
2. labour information: fetal presentation (i.e. cephalic, breech, shoulder dystocia, transverse, or other), labour complication (i.e. prolonged labour, obstructed labour, preeclampsia, eclampsia, uterine rupture, haemorrhage, cord prolapse, CS, and vacuum extraction), FHR (normal was defined as 120–160 BPM, abnormal as < 120 or > 160 BPM, not detected, or not measured), and mode of delivery (i.e. spontaneous vaginal delivery, CS, assisted breech delivery, and vacuum extraction);
3. neonatal information: transitional newborn adaption including time intervals from birth to initiation of spontaneous respirations and cord clamping, gender, BW, GA, and Apgar scores at one and five minutes;
4. interventions in the delivery room i.e. stimulation, suction ± FMV with a self-inflating bag, time interval to initiation of FMV, as well as the time interval from initiation of FMV to the onset of spontaneous breathing or death, and the presence or absence of any newborn heart activity;
5. perinatal outcome at 24 h postpartum categorized as either normal, admitted to the designated neonatal area, death within 24 h, or stillbirths (macerated/antepartum or fresh/intrapartum).

| $P_{CO_2}$ | 45 | 100 | 150 | 200 | 40 |
| pH         | 7.3 | 7.0 | 6.8 | 6.75 | 7.1 |

![Fig. 1. Cardio-respiratory changes in the asphyxiated monkey over time. Adapted from Ref. [10].](image-url)
GA was based on self-report of the last menstrual period and distance from symphysis pubis to the fundus. Normal term GA at HLH is routinely defined as 36 weeks.

Prematurity was defined as a GA < 36 weeks.

Low birth weight was defined as BW < 3rd centile for GA.

Birth asphyxia was defined as a failure to initiate spontaneous respirations and/or 5 min Apgar score < 7.

Normal was defined as survival > 24 h without any detected difficulties.

Fresh/intrapartum stillbirth was defined as an Apgar score = 0 at both 1 and 5 min with intact skin and suspected death during labour/delivery.

Macerated/antepartum stillbirth was defined as an Apgar score = 0 at both 1 and 5 min with macerated skin and suspected death before start of labour.

2.1. Data management at HLH

The research assistants are continuously supervised and retrained by the local research manager (EM) who reviews the data collection forms on a daily basis for quality control issues including missing information or potential errors. The data are double entered in EpiData 3.1 by two different people. Random crosschecks of the entered data are undertaken intermittently, with double data extraction and data entry of all cases. If there is any discrepancy between the two entered databases, the data entering individuals recheck the original data together and correct where necessary. For this report the data collection was from August of 2009 through October of 2010.

2.2. Statistical analysis

Statistical analysis has been performed using Statistical Package for Social Sciences (SPSS) 15 and 17 and includes descriptive statistics, chi-square calculations, independent-samples t-tests, and multiple logistic modelling. All data are presented as mean ± standard deviation unless as otherwise stated.

2.3. Ethical considerations

The Regional Committee for Medical and Health Research Ethics, Western Norway (REK West) consider the project – reference number 2009/302 – to be an evaluation program among certified health care workers. Formal approval from Norwegian ethical committee is thus not required. The National Institute for Medical Research in Tanzania has approved the ongoing study.

Table 1
Perinatal outcome 24 h after birth as normal, admitted neonatal area, death, stillbirth (SB) fresh, and stillbirth (SB) macerated with related characteristics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Normal n = 5613</th>
<th>Admitted n = 20</th>
<th>Death n = 56</th>
<th>SB Fresh n = 93</th>
<th>SB Macerated n = 63</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g)</td>
<td>3159 ± 482</td>
<td>2812 ± 648</td>
<td>2958 ± 801</td>
<td>2899 ± 721</td>
<td>–</td>
</tr>
<tr>
<td>Gestational age (w)</td>
<td>36.6 ± 1.5</td>
<td>35.4 ± 2.7</td>
<td>35.0 ± 2.9</td>
<td>36.1 ± 2.4</td>
<td>35.1 ± 3.3</td>
</tr>
<tr>
<td>Female</td>
<td>2656 (47%)</td>
<td>6 (30%)</td>
<td>22 (39%)</td>
<td>40 (44%)</td>
<td>34 (54%)</td>
</tr>
<tr>
<td>Male</td>
<td>2952 (53%)</td>
<td>14 (70%)</td>
<td>34 (61%)</td>
<td>52 (56%)</td>
<td>29 (46%)</td>
</tr>
<tr>
<td>Time Birth – CC sec</td>
<td>49.5 ± 37.7</td>
<td>30.3 ± 24.9</td>
<td>30.1 ± 27.2</td>
<td>28.6 ± 23.6</td>
<td>–</td>
</tr>
<tr>
<td>Time Birth – SR sec</td>
<td>10.2 ± 4.9</td>
<td>6.2 ± 4.3</td>
<td>21.6 ± 18.3</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Resuscitation</td>
<td>857 (15%)</td>
<td>15 (75%)</td>
<td>47 (84%)</td>
<td>22 (24%)</td>
<td>–</td>
</tr>
<tr>
<td>Stimulation</td>
<td>830 (15%)</td>
<td>15 (75%)</td>
<td>46 (82%)</td>
<td>19 (20%)</td>
<td>–</td>
</tr>
<tr>
<td>Suction</td>
<td>646 (11.5%)</td>
<td>14 (70%)</td>
<td>47 (84%)</td>
<td>21 (23%)</td>
<td>–</td>
</tr>
<tr>
<td>FMV</td>
<td>399 (7%)</td>
<td>14 (70%)</td>
<td>45 (80%)</td>
<td>21 (23%)</td>
<td>–</td>
</tr>
<tr>
<td>Time Birth – Start of FMV sec</td>
<td>79 ± 55</td>
<td>115 ± 138</td>
<td>96 ± 76</td>
<td>66 ± 40</td>
<td>–</td>
</tr>
<tr>
<td>Duration of FMV in sec</td>
<td>352 ± 511</td>
<td>543 ± 596</td>
<td>2027 ± 4025</td>
<td>757 ± 710</td>
<td>–</td>
</tr>
</tbody>
</table>

SB = stillbirth, g = grams, w = weeks, CC = cord clamping, sec = seconds, SR = spontaneous respirations, FMV = face mask ventilation.

1 Infants who died versus normal (p = 0.0005).

2 Time to initiation of spontaneous respiration was delayed in infants who died compared to normal infants (p = 0.03).

3 Duration of applied FMV was longer in infants who died compared to normal infants (p = 0.004).

3. Results

During the 14 months of the observational period, 5845 newborns were born and evaluated. Of these 5689 infants (97.3%) were liveborn; 56 infants (0.9%) (9 per 1000 live births) died within 24 h and 20 infants (0.5%) remained in the neonatal area at 24 h. Infants who died were of lesser BW (p < 0.0005) and GA (p < 0.0005) as compared to normal infants (Table 1). There were 156 (2.7%) stillborns of whom 93 (1.6%) were categorized as fresh/intrapartum (16 per 1000 births) and 63 (1.1%) as macerated/antepartum.

3.1. Normal transitional respiratory adaption

Of the liveborn babies 4769 (83.8%) initiated spontaneous respirations and did not require any intervention (Fig. 2). The majority i.e. 4435 (93%) started breathing within 30 s, and 4735 (99.3%), were breathing spontaneously within one minute after birth. Five babies initiated spontaneous respirations between two and three minutes, one between three and four minutes, and three after four minutes; they were all classified as normal at 24 h. The mean time to spontaneous respirations was 10.2 ± 15.0 s (median 5.0 s) (Table 1). The outcome was as follows: 4755 infants (99.7%) were classified as normal at 24 h, nine (0.2%) died, and five (0.1%) remained in the neonatal area at 24 h (Fig. 2). The time to initiate spontaneous respirations was delayed among newborns who died as compared to those with normal outcome (p = 0.03) (Table 1).

3.2. Respiratory responses to basic resuscitation

Overall, basic resuscitation, i.e. stimulation, suction ± FMV was attempted in 942/5845 (16.1%) infants; 22 of the newborns were fresh/intrapartum stillborns in whom stimulation/suction and FMV were initiated due to uncertainty about heart activity (Fig. 2). Of the remaining 920 infants, approximately 50% (n = 461) responded by breathing after stimulation and/or suctioning only, and the remaining infants (n = 459) received FMV in addition to stimulation and/or suctioning (Table 1 and Fig. 2).

Among the babies that started breathing following stimulation and/or suctioning 436/461 (95%) responded within four minutes of birth, and 25 began breathing after four minutes. Overall in the group who received stimulation/suctioning (Fig. 2), two newborn died, one was still admitted, and the rest were classified as normal at 24 h. Among infants who required FMV the majority i.e. 447/459 (97%) were ventilated within four minutes after birth. In 12 babies FMV was initiated after four minutes; the outcome in these infants was normal (n = 7), death (n = 4), and seizures (n = 1).
Of the 459 infants who received FMV 45 (9.8%) died (Fig. 2). Fifteen (33%) were never able to establish spontaneous regular respirations; therefore ventilation was discontinued after a median time of 23 min. The remaining 30 babies (67%) initiated spontaneous respirations in response to FMV before they died. Of the survivors, 400 were normal while 14 remained in the neonatal area at 24 h including five with seizures (Fig. 2). Thus infants who died i.e. 45/56 (80%) and those admitted to the neonatal area, i.e. 14/20 (70%) were more likely to receive FMV as compared to infants with a normal outcome, i.e. 399/5612 (7%) (OR = 42; 95%CI: 25–72, p ≤ 0.0005) (Table 1). The mean time from birth to application of FMV was delayed in infants who died or who were admitted to the neonatal area (100 ± 92 s) as opposed to those infants with normal outcome (79 ± 55 s) (p = 0.035). This risk for death and morbidity increases 16% for every 30 s delay in initiation of FMV up to six minutes (OR = 1.005; 95%CI: 1.000–1.010, p = 0.045) when adjusted for BW, GA, pregnancy, and labour complications.

The mean duration of FMV administration was 534 ± 1411 s (median time 248 s or approximately four minutes). Only 6/459 newborns (1.3%) were ventilated for less than one minute. The mean duration of FMV was longer in infants who died or who were admitted to the neonatal area (1694 ± 3601 s) as opposed to those infants with normal outcome (352 ± 511 s) (p = 0.003). More specifically, the likelihood for death increased when the duration of FMV was greater than four minutes, i.e. 34/226 as compared to 10/227 when the duration of FMV was less than four minutes (p = 0.0001). In 6/459 cases (1.3%) the duration of FMV was not specified. By logistic modelling the risk for death and morbidity increases six per cent for every minute of FMV (OR = 1.001; 95%CI: 1.000–1.001, p = 0.001). Pregnancy complications, labour complications, BW, GA, and time to initiation of FMV did not influence this risk when analysed by multiple logistic regression.

4. Discussion

The data in this report for the first time describe the natural transitional respiratory adaption of newborns delivered in a rural setting in a low-income country, and the population of newborns needing basic stabilization/resuscitation in the delivery room. Thus 84% initiated spontaneous respirations within the “Golden Minute SM”, with an additional 15% responding to stimulation/suctioning alone or with FMV by initiating breathing. This proportion of newborns in need of basic resuscitative interventions is much higher than estimated global numbers, but comparable to recent findings obtained from a district setting in Zambia.

An important observation is that death was significantly more likely to occur in infants who were administered FMV with almost ten per cent mortality noted in this group. Moreover, there was a significant relationship between a delay in the initiation of FMV and admission to the neonatal area and/or death. Specifically the risk for death and morbidity increases 16% for every 30 s delay in initiation of FMV up to six minutes, and more than two thirds of the deaths occurred when ventilation was administered beyond four minutes. The association between delayed FMV and adverse neonatal outcome was found after multiple logistic modelling and adjusted for BW, GA, pregnancy, and labour complications. Nevertheless, other potential confounding factors, i.e. severe fetal acidemia, might have influenced this association. The reasons for the delay in initiating FMV in some infants is unclear, but may reflect a gradual learning curve of some of the single providers to first manage a depressed baby rather than the mother.

The cardio-respiratory responses to asphyxia has been characterized in the newborn monkey (Fig. 1). Thus during the initial minute/s with apnea heart rate is greater than 60 beats per minute and blood pressure is still compensated – a state referred to as primary apnea. With intervention at this stage, and relief of the asphyxial process, there is an immediate increase in heart rate and blood pressure with initiation of spontaneous respirations. However, if there are no interventions and the asphyxial process is allowed to continue there is progressive bradycardia and hypotension with final gasping (after approximately four to five minutes) before secondary apnea develops. Once this state evolves it becomes more difficult to resuscitate and restore cardiorespiratory status and in those who do recover the likelihood for hypoxic–ischemic brain injury is markedly increased. The findings in this report are consistent with these observations. Thus almost 50% of the apneic infants responded to stimulation and suctioning only, and the outcome in this group was favourable (only two deaths). On the other hand, although half of the infants administered FMV initiated spontaneous respirations within four to five minutes of delivery, death was significantly more likely in this
5. Documentation

These observations are initial critical steps towards the understanding of “birth asphyxia” and by default interventions to reduce its occurrence in the developing world. Thus the data indicate that the overwhelming majority of lifeless babies at birth are in primary apnea and will respond to basic interventions with or without FMV particularly when initiated within the “Golden MinuteSM” 14. Moreover, if spontaneous breathing is initiated within four minutes in response to interventions the mortality rate is approximately 1.2 per 1000 live births i.e. comparable to that observed in the developed world. However, if there is a delay beyond four minutes in the onset of breathing, mortality increases and approximates 7.0 per 1000 live births. In this regard the predominant cause of death was secondary to “birth asphyxia”, with prematurity, low birth weight, and congenital abnormalities additional causes. 18

The association of duration of FMV and mortality may be related to several factors. First, some babies may have been in secondary apnea and depending on the extent of circulatory collapse unlikely to respond to stimulation, suction, and ventilation only. We have reported separately that many of the infants in need of resuscitation presented with obstetrical complications and fetal heart rate abnormalities. 19 Moreover, no infant received chest compressions, medications, or mechanical ventilation. It is unclear whether these interventions would have reduced mortality. Second, application and administration of FMV may have been suboptimal. Thus in a non breathing infant establishment of functional residual capacity, which is critical to effective ventilation, can be extremely difficult without the application of continuous positive airway pressure or prolonging the inspiratory time which are both difficult to achieve with a self inflating bag. 20

An interesting observation is that of a substantial delay in onset of spontaneous respirations and normal outcome at 24 h in a limited number of infants. Thus three babies initiated spontaneous respirations and 25 newborns began breathing when stimulated/suctioned after four minutes and 27/28 were classified as normal at 24 h. Even in the group of 12 babies who received FMV after four minutes almost 60% were classified as normal. This suggests that the infants were most likely in primary apnea and/or they had shallow breathing not detected by the provider or the observers. In this regard data from the Collaborative study in the United States noted in babies with a 20 min Apgar score <3 that 60% died and of the survivors 40% were normal. 21 These combined observations speak to the adaptive resilience of the fetus in response to a hypoxic environment.

5. Conclusion

The majority of newborn infants, delivered in a rural institution in Sub-Sahara Africa, spontaneously initiate respirations within one minute and a substantial number of apneic babies begin breathing in response to basic actions (stimulation/suction) and/or FMV with a favourable short term outcome in the majority of infants. Infants who required FMV were more likely to die particularly when the intervention was delayed or prolonged. Understanding the factors contributing to the delay in initiation of FMV and the need for prolonged ventilatory support is likely to be extremely important in potentially reducing mortality in this subset of infants. Documentation of strategies to improve the skills of basic neonatal resuscitative actions is needed.

Conflicts of interest

All authors have completed the ICJMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that (1) HLE has received research grants from The Laerdel Foundation for Acute Medicine for the submitted work; (2) Haydrom Lutheran Hospital has received project funds from The Laerdel Foundation for Acute Medicine for the submitted work, and (3) JMP has no conflict of interest. The financial source had no role in study design, data collection, data analysis, data interpretation, writing of the report, or in the decision to submit the paper for publication.

Acknowledgements

This study was made possible because of the research assistants and health providers working in the Maternity Ward at Haydrom Lutheran Hospital. Statistical assistance was provided by Bjørn Auestad, PhD, statistician at University of Stavanger. We thank Professors Johanne Sundby, University of Oslo and Eldar Søreide, Stavanger University Hospital for their support.

References

19. Ersdal HL, Mnduna E, Svensen E, Sundby J, Perlman JM. Obstetrical factors that increase the risk for fetal heart rate abnormalities, bag mask ventilation, 5 min Apgar Score <7, deaths and fresh stillbirths in a low-resourced hospital. In: Abstract Pediatric Academic Societies (PAS) annual meeting, 2011.