

# Decision-Making: Initiation and Withdrawing Life Support in the Asphyxiated Infants in Developing Countries\*

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## ABSTRACT

The issues of life support in the asphyxiated infant are not only whether cardiopulmonary resuscitation or CPR will be successful, but also whether if successful, the infant will be severely damaged. This is particularly important in the developing countries because the damaged infants may burden the society. The country has to allocate huge financial and human resources to look after them. When it comes to decisions in initiation and withdrawal of life support, there are differences between the East and the West. Physicians are searching for reliable predictors of outcome of term asphyxiated infants to enable early decision-making, initiation and withdrawal life support, as well as counselling and planning appropriate level of treatment including trials of cerebroprotective therapies. Markers commonly used to identify birth asphyxia are not good predictors of brain injury or death. There is a myriad of reports on clinical or laboratory tests, some using single parameter, to help determine neurological outcome of asphyxiated term infants. Much frequently used equipment in developed countries can be expensive and inaccessible to developing countries. There is an urgent need to look for relevant, simple and inexpensive methods. A combination of measurements may look promising in the early selection of at-risk neonates for decision and counselling. Recently measurement of urinary lactate: creatinine ratio to identify early newborn infants at risk for HIE was proposed.

Withdrawal of life support is an ethical issue. In withdrawing life support of the severely asphyxiated infants, one must be aware of the differences of approach. There are differences in religion and culture; in beliefs and philosophies, between the East and West.

The importance of neonatal resuscitation should be emphasised. Some regions still adhere to obsolete resuscitation methods. Neonatal Resuscitation

Program (NRP) should be promulgated and organised resuscitation should be introduced. There is an urgent need to train the trainers in CPR in the developing countries.

**Keywords:** predictors, neurodevelopmental outcome, prognostic markers, CPR (cardiopulmonary resuscitation), Neonatal Resuscitation Program (NRP)

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## INTRODUCTION

Birth asphyxia is a serious problem in perinatal care because medical, social, economical problems that ensue could burden the country that bears the responsibility to manage the damaged children. These children drain off enormous resources, both financial and manpower, of the country. Sadly the investment is usually not cost effective.

According to reports from the World Health Organisation (WHO): One million or more neonatal deaths are attributable to birth asphyxia each year<sup>(1)</sup>. The figure may be grossly underestimated, as cases of birth asphyxia are not notifiable. The number of children who suffered from neurodevelopmental damage as a result of birth asphyxia were not documented or published. The magnitude of birth asphyxia is not known unless one can retrieve reliable data from various sources such as indexed medical journals, official reports from government health departments. In USA, of the four million babies who died, 3,378 can be ascribed to birth asphyxia or delivery-related complications<sup>(2)</sup>.

In China, if the fatality rate of asphyxia remains at 10% and working on the total annual deliveries of 20 million and the mean asphyxia prevalence of 8%, there would be 160,000 neonatal deaths a year as a result of asphyxia<sup>(3)</sup>.

Generally the impact of birth asphyxia is smaller in more developed countries because of better organised perinatal health care, especially wide introduction of NRP.

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## INITIATION OF LIFE SUPPORT

When considering initiation of life support in perinatal asphyxia, the issues are not only whether the CPR (cardiopulmonary resuscitation) will be successful, but also whether if successful, the infant will be severely damaged. Ideally, physicians need predictors of poor neurological outcome for decision of initiation of life support. There is no single clinical factor that can reliably predict the outcome (death or neurodevelopmental abnormality) with absolute certainty. Neurological prognosis soon after birth can be difficult. Very often it is uncertain whether a foetus had suffered problems earlier in pregnancy. It is also not known whether HIE (hypoxic ischaemic encephalopathy) occurred immediately prior to birth or some hours earlier. The problem is also compounded by not knowing whether asphyxia was a single or repeated episode. Cerebral damage evolves over several days, with significant changes in pathophysiology over time.

Often CPR of asphyxiated infants is an emergency situation, denying the resuscitating physician a chance to know the wishes of the parents whether to institute immediately resuscitation. In this situation, especially in the West or developed countries, physicians have to act with the "presumption of consent" in the delivery room if they possess appropriate level of competence and use "reasonable judgement." Physicians functioning in an ethical manner should meet both of these qualifications. Practice of techniques and completion of appropriate refresher courses such as the Neonatal Resuscitation Program (NRP) should achieve appropriate level of competence through a continuing effort to maintain resuscitation skills. Recertification in this programme should be achieved every two years. "Reasonable judgement" is the application of these skills by a knowledgeable clinician who understands the medical, social, legal, and economic issues surrounding the resuscitation of the severely asphyxiated neonates.

## EARLY PREDICTORS OF ADVERSE OUTCOME

In Singapore, Toh has looked into early prediction of asphyxia outcome. She studied 35 term infants who suffered from HIE. There were 13 deaths, and 10 had major neurological sequelae. Despite standard neonatal intensive (NICU) care, the mortality and morbidity rates infants remained high, and neurodevelopmental outcome of these infants was poor<sup>(4)</sup>. She noted that the following were favourable prognostic markers: 1. The five minute Apgar score >5; 2. First pH >7.1; and 3. Stage I HIE<sup>(5)</sup>.

The significant risk factors for neurological damage were 1. Low Apgar score of less than four at five minute of life; 2. The use of adrenaline in resuscitation; 3. Low first arterial pH (<7.1); and

4. High base deficit (-20 mEq/L). She found that in using single markers for prediction of outcome, there were limitations in prognostic value. However, the initial base deficit =>20 mEq/L is predictive, and it is so in many other studies. To improve the predictive value of outcome, she examined a cluster of factors. She found these factors were more sensitive for risk of death or neurological outcome and the positive predictive value achieved 100% for death or major motor handicap. (Base deficit =>20 mEq/L and 5 min Apgar <4 were predictive; but pH =<7.1 with 5 min Apgar <4 were less sensitive<sup>(5)</sup>). These tests are relatively simple and cheap.

Recently Taiwan has come up with the measurement of urinary lactate:creatinine ratio to identify early newborn infants at risk for HIE. The test was simple and predictive. A sensitivity and specificity of ratio of >0.64 6 hours after birth predicts HIE (94% and 100%). It was postulated that when lactate was used as alternative energy substrate, the asphyxiated infants had more favourable outcome. The disadvantage is that urine sampling from these infants may not be possible as they may be oliguric<sup>(6)</sup>.

## MARKERS OF ASPHYXIA AND PREDICTORS OF NEONATAL BRAIN INJURY – THE UNECONOMICAL TESTS

There are many tests that may give fairly reliable predictions of neurological outcome of asphyxiated babies. They can have high positive predictive values even used soon after birth<sup>(7)</sup>. These include single-channel amplitude-integrated electroencephalogram (EEG) recordings; visual and somatosensory evoked potentials, cerebral haemodynamics e.g. Pourcelot resistance index, as well as neuroimaging techniques such as higher-frequency cranial ultrasound, magnetic resonance imaging (MRI), computerised tomography (CT), Near infra red spectrometry, Positron emission tomography (PET), MR spectroscopy to study cerebral energy failure. Biochemical markers of cerebral damage such as excessive GFAP (glial fibrillary acidic protein), and neurone specific enolase (NSE), a glycolytic enzyme.

Nevertheless most of those with high positive predictive values require some element of special equipment and expertise and many are not widely available. These are problems faced by people in developing countries. Special equipment is costly and inaccessible and can only be found in tertiary centres. Ironically, the equipment is not available in places where birth asphyxia commonly occurs. Also training people to acquire reasonable skill to operate these technologies can be difficult, and it takes time to do so. Therefore simple clinical examination and cheap tests are required.

Physicians have to look for less costly methods as good alternatives. Delivery room resuscitation, foetal heart rate patterns, cord blood gas, and Apgar scoring have been proposed. Low Apgar scores, signs of neonatal encephalopathy, and seizures predict a high rate of cerebral palsy.

#### **HIGH-RISK INFANTS IDENTIFIED BY COMBINATION OF MARKERS**

In recent clinical studies, a combination of markers such as progressive foetal heart-rate abnormalities shortly before delivery, severe foetal acidosis, very low Apgar scores and delivery room resuscitation increased risk of moderate-to-severe HIE. Such combination of measurements may look promising in the early selection of at-risk neonates for decision and counselling. However, these require refinement or serial determination of physiological measurements. Markers should be few, simple, cheap<sup>(8,9)</sup>.

#### **THE ETHICAL ISSUES**

When it comes to the ethical issues and decision of initiation and withdrawal of life support, it must be relevant to cultural, economical, social, philosophical and religious differences between the East and the West, rich and poor, and developed and developing countries. One should not try to apply or compare neonatal health care in the developing countries to systems existing elsewhere.

When the question of stopping ineffective treatment of a severely asphyxiated child arises, effective doctor-parents communications, especially in the developed countries and in the West, play an important role in deciding further management. Effective doctor-patient communication such as use of right words and terms, simple language to explain the values, applications and limitations of technologies to ensure understanding of the situation is utmost important. When counselling the parents, the best or worst scenario of outcome should be presented<sup>(10)</sup>. As agent speaking on behalf of the baby's interest, the parents need to know the range of options, risks and likely outcomes such as palliative care and aggressive treatment. The wishes of parents should predominate in expressing the interest of the infant. Most parents do not want the baby to suffer, be unwanted, or die alone. They should be given an opportunity to do something and people related to the very ill infant should be involved. The principles of autonomy and fidelity should be respected and applied. Well-informed families should have the right to refuse treatment.

The physicians of the East may be different. They normally behave paternalistically and their decisions

are accepted without much criticism. Generally the family is consulted and the decisions will be accepted. Many people in the East consider quality of life rather than sanctity of life because of a strong belief in rebirth and fatalism. Patients obey prestigious physicians who have professional responsibility. They respect the doctors whom they think know best and feel that if knowledgeable and respectable physicians cannot make decisions, who else can<sup>(11)</sup>?

One must understand it is medicine's role to serve the needs of patients and families. The role of medicine is not to define and impose the agenda on the patients and families.

#### **WITHDRAWAL OF LIFE SUPPORT IN PERINATAL ASPHYXIA**

Withdrawal of life support is an ethical issue<sup>(12)</sup>. Often a severely asphyxiated infant with clear clinical evidence of inevitable or imminent death is kept alive on life support system, maintained on anti-convulsive drugs as well as parenteral therapy. All possible methods of treatment were exhausted. Yet many doctors rigidly require brain deaths as the sole criterion for discontinuation of life support. They allow the dying process be prolonged, and avoid withdrawal or withholding of treatment.

In withdrawing life support of the severely asphyxiated infants, one must be aware of the differences of approach and philosophies, between the East and West. One also faces the following questions:

1. At what stage when further CPR becomes an exercise of futility?
2. Are predictors or markers reliable and necessary?
3. Is it true once resuscitation is initiated, it is hard to withdraw?
4. Who should make decision of withdrawal?
5. What is the situation in the developing countries?

Generally most people chose to discontinue CPR in term infants<sup>(13)</sup> when:

1. The cord or neonatal (arterial) blood is pH <6.8
2. The base deficit is at least -20 mEq/L
3. There was no spontaneous respirations at 30 minutes of life
4. There was no heart rate by 10 minutes of life (Apgar 0>10') despite adequate resuscitation and failure to respond to adrenaline.
5. There were attendant adverse prenatal conditions

#### **BACK TO BASICS**

Physicians should not forget the basics. Where possible, births asphyxia, or even intrapartum asphyxia, should be avoided or even prevented. It has been observed that in many medical meetings, a myriad of reports on research in birth asphyxia, including post asphyxial

physiological and metabolic changes, the molecular biology and neuroprotective treatment. People tend to forget that management of birth asphyxia should begin with good perinatal care and recognition and prompt supervision of high risk babies, organised neonatal transport team as well as resuscitation team including the neonatologists, obstetricians, nurses, radiologists, physiotherapists, laboratory technicians, etc.

For organised resuscitation team, the new International Liaison Committee on Resuscitation (ILCOR) recommendations are based on the ease with which the resuscitation measures can be taught and the degree to which the skill taught can be retained ("construct validity")<sup>(14)</sup>.

Consensus guidelines on resuscitation will ultimately benefit many infants, particularly in the less technically developed countries.

#### **NRP: TRAINING AND RETRAINING, TRAIN THE TRAINERS (TTT)**

The experience from China is encouraging. Zhu et al introduced the NRP in 1993 and the group was able to reduce the perinatal neonatal mortality rate to almost three times after its implementation<sup>(3)</sup>. Zhu's experience testifies the importance of NRP, particularly in the developing countries. To ensure success in NRP, these countries should focus on TTT or train the trainers.

The Guidelines for Perinatal Care, third edition, requires one skilled resuscitator to be present at every delivery. This is an ideal setting if all the babies are delivered in the hospitals. But what about the developing countries where women deliver their babies at home or babies are delivered by traditional birth attendants most of whom are unqualified? Therefore, is the concept of "Reasonable judgement" relevant in such a case.

In the Report of the Regional Expert Group Meeting, organised by the WHO Collaborating Centre for Training and Research in Newborn Care, held in November 1998, it was recommended that NRP be launched in all countries in SEAR (South East Asia Region), wherever this activity has not been initiated<sup>(15)</sup>.

#### **CONCLUSIONS**

Decision-making in initiation and withdrawing life support in the asphyxiated infants in developing countries is different from that of the developed countries. There is a need to look for reliable predictors

of outcome of term asphyxiated infants so that proper planning and management is possible. There is an urgent need to look for relevant, simple and inexpensive methods to predict outcomes in the developing countries. The recent method of measurement of urinary lactate: creatinine ratio to identify early newborn infants at risk for HIE may be promising.

When addressing the issues of withdrawal of life support of the severely asphyxiated infants, one must be aware of the cultural, religious and philosophical differences in approach between the East and West. The importance of neonatal resuscitation should be emphasised, and obsolete resuscitation methods should be eliminated. Neonatal Resuscitation Program (NRP) should be promulgated and organised resuscitation should be introduced. There is an urgent need to train more trainers in CPR in the developing countries.

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