Post - resuscitation management of an asphyxiated neonate

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Introduction

Perinatal asphyxia is a common neonatal problem and contributes significantly to neonatal morbidity and mortality. It ranks as the second most important cause of neonatal death after infections, accounting for around 30 % mortality worldwide. In India, between 250,000 to 350,000 infants die each year due to birth asphyxia, mostly within the first three days of life. In addition, ante-partum and intra-partum asphyxia contributes to as many as 300,000 to 400,000 stillbirths.

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Perinatal asphyxia

Perinatal asphyxia is an insult to the fetus or the newborn due to lack of oxygen (hypoxia) and/or a lack of perfusion (ischemia) to various organs. The common denominator of hypoxic ischemic injury is deprivation of the supply of oxygen to the central nervous system. An oxygen deficit may be incurred by either hypoxemia or ischemia. Hypoxemia is defined as a diminished oxygen content of the blood and ischemia is characterized by reduced perfusion of that particular tissue; generally the two tend to occur simultaneously or in sequence. Asphyxia is an impairment of gas exchange that results not only in the deficit of oxygen in blood but also an excess of carbon dioxide causing acidosis. The acidosis further leads to hypotension and ischemia culminating in hypoxic-ischemic injury. The brain is especially vulnerable to damage by hypoxia and ischemia because it has one of the highest oxygen requirements and base line blood flow of all the organs in a term fetus. Within the full term brain, the highest base line metabolic rates and blood flow occur in the thalamus and certain brain stem nuclei.

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Definition

There is no unanimity or consensus regarding the definition of birth asphyxia and various workers have used different definitions making it difficult to ascertain the incidence of asphyxia. The World Health Organization has defined birth asphyxia as "failure to initiate and sustain breathing at birth" and based on Apgar score as an Apgar score of <7 at one minute of life. The National Neonatal Perinatal Database (NNPD) 2000, used a similar definition for perinatal asphyxia and defined moderate asphyxia as slow gasping breathing or an Apgar score of 4-6 and severe asphyxia as no breathing or an Apgar score of 0-3 at one minute of life. The National Neonatology Forum of India has defined asphyxia as "gasping or ineffective breathing or lack of breathing at one minute of life".

The essential criteria for diagnosing perinatal asphyxia as outlined by ACOG & AAP are

- Prolonged metabolic or mixed acidemia
  (pH <7.0 on cord arterial blood sample)
- Persistence of an Apgar score of <3 for 5 min or longer
- Clinical neurologic manifestation as seizures, hypotonia, coma or HIE in the immediate neonatal period
- Evidence of multi-organ system dysfunction in the immediate neonatal period

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Etiology

Ninety percent of asphyxial insults occur in the antepartum or intrapartum periods as a result of placental insufficiency resulting in an inability to provide oxygen and remove carbon dioxide and hydrogen ion from the fetus. The remaining 10% are post-partum usually secondary to pulmonary, cardiovascular or neurologic insufficiency. Normally during labour with every uterine contraction there is a decrease in the blood flow and thus oxygen delivery to the fetus along with increase in the fetal and maternal oxygen requirements. The newborn is fairly resistant to the effects of this transient lack of oxygen and thus late decelerations are not seen until a PaO_2 of <20mm Hg and a SaO_2 of <31 % is reached.

In addition, if any of the following factors operate they pose hypoxic ischemic challenges to the fetus and initiate protective reflexes which sustain the cerebral circulation for some time before the neonate manifests with an asphyxial insult. These factors are

- Impaired maternal oxygenation: as in maternal hypoxia due to pulmonary, cardiac or neurologic disease in the mother.
- Decreased blood flow from the mother to the placenta: as in maternal infection, shock, dehydration, hypotension and anemia.
- Decreased blood flow from the placenta to the fetus: as in placental abruption, cord prolapse, cord entanglement, true knot, cord compression and abnormality of the umbilical vessels.
- Impaired gas exchange across placenta or fetal tissues: as in maternal hypertension (PIH or essential), post maturity, maternal vascular disease, maternal diabetes, drug abuse, placental calcification, infarct or fibrosis
- Increased fetal oxygen requirement: as in fetal anemia, fetal infection or IUGR.

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Clinical consequences

Perinatal asphyxia may result in adverse effects on all major body systems. Many of these complications are potentially fatal. In a term infant with perinatal asphyxia renal, neurologic, cardiac and lung dysfunction occurs in 50%, 28%, 25% and 23% cases respectively. The extent of multi-organ dysfunction determines the early outcome of an asphyxiated neonate with either the neonate succumbing as a consequence of organ damage or recovering completely. Generally there are no long term sequelae associated with these organ system derangements. Hypoxic ischemic encephalopathy (HIE) refers to the CNS dysfunction associated with perinatal asphyxia. HIE is foremost concern in an asphyxiated neonate because contrary to other system derangements this has the potential to cause serious long term neuromotor sequelae among survivors.

The clinical features in asphyxiated babies range from mild to severe impairment. In the most severely affected babies there are signs of cerebral dysfunction during the first twelve hours in the form of stupor or

coma, periodic breathing or irregular respiration, hypotonia and loss of complex reflexes like Moro's and sucking. The pupillary response may be intact or sluggish. 6-24 hours after the insult about 50 % of the moderate to severely asphyxiated babies may have subtle tonic or multifocal clonic seizures. Between 12-24 hours there may be apnea requiring respiratory support reflecting brain stem dysfunction. Severely affected babies may have progressive deterioration of the CNS function in terms of decreasing tone, increasing degree of coma and prolonged apneas over the next 48 hours. These neonates would eventually die or have permanent neurologic sequelae. The Sarnat's staging system to estimate the severity of asphyxial insult to infants > 36 wks gestation is fairly accurate for early assessment of prognosis in neonates with HIE. The prognosis is good if a neonate does not progress to or remain in stage III & if total duration of stage II is less than 5 days. In the universal absence of continuous EEG monitoring, Levene's system of grading clinical severity of HIE is functionally appropriate, easy to use and serves as a useful clinical guide which is based on assessment of consciousness, tone, seizure activity, autonomic disturbances and abnormalities of peripheral & brain stem reflexes.

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Principles of management

The management consists of supportive care to maintain temperature, perfusion, ventilation and a normal metabolic state including glucose, calcium and acid-base balance. Early detection by clinical and biochemical monitoring and prompt management of complications must be done to prevent extension of cerebral injury.

Temperature should be maintained in the normal range of 36.5 – 37.5 ^{O}C as hypothermia imposes additional stress to the baby by increasing the metabolic needs. This may lead to acidosis, myocardial depression, hypotension, bleeding tendency and pulmonary hemorrhage. Hyperthermia is detrimental by way of increasing the metabolic and energy expenditure and inducing neuronal injury. **Oxygenation** should be kept in the normal range by monitoring transcutaneous or arterial PO_2 or percent oxygen saturation (SO_2) by pulse oximetry. PaO2 should be maintained between 60-80 mmHg and SpO2 should be maintained between 90-93 %. Hypoxia

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should be treated with O_2 and if required ventilation. Hyperoxia should always be avoided. **CO_2** levels should be kept in the normal range by maintaining pCO2 between 35-45 mmHg. **Blood glucose** level should be kept at 75-100 mg/dl to provide adequate substrate for the brain. If the baby is hypoglycemic, a bolus of 2 ml/kg of 10% dextrose should be administered followed by a continuous glucose infusion at a rate of 6 to 8 mg/kg/minute . Rates as high as 9 to 15 mg/kg/minute may be required for short periods. If necessary a central line should be put to give the higher concentration. **Calcium** level should be kept in the normal range and serum calcium should be maintained between 9-11 mg/dl. Hypocalcaemia is a common metabolic alteration in the neonatal post asphyxial syndrome. A subnormal serum Ca^{++} level may compromise cardiac contractility and may cause seizures.

It is of utmost importance to maintain the blood gases within the normal range by ensuring good oxygenation and adequate ventilation in an asphyxiated neonate. Hypoxia can decrease cerebral blood flow and cause ischemia whereas hyperoxia causes vasodilatation and may increase blood flow to injured cerebral areas with compromised vascular integrity leading to hemorrhages. Similarly, hypercapnia may cause cerebral vasodilatation, which may direct more flow to uninjured areas with relative ischemia to damaged areas (Steal phenomenon) and extension of infarct size. Excessive hypocapnia may decrease cerebral blood flow and cause ischemic infarcts. Hyperventilation is therefore not recommended.

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Initial management

The initial management of all such neonates consists of placing the baby under a servo-controlled radiant warmer and nursing them in the thermo-neutral range of temperature. Immediate clinical assessment should be made by recording respiratory rate, heart rate, capillary filling time, blood pressure, temperature and oxygen saturation. Urine output should be monitored on an hourly basis. Check hematocrit, sugar, blood gases and serum electrolytes. Place an intravenous line and start 10% dextrose at

60ml/kg/day. Injection vitamin K 1mg must be administered to all these babies.

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Clinical monitoring

All neonates who have suffered asphyxia must be closely monitored clinically as well as by performing certain bedside tests. This monitoring aims to detect derangements in the clinical, metabolic and hemodynamic milieu so as to ensure prompt management. The present day management of an asphyxiated neonate is largely supportive with an aim to prevent any further exacerbation of the existing injury. Inability to detect and treat complications has the potential to aggravate the insult. The respiratory status must be monitored by meticulous record of the RR, B/L adequate chest expansion & air entry. The CVS status assessment should include HR, color, CFT, Pulse oximetry, NIBP & temperature. Assessment of the neurologic status should include Sarnat & Sarnat staging or Levene's staging for HIE along with assessment of anterior fontanel, tone, seizures, pupillary size & reaction every 12 hrly. This is essential to document the progression and evolution of HIE which is helpful in prognostication. The abdominal circumference should be recorded to rule out any ileus due to gut ischemia. The urine output should be measured as it is a direct indicator of the state of peripheral perfusion. Moreover, this entity is also used as a prognostic sign and the outcome is uniformly poor if the output remains <1ml/kg/hr beyond 36 hrs of life.

The subsequent management is largely supportive with monitoring and maintenance of normal oxygenation & ventilation, adequate perfusion, normal glucose, calcium and hematocrit. Seizures should be treated energetically. Continuous monitoring of vital parameters must be aimed at early detection of derangements and complications and their timely management.

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Biochemical monitoring

The biochemical monitoring should aim at measuring the blood sugar by Dextrostix, the hematocrit, serum electrolytes (Na, K), serum calcium, BUN, creatinine, blood gases & pH. All these need to be maintained in the normal range to prevent extension of the neuronal damage.

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Investigations

Investigations in a baby with perinatal asphyxia do not alter the acute management but help in prognostication (imaging studies). It is important to perform a sepsis screen as most of these neonates would have undergone extensive resuscitation and are candidates for invasive monitoring and therapy. It further helps to minimize antibiotic usage and prevents unnecessary antibiotic resistance. X-ray chest should be done to look for pneumothorax, cardiac enlargement or any malformations.

Neuroimaging such as Ultrasound and CT Scan and subsequent investigations like EEG are mainly required for prognostication and do not aid in the immediate management of the asphyxiated neonate.

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Aims of specific management

The principles of management in an asphyxiated neonate consist of supportive care to maintain temperature, perfusion, ventilation and a normal metabolic state including glucose, calcium and acid-base balance. Early detection by clinical and biochemical monitoring and prompt management of complications must be done to prevent extension of cerebral injury.

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Specific management - perfusion

Normal neonatal cerebral blood flow and thus the perfusion are achieved as a consequence of cerebral auto regulation which prevents major fluctuations in the cerebral blood flow. For instance, in a neonate who

develops hypotension, cerebral vasoconstriction maintains the cerebral blood flow and thus the perfusion. However, in an asphyxiated neonate this auto regulation is lost and the cerebral circulation becomes pressure passive.

It is important to maintain cerebral perfusion pressure (CPP) within a narrow range to optimally perfuse the brain. Too little can cause ischemic injury and too much can cause hemorrhage in the areas of damaged blood vessels. Because cerebrovascular auto regulation is lost, cerebral perfusion entirely reflects systemic BP in a pressure passive fashion. Hence, to maintain cerebral perfusion, a systemic mean arterial BP of at least 45 to 50 mm of Hg is desirable for term infants, 35-40 mm for infants weighing 1000-2000 g and 30-35 mm for infants <1000 g.

Frequent pushes of colloids or sodium-bicarbonate should be minimized. Regular replacement of intravascular volume losses should be done to avoid lactic acidosis. Volume replacement should be given slowly. If the infant is well hydrated and urine output is normal (>1 ml/kg/hour) intravenous fluids should be restricted to replacing insensible losses plus urine output. Pressor agents like dopamine should be used judiciously if BP is low.

A clinical assessment of the perfusion status should be done by assessing the capillary filling time, monitoring the urine output and the blood pressure at regular intervals. Adequacy of the end organ perfusion (skin & kidney) as assessed by CFT<3 seconds and urine output >1ml/kg/hour is a reliable indicator of adequate vital organ perfusion, which are preferentially perfused at the cost of non-vital (end organs) organs in asphyxiated neonates. If the CFT is prolonged, a fluid bolus of 10ml/kg of normal saline or ringer lactate is infused slowly over 20-30 minutes and CFT is reassessed. Further fluid boluses/ vasopressor use is best decided based on the CVP measurement. A low CVP indicates poor intravascular volume and dictates additional fluid therapy whereas neonates with normal or high CVP should be started on vasopressors. Dopamine followed by dobutamine if required should be used to increase the blood pressure. Sodium bi carbonate should be used judiciously and only if there is documented metabolic acidosis.

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Specific management - seizures

Seizures should be controlled as far as possible. In neonatal HIE they are typically focal or multifocal and are characteristically seen in stage 2 of Sarnat staging on the first or second day. When seizures occur, phenobarbitone as a loading dose 20 mg/kg should be given slowly at the rate of 1 mg/kg/min intravenously. The bolus should be followed by maintenance dose of 5 mg/kg/day. Additional boluses of 10 mg/ kg (maximum two) may be administered if seizures continue or recur. One should always be vigilant for respiratory depression and/or cardiovascular compromise with hypotension during administration of the drug. If seizures persist, phenytoin may be administered slowly as a second drug (20 mg/kg intravenously as the loading dose followed by 4 to 8 mg/kg/day as a maintenance dose). Before starting anticonvulsants one should ascertain that metabolic derangements that may complicate asphyxia and cause seizures (hypoglycemia, hypocalcaemia, hyponatremia) have been taken care of. Nevertheless, if seizures persist, a benzodiazepine e.g. lorazepam 0.05 to 0.10 mg/kg/dose intravenously may be given transiently as a third drug.

When the infant's condition has been stable for 3 to 4 days, all anticonvulsants are weaned except phenobarbitone, dose of which may be reduced. If seizures have resolved, neurologic findings are normal and EEG is normal, anticonvulsants are stopped in the neonatal period. If anything is abnormal, anticonvulsants are continued for 1 to 3 months. If the neurologic findings are then normal with no recurrent seizures, Phenobarb is tapered over 4 weeks. If the neurologic findings are still not normal, thorough investigative workup should be carried out to know the initial cause of seizures and anticonvulsants continued. Infants with a higher risk of subsequent seizures are those with a persistent neurologic deficit (50% risk) and those with an abnormal EEG between seizures (40% risk).

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Predictors of outcome

The presence of one or more of the following features has been found to be a predictor of poor neurodevelopmental outcome in the long term. These are:

1.   Failure to establish respiration by 5 minutes of life
2.   Apgar score of 3 or less at 5 minutes
3.   Onset of seizures with in 12 hours
4.   Refractory seizures
5.   Stage III HIE
6.   Persistent oliguria (<1 ml/kg/hr) for the first 36 hrs of life
7.   Inability to establish oral feeds by 1 wk
8.   Abnormal EEG & failure to normalize by D7
9.   Abnormal CT, MRI, MRS in neonatal period

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Prevention of asphyxia

The absence of satisfactory cure for asphyxiated neonates despite extensive work on this condition for the last few decades once again poses the most primitive question as to whether asphyxia can be prevented. If yes, to what extent? The answer is not simple or straight forward but certainly some of the cases of asphyxia can be prevented by better antenatal and intranatal management of high risk cases. The approach should be regular antenatal check ups to detect high risk cases and adoption of an 'at risk approach' to anticipate complications so that timely intervention in terms of emergency LSCS can be instituted. An alternative strategy for the not so well equipped centers can be appropriate timely referral to a well equipped neonatal and obstetric centre with active surveillance and timely delivery. Prompt and efficient resuscitation followed by management of neonatal complications in a level III NICU should go a long way in preventing some of the morbidity and mortality related to asphyxia.