

Futility and Withdrawal of Intensive Care in Term Infants with Brain Injury

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Neonatal brain injury is a major challenge in modern perinatal care, including obstetric and neonatal care. Advances in the care of the newborn, including resuscitation improvements and the introduction of therapeutic hypothermia (TH) for the management of neonatal encephalopathy, have allowed us to sustain and improve life for babies that previously may have been deemed too unwell to continue life-sustaining treatments. From an obstetric perspective, there has been an increase in the detection of serious fetal anomalies with better antenatal scanning regimes and the use of MR imaging in fetal medicine to detect congenital brain malformations.

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The decision to redirect the focus of care to comfort-only measures usually follows a detailed neurological examination of the baby in conjunction with neuroimaging (typically MR imaging) aided by EEG monitoring when available. Congenital causes of severe brain dysfunction, such as severe congenital brain malformations (e.g., giant encephalocele, lobar holoprosencephaly) leading to a plan for palliative care following delivery, are encountered. However, most term babies where palliative care is initiated do so following acquired perinatal brain injury. Major conditions that lead to the development of perinatal brain injury include hypoxic ischaemic encephalopathy (HIE), perinatal stroke, perinatal central nervous system infection, and intracranial haemorrhage. Hypoglycaemia can result in brain injury or potentiate injury due to other causes, e.g., HIE.

HIE is one of the commonest reasons for acquired brain injury in the normally formed term newborn. The incidence of HIE is approximately 1.5 per 1000 births, and globally there are 700,000 cases of death or disability from birth asphyxia annually (1). Therapeutic hypothermia (TH) has resulted in significant improvements in the outcomes of neonates with HIE. However, greater than 40% of neonates who undergo TH will still have impaired neurological outcomes at school-going age (2). TH does not improve outcomes in babies with severe HIE.

A perinatal stroke is a cerebrovascular event occurring between

20 weeks gestation and up to 28 days after birth(3). Prevalence has been estimated at 1/1600 to 1/5000 live births and is recognised as the second most common cause of neonatal seizures after neonatal encephalopathy accounting for up to 20% of neonatal seizures (4). Presentation is usually in the first three days after birth. The outcome of neonates with perinatal stroke is difficult to predict (5).

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Intracranial haemorrhage in term infants is rare but can result in significant neuro disability. Intracranial haemorrhage can be epidural, subdural, subarachnoid haemorrhage, or intracerebral.

Central nervous system infections, including meningitis and encephalitis, can be bacterial, viral, or fungal in aetiology. The incidence of early-onset meningitis is approximately 0.39 per 1000 live births. Herpes virus infection is the most common non-bacterial cause of central nervous system infection, with an estimated incidence of 1 in 50,000 live births, and can lead to severe neurodevelopmental delay.

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Being told that their newborn has a brain injury is amongst the most devastating news that parents can receive. Existing data suggests that parents of encephalopathic neonates experience predictable communication difficulties. Medical information is complex and uncertain prognosis is challenging. It is well-accepted that parents value participation in medical decision-making. Parent-centred decision-making is preferred in the NICU when discussing longer-

term goals and potential harm(6). The fundamental goal of shared decision-making is to open the process to benefit from both the physician's and the parent's respective experiences, knowledge, and beliefs. This does not imply a value-neutral role for clinicians but instead requires a more delicate balancing as an advocate for the baby while respecting parental views(7). Parents who perceive a shared role in end-of-life decision-making may experience less long-term grief than parents who perceive either making the decision on their own or having no involvement (8). Palliative care teams are an important source of added support to all caregivers. Attempting prognostication in neonatal encephalopathy is essential to help parents formulate their concept of best interest for their newborn. However, estimating prognosis is complicated by the wide range of potential neurodevelopmental outcomes, evolving course, and role of extrinsic factors like access to rehabilitation. Even in cases of anticipated death, infants may unexpectedly survive. In the face of uncertainty, describing the best case, worst case, and most likely outcome is an effective strategy to characterize the potential range of outcomes(6).

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Clinical history, neurologic examination, serum biomarkers, neurophysiology [amplitude-integrated electroencephalography (aEEG) or EEG], near-infrared spectroscopy, and magnetic resonance imaging have all been studied as predictors of severe neurologic injury and poor outcome, although none is 100% predictive. Serial evaluation over time facilitates discussion regarding anticipated poor prognosis and decision-making for transition to comfort care. Serial assessments with a particular test are more predictive than a single observation. The time over which a test remains abnormal together with the trend over time yields the best information(9). Thus far, brain monitoring in the form of aEEG and conventional EEG seems to be the best objective tools to identify the highest-risk patients (10). Specifically, a severe depression or burst suppression pattern which persists is suggestive of poor outcome. Magnetic resonance imaging (MRI) is known to retain its predictive abilities when performed in the window of 5-10 days after birth. Where MRI is performed, the pattern and extent of injury remain important predictors of outcome even after TH (11-13). However, MRI is sometimes not possible due to clinical instability or accessibility. In these cases, cranial ultrasound is important and predictive if it shows hyperechogenic subcortical grey matter structures (basal ganglia and thalamus) and/or focal parenchymal lesions. The presence of cystic lesions early in the neonatal course is also predictive of poor outcome and helps to identify prenatal injury. Many scoring systems are available and can be

applied to help predict outcomes, including the Barkovich and the Rutherford scoring system (14,15). The Weeke scoring system(16) is a comprehensive scoring system that assesses several different functional areas of the brain, including motor, visual, and memory. Complete and careful neurological examination remains of critical importance. In predictive models, time to improvement in stage and time to reach no or mild HIE were important predictors of death/disability (10). The advent of bedside aEEG allows neonatologists to continuously trend the background pattern and hence the degree of recovery alongside serial clinical examination during TH. In cases where clinical examination and EEG are in keeping with profound injury, and there is no sign of improvement over 24-48 hours, MRI brain does not add greatly to prognostication. However, MRI should be considered in this setting if the baby has received anti-epileptic medications, which may affect the reliability of both clinical examination and EEG findings.

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The term life-limiting condition refers to any illness for which there is no reasonable hope of cure and where the child is unlikely to survive beyond early adulthood(17). Many of these conditions cause a progressive deterioration leaving the child increasingly dependent on their family or carers. Such illnesses have been categorised into four categories (18). The fourth category includes conditions leading to severe disability and the likelihood of premature death, such as severe cerebral palsy and multiple disabilities following brain injury.

Decisions that involve the withdrawal or withholding of life-sustaining treatment should have the child's best interest as the central focus(7). A futile intervention is different from an intervention that is not pursued because it is not perceived to be in the overall best interests of the child. With shared decision-making, medical facts must be reflected alongside the family's preferences, values, and goals. Even when care is not futile, care may be against the child's best interests when the likely harms outweigh possible benefits (6). Perinatal palliative care input is paramount in the care of the term neonate with significant brain injury. Palliative care stages have been defined in the British Association of Perinatal Medicine Framework for Clinical Practice in Palliative Care(19). This describes a transition period from routine or intensive care to palliative care. Supportive care includes considerations for oral nutrition, hydration, and analgesia. The overall goal of palliative care is to achieve the best quality of life for patients and their families.

In conclusion, decisions around the futility of care and redirection to comfort measures for newborns with brain injury is a complex decision that should only occur following a process of shared decision-making involving all caregivers for the baby. Certainty about prognosis is not possible despite advances in medical care,

but clear and honest discussions with parents are paramount to the decision-making process. The involvement of palliative care physicians is recommended in patients with severe brain injury leading to a life-limiting condition.

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