Identification and management of birth asphyxia

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The pathogenesis of brain damage following hypoxic-ischaemic injury in the developing brain is complex and incompletely understood. However, noninvasive studies using 31P magnetic resonance spectroscopy (MRS) have shown that hypoxia-ischaemia followed by resuscitation leads not only to primary cellular injury during the period of the insult, but to a delayed secondary injury 24 to 48 hours later. The degree of later neurodevelopmental impairment is directly related to the severity of the secondary injury.

The interval between resuscitation from hypoxia-ischaemia and secondary injury has been investigated by several techniques. In infants suffering a hypoxic-ischaemic insult there is a derangement of cerebral vascular control, but no decrease in global cerebral perfusion. Measurements using the 113Xe clearance technique or near infrared spectroscopy have shown that cerebral blood flow is increased, although the normal response to changes in carbon dioxide is lost. Despite the high cerebral blood flow during this period, there is an accumulation of lactate within the brain, and there is a direct correlation between the severity of delayed cerebral injury and the concentration of lactate in the brain soon after birth.

Magnetic resonance imaging has also helped to demonstrate the process of brain injury. Soon after an insult, diffusion weighted images are abnormal, while conventional T1 and T2 images become abnormal some days later. It is also clear that brain injury and repair is a prolonged process: the concentration of Lactate remains high for many weeks in the brains of infants who develop neurodevelopmental impairment, and brain structure shows significant alterations, including both the development of atrophy distant from the original site of injury, and in some cases accelerated growth in areas of focal infarction.

The mechanisms of secondary injury are poorly understood, but probably involve cellular injury mediated by excess concentrations of excitatory neurotransmitters, free radical formation and lipid peroxidation, activation of immune mechanisms and removal of trophic factors which normally support cell survival. Recent studies have demonstrated that the mechanisms of programmed cell death are activated after hypoxia-ischaemia, and considerable proportion of cells die not by necrosis but by apoptosis.

The period between resuscitation from hypoxia-ischaemia and secondary injury offers the potential for therapeutic interventions to ameliorate delayed damage and concomitant neurodevelopmental impairment. Many potential interventions are being investigated, including drugs which block the actions of glutamate in the brain, growth factors such as insulin-like growth factor-1 which is a potent anti-apoptotic factor, and moderate hypothermia applied following resuscitation.

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