Outcome following preterm intraventricular haemorrhage – what to tell the parents

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Abstract

Despite advances in neonatal care and overall improved survival rates of preterm infants, intraventricular haemorrhage (IVH) remains an important cause of mortality and long-term neurodevelopmental morbidity in the preterm population. Counselling parents regarding possible outcomes following IVH can be very challenging, particularly as prognostication can be difficult in the early stages. This article gives an overview of the incidence, pathophysiology, clinical manifestations, treatment and classification of IVH. In addition, it reviews the currently available outcome data following IVH including recent publications on less severe IVH previously not thought to be of particular clinical significance. It includes best practice recommendations for parental discussions and decision-making.

Keywords cerebral palsy; extremely low birth weight; intraventricular haemorrhage; neuro-developmental outcome; post-haemorrhagic ventricular dilatation; prematurity

Background

With improvements in neonatal intensive care survival rates in preterm infants in most countries have shown continuous improvements over the last 25 years. At the same time the incidence of intraventricular haemorrhage (IVH) in preterm infants has reduced, most noticeably since the introduction of antenatal steroids. However, IVH remains an important cause of preterm mortality and long-term neurodevelopmental morbidity. It occurs in 20–30% of very low birth weight infants less than 1500 g, and is reported to be as high as 45% in extremely low birth weight infants less than 1000 g. IVH is relatively rare in term infants and usually occurs as a secondary complication in disease processes such as trauma, sepsis, hypoxic-ischaemic encephalopathy, coagulopathy or vascular malformations.

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Pathophysiology of intraventricular haemorrhage

IVH in preterm infants is different from IVH in term babies

Intraventricular haemorrhage in preterm infants occurs most commonly as a result of bleeding in the germinal matrix (GM). The GM is a highly cellular and vascularised area located over the head of the caudate nucleus just below the ependymal lining of the lateral ventricle. Within the GM new glial cell development and neurogenesis occurs. The GM blood vessels supply the high metabolic demand of this area. These vessels are only transiently required and they are very fragile hence prone to damage which results in bleeding. The GM starts to involute from 28 weeks gestational age onwards, regresses by 32–34 weeks gestational age, and is generally completely absent in term infants.

The fragility of the capillaries in the GM makes preterm infants vulnerable to the development of germinal matrix-IVH. Additional risk factors associated with IVH are male sex, lack of antenatal steroids, perinatal asphyxia, vaginal delivery, postnatal transport during the first three postnatal days, respiratory distress syndrome, early hypothermia, hypocarbia, pneumothorax, blood pressure instability, persistent ductus arteriosus, and sepsis, as well as thrombocytopenia and coagulation abnormalities. The proposed pathophysiological mechanisms for these are disturbances and rapid fluctuations in cerebral blood flow including impaired autoregulation, increased fragility of the GM, and bleeding diathesis.

IVH in term infants most commonly arises from the choroid plexus rather than the GM, which indicates that term and preterm IVH are separate entities with different pathophysiological mechanisms.

Clinical manifestations

Most intraventricular haemorrhages occur within 72 hours of birth, with more than half occurring during the first 24 hours. Clinical manifestations of IVH include sudden respiratory and cardiovascular instability accompanied by a sudden fall in haemoglobin, metabolic acidosis, bulging anterior fontanelle, agitation and seizures due to cerebral irritation. However, around 50% of infants remain relatively stable without obvious clinical signs.

Diagnosis and treatment

Diagnosis is most commonly made via bedside cranial ultrasound scan (USS). This is performed routinely for preterm infants in most neonatal units in the UK. This enables accurate timing of the onset of lesions and monitoring of their evolution to assist in final classification and prognostication. In our centre, we perform scans on day 1, 3, 7, 14 and 28, followed by a term-corrected scan. In cases of known IVH, more regular scanning may be indicated.

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No specific treatment exists for the management of IVH. Treatment largely consists of supportive management with correction of anaemia, thrombocytopenia and coagulation abnormalities, correction of acidosis, as well as respiratory and cardiovascular support, and treatment of seizures.

Classification of IVH

Papile and Volpe classification

Intraventricular haemorrhage is usually classified using either the Papile (1978) or Volpe (2008) grading systems, which range between grade I and grade IV IVH. The classification system is fully described and illustrated in Table 1. Papile's classification was developed in 1978 based on computer tomography findings, whilst at the time of publication of Volpe's classification, bedside cranial USS had been introduced in most centres. Ultrasound is reliable for the diagnosis of IVH. Sensitivity and specificity improve with more severe grades of IVH. To make a formal diagnosis of IVH, abnormalities must be correlated on both coronal and para-sagittal views. Findings on the left and right sides should be graded separately, and size, extent, and location of the lesions noted.

Grade IV IVH in both classification systems describes a parenchymal infarct, also called periventricular haemorrhagic infarction (PVHI). PVHI is a result of intraventricular blood compressing the terminal vein within the GM, causing congestion of the medullary veins, which leads to infarction of the adjacent white matter. Hence it should not be considered as a continuum of grades I–III IVH and the term PVHI is therefore used in this article. In practice however, it is often referred to as grade IV IVH. Following a PVHI the brain parenchyma affected is replaced by a porencephalic cyst over the subsequent weeks.

Incidence of IVH according to Papile classification

Most preterm infants do not have evidence of IVH. The incidence and severity of IVH decreases with increasing gestational age. The French national prospective EPIPAGE 2 cohort study recruited all infants born alive between 22 and 34 weeks' gestational age in 2011. The incidence of IVH among a sub-group of 3495 infants born between 22 and 31 weeks' gestational age was assessed using cranial USS, and lesions were classified according to Papile criteria. Sixty-four percent (n = 2193) had no IVH. Seventeen percent (n = 591) had grade I; 12% grade II; 3% grade III; and 4% had evidence of PVHI on cranial USS. This trend is corroborated by other studies. The EPIPAGE study also demonstrated that 25% of IVH consists of PVHI in babies born at 24–26 weeks' gestational age, yet PVHI makes up only 5% of all IVH at 30–32 weeks' gestational age. Table 2 summarises the incidence of severe IVH (grade III and PVHI) by gestational age.

Grading systems for intraventricular haemorrhage

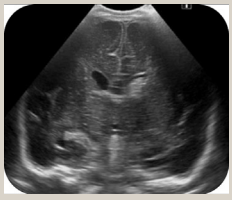
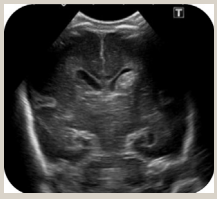
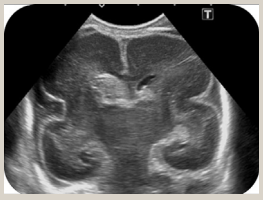
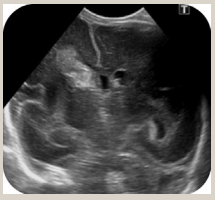
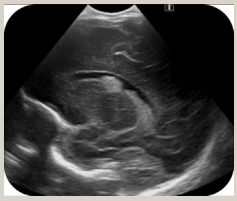
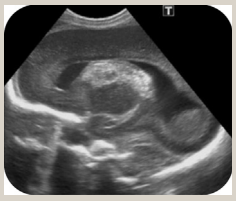
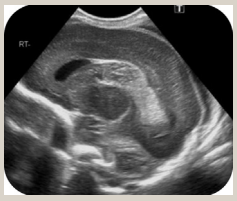
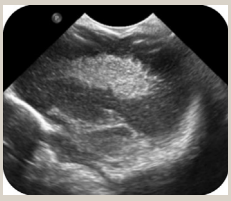
System	Grade			
	I	II	III	IV or PVHI
Papile et al., 1978	Subependymal haemorrhage	Intraventricular haemorrhage without ventricular dilatation	Intraventricular haemorrhage with ventricular dilatation	Intraventricular haemorrhage with parenchymal haemorrhage
Volpe et al., 2008	Germinal matrix haemorrhage with no or minimal intraventricular haemorrhage (<10% of ventricular area on para-sagittal view)	Intraventricular haemorrhage (10–50% of ventricular area on parasagittal view)	Intraventricular haemorrhage (>50% of ventricular area involved on parasagittal view; usually distends lateral ventricle)	Periventricular echodensity or periventricular haemorrhagic infarction (location and extent)
Coronal view on cranial USS				
Para-sagittal view on cranial USS				

Table 1

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