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Neonatal Prediction Of Late Neurodevelopmental Deficits

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Comprehensive long-term follow-up of graduates of newborn intensive care have shown that a small but significant number will have neurodevelopmental deficits that will ultimately result in disabilities. In the case of very premature (<32 weeks gestation) babies with a very low birth weight (<1500 g), about 10% - 15% have been reported to have deficits. Awareness of the plasticity of the infant brain and observations on affected children have confirmed that appropriate interventions beginning early and in the nursery and continuing into the classroom will reduce the likelihood of disabling secondary and primary deficits and improve the child's ability to function. At the other end of the scale, observations have also revealed that there is a subset of unfortunate survivors who appear to be beyond rehabilitation. Most of such children would, in the newborn period, have been critically ill and in receipt of extraordinary life-sustaining care. If the dismal outcome was reasonably certain, then the possibility of discontinuation of life-sustaining care could have been considered and effected. The benefits of identifying the neonate who is at risk for neurodevelopmental deficits are thus tremendous and at least two-fold.

The incidence of these neurodevelopmental deficits is most strongly associated with the identification of cerebral pathology in the newborn period. The advent of real-time cranial ultrasonography (US) about one and a half decades ago greatly facilitated the identification of cerebral pathology associated with later neurodevelopmental deficits. The lesions that are most commonly identified in prematures are periventricular haemorrhage (PVH), intraparenchymal echodensities (IPE), and periventricular leukomalacia (PVL).

The majority (50%) of the haemorrhagic lesions occur within a day of birth and only 10% occur after 72 hours of birth. As much as 40% of bleeds are however noted to progress over the first 3-5 days. The severity of the bleed is graded (I-IV) on the presence of blood in the germinal matrix in the coronal scan and on the amount of blood in the lateral ventricle on the parasaggital scan. Grading goes up to IV when there is intraparenchymal "extension". It is now believed that the "extension" is actually a bleed into an area of probably venous infarction, rather than an actual extension from the ventricle or the germinal matrix. It is therefore more appropriate that this "extension" be identified with its different etiology and consequence by separating it from the grading scheme and giving it the new name of intraparenchymal echodensity (IPE). The good correlation of US findings with pathological studies has enabled validation of the US for the diagnosis of germinal layer - intraventricular haemorrhage (IVH)[1].

In the case of ischaemic lesions, there is concern as the recognition and interpretation rely more heavily on the quality of the equipment, the timing of scanning and the operator's experience. As much as 70 % of periventricular white matter injury, presumed to be hypoxic-ischaemic, is missed by neonatal US[2]. The missed lesions are principally focal areas of necrosis (generally < 1.0 cm), diffuse gliosis and myelin loss. Specificity is decreased because echodensities in the posterior parietal and parieto-occipital regions, the most common site for PVL, are common in premature infants with no neuropathologic correlation. The magnitude of the intra and inter-reader non-reliability of the interpretation of cranial ultrasound for the diagnoses of subependymal, intraventricular haemorrhage and intraparenchymal echodensities was documented recently with the authors concluding that the resultant misclassification was unacceptable for the purposes of clinical research[3].

There are many reports on the long-term outcome of babies born in the early 1980s and who sustained GMH and/or IVH. Volpe (1994) concluded that the incidence of definite neurological sequelae in Mild, Moderate, Severe and Very Severe with periventricular haemorrhagic infarction are 5%, 15%, 35% and 90% respectively[4]. The prognosis was found to be refined further by considering the severity of the IPE[5]. When the IPE was extensive ie including the fronto-parietal-occipital regions, 81% died and the survivors had severe motor deficits with only 1 having an IQ greater than 80% of the mean. Among infants with localised IPE, only 37% died, and of the 15 survivors that could be studied, 10% had no motor or severe cognitive deficit. In the subset of 8 infants with localised and unilateral IPE, only 1 had a severe cognitive deficit. A more recent report revealed that unilateral localised lesions located in the frontal white matter had a more favourable outcome than those located in the parietal-occipital (trigonal) white matter[6].

The particular propensity for lesions affecting the posterior cerebral white matter to produce cerebral visual deficits has been documented in the recent literature[7].

The major long-term sequela of PVL is spastic

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diplegia with greater affection of the lower limbs than upper limbs. Particularly vulnerable is the preterm who is also small for gestational age[8]. When the diplegia becomes extensive ie with prominent upper extremity involvement, intellectual impairments become obvious. Of concern is the subtle intellectual deficits that might be predicted from the involvement of cerebral white matter containing fibres subserving association of visual, auditory and somesthetic functions and the overt visual perceptual deficits which can adversely affect cognitive function. In the series reported by Pharoah et al, moderate and severe mental retardation was present in 15% and 17% respectively of 81 former low birth weight children with spastic diplegia[9]. In the 956 children with spastic quadriplegia, the proportion with moderate and severe mental retardation rose to 21% and 54% respectively.

The degree of disability that results from a deficit is very much influenced by the physical, emotional and financial support that the child can receive from society because in most instances, the support needed will exceed the family's resources. Thus a deficit that will result in no disability in one family - society unit can, in another unit, be a source of much disability. Most reports of the extent of disability originate in societies that have had a long tradition of providing maximal support for children with neuro-developmental deficits. Physicians and counsellors need to be cognizant of this when prognosticating on the basis of published reports.

The possibility of increasing the reliability of prediction of neurodevelopmental deficits is being extensively studied. However, no one single measure has been able to achieve the sensitivity and specificity that cranial US is able to attain. The addition of serial ultrasound doppler measurements of CBFV did not improve the prediction of outcome obtained by using ultrasound imaging alone[10]. Likewise, MRI at 44 weeks post-menstrual age did not result in better reliability[11]. Boal, in a recent paper, reported that routine delayed (second week) US when compared to early (first week) US resulted in a decrease in the number of scans per patient, a decrease in the number of patients with questionable PVL and no change in the incidence of the major and minor abnormalities[12]. The disadvantage though of late screening will be the loss of the opportunity of parents to opt for the discontinuation of extraordinary care in their babies with extensive IPE or PVL. This is because once such babies survive into the third week, they are usually able to survive without life support systems and go on to live with major deficits and disabilities at a tremendous cost to the family and society.

In looking at published risk figures, the neonatologist is immediately concerned of their universal applicability. Can the risk for deficits with a certain cerebral lesion be the same all over the world and can it be the same today as it was 15 years ago? There has been an overall improvement in all aspects of foetal and neonatal care of the premature newborn. Nevertheless this level of care is not uniformly available or present in many centres. Thus, inadequacies in the management during the acute stage and in the management of the other system pathology (eg hypoglycaemia, hyperbilirubinaemia, protein calorie malnutrition, will most certainly bring further insults to the brain.

In the climate of meritocracy and competitiveness that developing societies like ours are in, the presence of even minimal deficits could translate into major disabilities especially if undiagnosed or inadequately managed. Most parents have only 2 or less children and they have great expectations of their children. There is also increasing parent awareness of prognostic factors, the need and value of intervention and rehabilitation programmes and a desire to have a significant say in the care extended to their child. Therefore there is a necessity to promptly and accurately identify the presence of cerebral pathology and to be able to offer the risks for the development of deficits and their long-term effects, particularly on scholastic achievement and social integration. These risks further need to be based on the local experience and not on the experience in other societies. Thus all newborn intensive care units should possess this ability and also have a system of ensuring that parents are brought into the knowledge of the state of their child and allowed and encouraged to make an informed decision on the continuation or termination of extraordinary care or in the commencement of early rehabilitation. Failure to do so represents a major deficiency on the part of the neonatal team and can lead to litigation.

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