Sharks, ice cream, chickens and eggs in neonatal seizures

A DMCN reader queries the conclusions of a recent paper and commentary, and emphasises the value of EEG grading in neonatal hypoxic-ischaemic encephalopathy.

Sir,

I read with interest the paper by Kharoshankaya et al.1 and its accompanying commentary.2 They touch on the old and still unanswered question about the existence of seizure-induced brain injury. This problem has huge practical implications and pervades the everyday life of neonatologists, neurologists, intensivists, and neurosurgeons.

As also observed in similar studies of older children with hypoxic-ischaemic and other encephalopathies,3 Kharoshankaya et al. found that total seizure burden was independently associated with abnormal neurodevelopmental outcomes. They claim that their results ‘indicate that, in hypoxic-ischemic encephalopathy, a high accumulation of seizures plays a more significant role for long-term developmental outcome than the presence of seizures per se.’1

An independent association does not necessarily mean that electrographic seizures themselves have a direct causal role in brain injury or worse neurodevelopmental outcomes. Another view would be that an independent association could suggest that the electrographic grading is a more reliable marker for worse outcomes than the clinical grading.

The authors cite evidence supporting the notion of seizure-induced brain injury. However, designing clinical studies is extremely difficult or even impossible, considering that you will never know if more frequent, prolonged, or refractory seizures are the cause or just a marker of a more severe brain insult. The animal models are far from emulating a real clinical scenario of seizures coming from an intrinsically dysfunctional brain, considering that in most of them a potentially harmful agent is used to produce seizures. Similarly, evidence supporting that seizures themselves lead to signal MRI abnormalities is fragile.4

Current available evidence does not rule out any of the following hypotheses about the existence of seizure-induced excitotoxicity (SIE): (1) SIE always occurs if duration and/or frequency of the abnormal electrical activity reach a threshold; (2) SIE never occurs; and (3) SIE does occur if an underlying condition is present as a hypoxic–ischaemic or metabolic insult, hereditary, or acquired ion channel dysfunction.

An alternative to the ‘shark and ice-cream metaphor’2 would be the ‘chicken or the egg’ causality dilemma.

Before these issues are elucidated, the old precept of non-maleficence should be contemplated in the management of electrographic seizures in the neonatal encephalopathy.

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REFERENCES


