When should term or preterm neonates with convulsions be treated with drugs (phenobarbitone, phenytoin, clonazepam or midazolam) and when should these be stopped?

The duration of convulsions or seizures in the neonate may be brief and the signs subtle, making it difficult to decide when drug treatment should be started and stopped. As a generalisation, most neonatologists treat if more than 3 brief seizures occur in an hour, or a single seizure lasts more than 3 minutes (Rennie, 1999).

Neonatal convulsions are resistant to most standard antiepileptic drugs (Sankar, 2005; Booth, 2004; Zupanc, 2003), with, for example, phenobarbitone being effective as a first-line treatment in only around one-third of cases (Rennie, 2003). A study in 59 neonates comparing phenobarbitone and phenytoin (Painter, 1999) found that the two drugs were equally effective, but that each failed to control seizures in more than half of cases when administered alone. Failure is often associated with a significantly abnormal background EEG (Boylan, 2002).

Phenytoin as a second-line treatment is generally more effective than a benzodiazepine, although large evaluation studies are lacking (Rennie, 2003). Clonazepam is effective in stopping seizures in doses as low as 0.1 mg/kg (Andre, 1986). Nasal midazolam stopped 122 of 125 seizures (98%) within 10 minutes (average 3.6 min) in a small study involving 26 children both in and out of hospital (Jeannet, 1999). In another study, in 6 neonates whose convulsions were refractory to high-dose phenobarbitone and phenytoin (Sheth, 1996), midazolam controlled the seizures in all 6 within 1 hour.

In a small retrospective study (Brod, 1988), a normal EEG was found to be a reliable predictor for discontinuing drug treatment in 18 of 22 term infants and 9 of 10 premature infants. As long-term use of phenobarbitone is associated with impaired cognitive function in infants and toddlers, and the risk of recurrent seizures is less than 10% in the absence of neurologic damage, early discontinuation of treatment is advisable (Hellstrom, 1995; Gal, 1985; Labrecque, 1984). Continuing evidence from animal studies confirms that increased apoptotic neurodegeneration occurs in the developing brain after exposure to phenytoin and benzodiazepines as well as phenobarbitone (Rennie, 2007).


Sankar R, Painter MJ. Neonatal seizures: after all these years we still love what doesn’t work. Neurology 2005;64:776-7


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