LETTER TO EDITOR (VIEWERS' CHOICE)

MANAGEMENT OF STATUS EPILEPTICUS IN PYRIDOXINE DEPENDENT SEIZURES (PDS)

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A boy was born at term vaginally and had birth weight of 2.35kg with low Apgar scores. At 2 hours of life the child had refractory seizures which were controlled only after intravenous pyridoxine. Electroencephalogram (EEG) done at day 10 of life showed spikes originating from both temporal areas. MRI brain was suggestive of normal myelination. Repeat EEG after 3 weeks was normal. The child was put on phenobarbitone, phenytoin, levetiracetam and 100 mg oral pyridoxine. The child had significant developmental delay. Since the child was seizure free since the neonatal period, to confirm pyridoxine dependency as per the criteria proposed by Baxter et al (1), we decided to stop pyridoxine in this case. Two weeks after stopping pyridoxine, the child was brought in status epilepticus which were not controlled with conventional anticonvulsants and aborted only after administration of 100 mg of IV pyridoxine. No EEG monitoring was done. The child was restarted on 100mg oral pyridoxine. Six months later this child again presented with status epilepticus after an episode of viral fever inspite of regular oral pyridoxine and this time also, responded only after IV pyridoxine was given. Subsequently the maintenance dose of oral pyridoxine was increased to 150 mg per day.

Pyridoxine dependent seizure (PDS) is a rare autosomal recessive disorder, localized to chromosome 2q31. (2) It results from an abnormality of the enzyme glutamic acid decarboxylase (GAD), which results in pyridoxine dependent reduced synthesis of the inhibitory neurotransmitter gamma amino butyric acid (GABA) from glutamate. Mutation in ALDH7A1 is known to cause PDS. (3) Elevated concentrations of pipecolic acid in plasma and CSF, elevated urinary concentration of α-aminoadipic semialdehyde (AASA) are shown to be associated with PDS. (3) The clinical features are varied. The full range of symptomatology is unknown. (2)Classically seen in neonatal period but may be seen in later age group too and may be associated with autism, breath holding spells and severe mental retardation. (2) Other reported features include hepatomegaly, bilious vomiting, transient visual agnosia, squint, severe articulatory apraxia, motor dyspraxia and microcephaly. Most common seizure type is generalized tonic clonic seizures that progress to status epilepticus. Other types of seizures reported in the literature include brief partial seizures, atonic and myoclonic seizures and infantile spasms. (4) Criteria for the diagnosis of pyridoxine-dependent epilepsy include (i) seizures resistant to traditional antiepileptic therapy and cessation of clinical seizures with administration of parenteral or oral pyridoxine, (ii) complete seizure control on pyridoxine monotherapy, (iii) recurrence of seizures upon pyridoxine withdrawal; and (iv) no clinical evidence of pyridoxine deficiency. (4) Baxter et al (1) have proposed new criteria. Definite cases have recurrent (two or more) seizures of any type that (i) cease within seven days of the administration of oral pyridoxine (usual dose, 30 mg/kg/day; minimum dose, 15 mg/kg/day; maximum dose 50 mg), (ii) recur when pyridoxine supplementation is withdrawn, and (iii) cease again when pyridoxine is given as above.

The case highlights the fact that pyridoxine dependent seizures can recur within 2 – 23 days of stopping pyridoxine (5) and there can be break through seizures despite maintenance doses of pyridoxine (Vitamin B6) during febrile period. (1) The exact dose of vitamin B6 is still debated. There is a relatively wide range for the daily B6 dose necessary to control the seizure i.e., 10-200 mg/day. In the literature doses as high as 680 mg initially and 200 mg/day subsequently have been reported. (6)Studies show that the dose of vitamin B6 required to normalize the cerebrospinal fluid (CSF) glutamate is 10mg/kg/day than the dose required to control seizures, and the higher dose to achieve normal glutamate level was associated with a normal developmental outcome and improvement in the motor/performance subscale. (7,8)

To conclude, bolus parenteral pyridoxine should be given in all cases of PDS if they present with breakthrough seizures and maintenance dose should be increased. Since measurement of CSF glutamate levels may not be feasible, clinical judgment should be used while deciding on the dose.

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References :

1. Baxter P. Epidemiology of pyridoxine dependent and pyridoxine responsive seizures in UK. Arch Dis Child 1999; 81: 431-433
2. Burd L, Stenehjem A, Fraceschini LA, Kerbeshian J. A 15 year follow up of a boy with pyridoxine-dependent seizures with autism, breath holding and severe mental retardation. J Child Neurol. 2000; 15: 763-765
3. Gospe SM. Pyridoxine –dependent seizures: new genetic and biochemical clues to help with diagnosis and treatment. Curr Opin Neurol. 2006; 19:148-153
4. Mikati MA, Trevathen E, Krishnamoorthy KS, Lombroso CT. Pyridoxine-dependent epilepsy: EEG investigations

and long-term follow-up. Electroencephalography Clin Neurophysiol 1991; 78: 215-222.
5. Goutieres F, Aicardi J. Atypical presentations of pyridoxine-dependent seizures: a treatable cause of intractable epilepsy in infants. Ann Neurol 1985 ;17: 117-120
6. Clarke TA, Saunders BS, Feldman B. Pyridoxine-dependent seizures requiring higher doses of pyridoxine for control. Am J Dis Child 1979; 133: 963-965.
7. Baumeister FAM, Gsell W, Shin YS, Egger J. Glutamate in pyridoxine-dependent epilepsy. Neurotoxic glutamate concentration in cerebrospinal fluid and its normalization by pyridoxine. Pediatrics 1994; 94: 318-321
8. Baxter P, Griffiths P, Kelly T, Gardner-Medwin D. Pyridoxine-dependent seizures: demographic, clinical, MRI and psychometric features, and effect of dose on intelligence quotient. Dev Med Child Neurol 1996; 38: 998-1001

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