

## **Pyridoxine Dependent Seizures**

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Pyridoxine dependency is a rare cause of seizures. Pyridoxine dependent seizures (PDS) occur despite normal vitamin B6 levels and is due to defective binding of pyridoxine to its apoenzyme, glutamate decarboxylase, which converts glutamic acid to gamma aminobutyric acid (GABA). The reduced concentrations of GABA result in lowered seizure threshold. Typically PDS occur within hours of birth and are unresponsive to anticonvulsant drugs but are controlled within minutes of intravenous pyridoxine administration. The mental development is usually impaired. Hunt, *et al.*(1) described the first case of PDS with autosomal recessive inheritance. Since then several cases have been reported with onset of seizures after neonatal period(2-6). This study was undertaken to determine the prevalence of PDS in children between the age of 1 month to 5 years.

### **Subjects and Methods**

One hundred and twenty patients, from 1 month to 5 years of age, with repeated and intractable seizures, who presented to us between September 1986-and September 1994 were studied. Children with seizures that were not controlled with phenobarbitone, carbamazepine, sodium

valproate and phenytoin in full therapeutic dosage and those with more than two episodes of status epilepticus were included. Patients with seizures secondary to head injury, meningitis, *etc.* were not included. All patients received pyridoxine either orally (50 to 100 mg twice daily) or by intravenous route (100 to 200 mg). Only 2 cases were diagnosed as PDS on the basis of response to pyridoxine administration, while the remaining 118 did not show any response.

*Case 1.* This apparently normal boy presented with an episode of convulsions and fever at 2½ years of age. The antenatal and neonatal periods were uneventful. Results of physical examination and all routine investigations were normal. A diagnosis of febrile convulsions was made. At 3 years of age he had status epilepticus, which was controlled by intravenous diazepam. All investigations including CT scan of the head were normal. The patient was seizure free on treatment with carbamazepine for only 4 weeks, when he started having 3-4 attacks of seizures per day. Subsequently other anti-convulsants like valproic acid, phenytoin and phenobarbitone were given in various combinations without any benefit. Following treatment with pyridoxine in a dose of 50 mg twice daily orally in addition to phenytoin and phenobarbitone, the seizures were controlled within 2 days. Phenobarbitone was stopped after 2 weeks and phenytoin after 2 months while pyridoxine was continued. He remained asymptomatic with normal mental development for one year while on pyridoxine therapy. Inadvertent stoppage of pyridoxine resulted in status epilepticus, which responded immediately to intravenous administration of pyridoxine in the dosage of 100 mg. The parents were advised to continue treatment with pyridoxine. At the age of 5 years the child showed normal mental development and was attending a normal school.

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*Case 2.* An 18-month-old girl with hypertonia of all the four limbs and severe degree of mental retardation was admitted with a history of repeated seizures, 2-4 attacks per day since the age of 2 months. The head circumference was 43 cm. She was previously treated with phenobarbitone, phenytoin, valproic acid and carbamazepine in various combinations without control of seizures. The antenatal and neonatal history was uneventful." The CT scan showed atrophy of cerebral cortex and EEG showed features of generalized seizures. All other investigations including CSF examination, and blood levels of sugar and calcium were within normal limits. Following treatment with oral pyridoxine in a dose of 50 mg twice daily the seizure frequency reduced and within one week the patient was seizure-free. All other anticonvulsants were tapered off and pyridoxine continued. On stopping treatment . with pyridoxine, the seizures recurred, but responded to intravenous administration of pyridoxine. At 3 years of age, the patient was seizure-free but the mental and motor development was markedly delayed.

### Discussion

PDS is characterized by onset within a few hours of birth; unusual fetal movements, may even suggest intrauterine

seizures(7,8). The combination of meconium staining, hypotonicity and seizures may often be misdiagnosed as due to perinatal asphyxia(9). PDS may initially respond to anticonvulsants(10) which may delay the diagnosis. PDS may occasionally present after the neonatal period(2-5). Goutieres and Aicardi(2) suggested that the diagnosis of PDS should be suspected , in children with convulsions starting in the first 18 months of life especially in those with: (i) no abnormal perinatal history, (ii) history of a severe convulsive disorder, often leading to death during status epilepticus in a previous sibling, (iii) consanguineous marriage, (iv) long lasting focal or unilateral seizures, often with preservation of consciousness and (v) irritability, restlessness, crying and vomiting preceding the actual seizures.

The diagnosis of post neonatal PDS was confirmed in our patients by the control of seizures within minutes of intravenous injection of pyridoxine and seizure-free period while taking pyridoxine.

The present study serves as a reminder to pediatricians that PDS must be suspected in patients with intractable seizures. A trial of pyridoxine therapy must be given in children with poorly controlled seizures or those with a family history of similar disorders.

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**NOTES AND NEWS**

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