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Letter to the Editor

Comments on 'Infantile hypophosphatasia without bone deformities presenting with severe pyridoxine-resistant seizures' in Molecular Genetics and Metabolism' 2014 Mar;111(3):404-7 by M.G. de Roo, N.G. Abeling, C.B. Majoie, A.M. Bosch, J.H. Koelman, J.M. Cobben, M. Duran, B.T. Poll-The

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Recently a case of an infantile hypophosphatasia (HPP) patient was published [1]. We would like to report supplemental data that were collected during the first 2 months of his life, when patient was admitted at our neonatal ward because of seizures.

After a first period of seizures, successfully treated with a single gift of phenobarbitone, pyridoxine and midazolam, patient went home at day 7.

At day 21 the patient was readmitted because of tonic seizures. After diagnosis of HPP, seizures were treated with pyridoxine without any effect. Levetiracetam was started, resulting in seizure freedom. However, 3 days after the start of pyridoxine treatment breath holding spells with severe desaturations occurred, which proved to be non-epileptic. Only treatment with high dose midazolam could stop these spells, but required mechanical ventilation. No other cause for the breath holding spells could be identified.

In the paper of de Roo et al. [1], the results of the metabolic investigation after long term pyridoxine treatment and at the end of the encephalopathic process are shown. In Table 1, we show the results of B6 vitamers and neurotransmitter levels in plasma and cerebral spinal fluid before and 5 weeks after the start of pyridoxine administration. We did not find any abnormalities in the levels of the neurotransmitters in the CSF. Before start of pyridoxine already high levels of pyridoxal-5′-phosphate (PLP) were present, suggesting that there was no functional shortage of PLP in the brain at the start of the seizures. It is therefore uncertain whether treatment with pyridoxine had any beneficial effect in this patient. This

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Table 1
Phosphoethanolamine (PEA), alkaline phosphatase (ALP), B6 vitamers, neurotransmitters, GABA and serine levels in plasma, cerebral spinal fluid (CSF) and urine before and after administration of pyridoxine.

Metabolite	Units	Before start pyridoxine maintenance therapy (day 21 of life)						After 5 week pyridoxine maintenance therapy (8th week of life)			
		Plasma	Reference values	CSF	Reference values	Urine	Reference values	Plasma	Reference values	CSF	Reference values
PEA	(μmol/mmol creat or μmol/L)			264	0–5	1202	5–45	36	0–5		
ALP	(U/L)	<5	100–360								
PLP	(nmol/L)	4082	54–136	111	13–22			45700	26–191	1820	13–22
PA	(nmol/L)			0.3	1.0–6.4			4000	11–60	196	1.0–6.4
PMP	(nmol/L)			nd	nd			nd	nd	nd	nd
PL	(nmol/L)			nd	16–36			5840	8–41	2120	16–36
PN	(nmol/L)			nd	nd			24	nd	724	nd
PM	(nmol/L)			nd	nd			nd	nd	nd	nd
HVA	(nmol/L)			1045	300–1250					399	300–1250
5-HIAA	(nmol/L)			954	200–1200					478	200–1200
3-OMD	(nmol/L)			243	24–245					63	24–245
GABA (free)	(nmol/L)			12	17–67						
GABA (total)	(nmol/L)			4810	4200–13400						
D-serine	(μmol/L)			7	4.6–34						
L-serine	(μmol/L)			49	37–96						

Abbreviations: PEA = phosphoethanolamine, ALP = alkaline phosphatase, PLP = pyridoxal-5′-phosphate, PA = pyridoxic acid, PL = pyridoxal, PN = pyridoxine, PMP = pyridoxamine-5′-phosphate, PM = pyridoxamine, HVA = homovanillic acid, 5-HIAA =5-hydroxyindole acetic acid, 3-OMD = 3-O-methyldopa, GABA = gamma aminobutyric acid, nd = not detectable.

is important, since pyridoxine administration can also be deleterious and cause encephalopathy and polyneuropathy [2].

Therefore, we would strongly recommend the measurement of PLP and other B6 vitamers in the CSF of patients presenting with infantile HPP before supplementation of pyridoxine is considered.

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