ELSEVIER

Brain & Development 33 (2011) 379–383

BRAIN & DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Original article

Effectiveness and safety of non-intravenous high-dose phenobarbital therapy for intractable epilepsy during childhood

Kenjiro Kikuchi [a,b,*], Shin-ichiro Hamano [a], Tomotaka Oritsu [a], Reiko Koichihara [a], Manabu Tanaka [a], Motoyuki Minamitani [a], Hiroyuki Ida [b]

[a] *Division of Neurology, Saitama Children's Medical Center, Japan*
[b] *Department of Pediatrics, Jikei University School of Medicine, Japan*

Received 12 February 2010; received in revised form 22 July 2010; accepted 23 July 2010

Abstract

High-dose phenobarbital (PB) therapy is effective for refractory status epilepticus. We reviewed medical records of patients with intractable partial epilepsies on whom performed non-intravenous high-dose PB therapy. Thirteen patients received PB rectally or orally at a dosage of 20–30 mg/kg/day initially, and the PB dosage was gradually reduced to a maintenance dosage of 5–10 mg/kg/day orally. We evaluated the effectiveness and safety of this procedure after 14 days at the maintenance dosage level. Twelve patients had partial seizures and one had secondary generalized seizures. In six of 13 patients (46%), seizure frequencies decreased more than 50%, and two of 13 patients (15%) became seizure free. In five of seven patients who were treated by continuous midazolam infusion therapy, we were able to discontinue the midazolam therapy. Adverse effects were found in seven of 13 patients. We were able to continue high-dose PB therapy in six patients because their adverse effects were transient and improved after a decrease in PB concentration, but we discontinued this therapy in the patient who developed Stevens–Johnson syndrome. Respiratory depression and hypotension were not found in our study. We conclude that high-dose PB therapy is effective and may be considered as an additional treatment for intractable partial epilepsy in childhood.

Keywords: High-dose phenobarbital therapy; Intractable partial epilepsy; Status epilepticus; Non-intravenous; Stevens–Johnson syndrome

1. Introduction

High-dose phenobarbital (PB) therapy, usually given intravenously, is effective for refractory status epilepticus [1,2]. In Japan, where intravenous PB therapy was not available until October 2008, there were some reports that non-intravenous high-dose PB therapy was effective for refractory status epilepticus [3–5]. In these reports, PB was given intramuscularly, rectally, or orally during high-dose PB therapy.

Only a few anecdotal studies reported that non-intravenous high-dose PB therapy was effective for intractable epilepsy in childhood as an additional therapy [6,7]. We performed non-intravenous high-dose PB therapy for intractable partial epilepsies during childhood, and evaluated the effectiveness and safety of this therapy.

2. Methods

We reviewed medical records of patients on whom non-intravenous high-dose PB therapy performed between January 1994 and July 2008 at Saitama Children's Medical Center, Saitama, Japan. Intractable partial epilepsy in this study was defined that epileptic partial seizures occurred daily even though we treated

* Corresponding author at: Division of Neurology, Saitama Children's Medical Center, 2100 Magome, Iwatsuki-ku, Saitama-city, Saitama 339-8551, Japan. Tel.: +81 48 758 1811; fax: +81 48 758 1818.
E-mail address: kikuchi.kenjiro@pref.saitama.lg.jp (K. Kikuchi).

0387-7604/$ - see front matter © 2010 The Japanese Society of Child Neurology. Published by Elsevier B.V. All rights reserved.
doi:10.1016/j.braindev.2010.07.009

Table 1
Patients' characteristics, outcome, and adverse effects in high-dose PB therapy.

Case	Sex	Age at high-dose PB therapy	Past history and/or complications	Seizure type (manifestations)	Concomitant AEDs	Duration of high-dose PB therapy (days)	PB serum levels at evaluation (μg/ml)	Seizure outcome	Adverse effect
1	F	2 mo	Neonatal asphyxia, mutlicystic encephalomalacia, West syndrome, MR	Tonic posturing of the legs, myoclonus of the arms	VPA	29	53	Effective	No
2	M	10 mo	MR	Rolling up of the eyes, apnea, clonic movements of the arms	CLB, ZNS, MDL infusion	21	69	Effective (seizure free)	Drowsiness
3	F	11 mo	Subcortical band heterotopia, MR	Head rotation to the right, tonic posturing of the arms	PHT, VPA	21	66	Effective (seizure free)	Drowsiness
4	M	4 yr 7 mo	MR	Rolling up of the eyes, tonic posturing of the arms	AZA, CZP, PRM, MDL infusion	24	38	Effective	No
5	F	5 yr 10 mo	Huntington disease, MR	Clonic movements of the arms	CBZ, VPA, MDL infusion	18	71	Effective	No
6	F	6 yr 9 mo	Acute encephalopathy, MR	Oral automatism, deviations of the eyes to the right	AZA, PB[b], PHT, MDL infusion	50	82	Effective	Emotional instability
7[a]	M	1 mo	Neonatal asphyxia, MR	Rolling up of the eyes, tonic posturing of the arms	MDL infusion	30	44	Not effective	No
8	M	3 mo	West syndrome, MR	Tonic posturing of the legs	MDL infusion	31	54	Not effective	No
9	M	5 mo	MR	Rolling up of the eyes, tonic posturing of the arms	PHT, VPA	41	27	Not effective	Drowsiness
10	F	8 mo	West syndrome, MR	Rolling up of the eyes	PHT	22	50	Not effective	Drowsiness
11	M	1 yr 7 mo Hypersecretion of saliva	West syndrome, MR	Clonic movements of the arms, oral automatism	CLB, VPA, ZNS	21	40	Not effective	
12	F	9 yr 7 mo	MR	Loss of consciousness,	CLB, ZNS, PB[b]	18	32	Not effective	No
13	M	11 yr 10 mo	MR	Tonic posturing of the arms, secondary generalization	CLB, PHT, TPM, VPA, MDL infusion	8	ND	Aborted	Stevens–Johnson syndrome, liver dysfunction

AEDs, antiepilptic drugs; AZA, acetazolamide; CBZ, carbamazepine; CLB, clobazam; CZP, clonazepam; F, female; M, male; MDL, midazolam; MR, mental retardation; MRI, magnetic resonance imaging; ND, not done; mo, month; PB, phenobarbital; PHT, phyntoin; PRM, primidone; TPM, topiramate; VPA, valpric acid; yr, year; ZNS, zonisamide.

[a] All cases, except Case 7, were received rectal high-dose PB therapy initially. Only Case 7 was received oral high-dose PB therapy initially.

[b] PB was administered orally at standard dose.