

# Appropriateness of Intravenous Loading Dose of Phenytoin Treatment in Srinagarind Hospital

Somsak Tiamkao MD\*, Numthip Chitravas MD\*,  
Suthipun Jitpimolmard MD\*, Kittisak Sawanyawisuth MD\*

\* Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen

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*Intravenous loading dose of phenytoin treatment (ILP) is a useful treatment but may cause serious adverse events. The present study assessed the appropriate use of ILP in Srinagarind Hospital. The authors reviewed all charts that ILP was ordered between January 1<sup>st</sup>, 2000 and December 31<sup>st</sup>, 2001, about indication, the infusion rate, and side effects. There were 206 cases treated with ILP. Thirty-two cases (15.7%) received inappropriate treatment by ILP. The most common indication was primary prophylaxis before brain surgery. There were 7 cases that developed side effects with 5 cases of high blood phenytoin level. These data showed that physicians should consider more carefully the use of ILP.*

**Keywords:** Phenytoin, Intravenous loading antiepileptic drug, Antiepileptic drug

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Phenytoin is an effective and widely used antiepileptic drug. On the other hand, it has a narrow therapeutic range and many side effects such as skin rash, hepatitis, cardiac arrhythmia, hypotension, and even seizures. An oral loading dose of phenytoin is now well established, as is its effectiveness, and seems to be safer and cheaper<sup>(1,2)</sup>. The present work studied the incidence of misuse of intravenous loading dose of phenytoin treatment (ILP) in Srinagarind Hospital.

## Material and Method

The authors reviewed all adult patients (age  $\geq 15$  years) who were prescribed ILP in Srinagarind Hospital (Khon Kaen University, Khon Kaen, Thailand) between January 1<sup>st</sup>, 2000 to December 31<sup>st</sup>, 2001. ILP is the infusion of phenytoin 10-15 mg/kg intravenously with the rate of infusion is not more than 50 milligram/minute. The indications of ILP<sup>(3-8)</sup> are status epilepticus, cluster of seizures or premonitory stage on status epilepticus, can not take phenytoin orally, or primary prophylaxis before brain surgery. The therapeutic range is 10-20 microgram/ml<sup>(6)</sup>. The authors studied patient characteristics, department of services, information of phenytoin treatment (indication, rate of infusion, and

solvent), side effects of phenytoin, and phenytoin level (in case of toxicity). In each case of inappropriate use of ILP, charts were reviewed by two neurologists.

## Results

There were 206 patients who received ILP. Of these, 117 cases were male (56.8%) and 89 cases were female (43.2%). Mean age was  $43.9 \pm 18.3$  years. Surgical and Medical ward were the most two common place of administration of ILP (51.5% and 35.9 %, respectively). The other places were emergency unit, otolaryngology, orthopedic, and psychiatric ward. ILP was commonly used in brain tumor cases (Table 1) and prescribed in 118 convulsive patients (57.2%). Primary generalized tonic-clonic seizure (GTC) was the commonest type of seizures (Table 2). One hundred and seventy four cases (84.5%) were treated with appropriate indication (Table 3). The other 32 cases (15.5%) were inappropriate use of ILP (Table 4). Twenty-two cases needed no antiepileptic agent (12 had no seizure and no brain surgery, 9 were metabolic seizures, 1 was pseudoseizure). One patient received phenytoin in dextrose water with an infusion rate of more than 50 milligram/min. The two most common doses were 750 mg (59.7%) and 600 mg. Seven patients (3.4%) who had serious side effects or phenytoin overdose are described in Table 5. Two of seven patients had

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Correspondence to : Tiamkao S, Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand. E-mail: [somtia@kku.ac.th](mailto:somtia@kku.ac.th)

**Table 1.** Diagnosis of ILP cases

Etiology	Number (Percentage)
Brain tumor	79 (38.3%)
Cerebrovascular accident	69 (33.5%)
Central nervous system infections	27 (13.1%)
Others	
Hypoxic-encephalopathy	10 (4.9%)
SLE with CNS vasculitis	8 (3.9%)
Cerebral concussion	3 (1.4%)
Metabolic disorder*	8 (3.9%)
No data	2 (1.0%)
<b>Total</b>	<b>206 (100%)</b>

\*Hypo/hyperglycemia 4 patients, hyponatremia 3 patients and hypercalcemia 1 patient

**Table 3.** Indications of ILP

Indications*	Number (Percentage)
Primary prophylaxis before brain surgery	79 (42.5%)
Can not take drug orally	76 (40.9%)
Cluster of seizure and premonitory-stage of status epilepticus	22 (11.8%)
Status epilepticus	9 (4.8%)
<b>Total</b>	<b>186 (100%)</b>

\* Some patients had more than one indication

**Table 5.** Side effect of ILP

Patient no.	Side effect	Blood level (microgram/ml)	Etiology	Indication
1	Hepatitis	29.28	Frontal lobe hemorrhage	Recurrent seizures
2	Seizure	65.92	Pituitary tumor	Primary prophylaxis
3	Skin rash	no data	Brain abscess	Primary prophylaxis
4	Drowsiness	49.79	CVA	Recurrent seizures
5	Seizure	49.44	Recurrent glioma	Primary prophylaxis
6	Seizure	30.00	Hyperglycemic seizure	Recurrent seizures
7	Skin rash	no data	Intracerebral hemorrhage	Primary prophylaxis

inappropriate indication for ILP. Neurological side effects such as seizure or alteration of consciousness were found in 4 cases.

### Discussion

Phenytoin is an antiepileptic drug that can

**Table 2.** Seizure types of ILP cases

Seizure types	Number (Percentage)
Generalized seizure	
Primary generalized tonic-clonic seizures	87 (73.7%)
Focal seizures	
Simple motor seizures	8 (6.8%)
Complex partial seizures	4 (3.4%)
Secondarily generalized tonic-clonic seizures	11 (9.3%)
Unclassified	8 (6.8%)
<b>Total</b>	<b>118 (100%)</b>

**Table 4.** Causes of inappropriate use of ILP (N = 32)

Causes	Number (Percentage)
Need no antiepileptic drug	22 (68.8%)
Primary prophylaxis before brain surgery (no surgery)	12 (37.5%)
Metabolic seizure	9 (28.2%)
Pseudoseizure	1 (3.1%)
Can take drug orally	10 (31.2%)
<b>Total</b>	<b>32 (100%)</b>

control many types of seizures such as primary GTC, secondarily GTC, or partial seizure. It can be used as a once daily dose because of its long half-life. The therapeutic level is narrow because it has a kinetic saturation. If we use dextrose water is used as a solvent for phenytoin, it will be saturated. The rate of infusion

should be less than 1 milligram/kg of body weight/minute to prevent cardiac arrhythmia, hypotension, and thrombophlebitis. According to the presented data, ILP was used as the primary prophylaxis before brain surgery in 79 of the 206 cases (38.3%). This informed us that primary prophylaxis before intracranial surgery with ILP is still commonly used among neurosurgeons in Srinagarind Hospital, but these may be harmful<sup>(3,8)</sup>. The present study found serious side effects of phenytoin in 3 of 7 cases that got ILP in terms of primary prophylaxis. The inappropriate use of ILP in Srinagarind Hospital was 15.5%. The most common indication in this group was primary prophylaxis in cases that had intracranial lesion. At present, even if the patient had an intracranial lesion, antiepileptic drugs are not necessary<sup>(3)</sup> if they do not have any seizure attack. Furthermore, seizures caused by metabolic derangement i.e. hyperglycemia, hyponatremia, etc. also need no antiepileptic drug. In the present study, there were 9 cases that had metabolic derangement and received ILP. The authors found side effects as follows: 4 neurological symptoms, 2 skin rash and 1 hepatitis<sup>(6,9)</sup>. All events occurred between 7-15 days after treatment. Fluconazole can increase the phenytoin level<sup>(10)</sup> but antiretroviral drugs have the opposite effect<sup>(11)</sup>. The authors also found a pitfall in treatment of status epilepticus, which was the slow infusion rate (data not shown). This may use a longer time to control status epilepticus and may cause brain damage.

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## ความเหมาะสมในการใช้ยาพีในโตอินทางหลอดเลือดดำที่โรงพยาบาลศรีนครินทร์

สมศักดิ์ เทียมเก่า, นัทธิพย์ จิตรवासัน, สุทธิพันธ์ จิตพิมลมาศ, กิตติศักดิ์ สวรรยาวิสุทธิ

การใช้ยาพีในโตอินทางหลอดเลือดดำเป็นการรักษาที่มีประสิทธิภาพและมีประโยชน์แต่ก็สามารถทำให้เกิดผลข้างเคียงที่รุนแรงได้ การศึกษานี้ต้องการศึกษาความเหมาะสมในการรักษาดังกล่าวที่โรงพยาบาลศรีนครินทร์ ผู้ศึกษาได้ศึกษาบันทึกเวชระเบียนของผู้ป่วยที่ได้รับการรักษาด้วยยาพีในโตอินทางหลอดเลือดดำตั้งแต่วันที่ 1 มกราคม พ.ศ. 2543 ถึง 31 ธันวาคม พ.ศ. 2544 เกี่ยวกับข้อบ่งชี้ วิธีการบริหารยาและผลข้างเคียงที่เกิดขึ้น พบว่ามีผู้ป่วยจำนวน 206 รายที่ได้รับยาพีในโตอินทางหลอดเลือดดำ โดยผู้ป่วยร้อยละ 15.7 ได้รับการรักษาด้วยความไม่เหมาะสม ข้อบ่งชี้ที่พบบ่อยที่สุดคือการให้เพื่อป้องกันการชกก่อนการผ่าตัดสมอง มีผู้ป่วยจำนวน 7 รายที่เกิดผลข้างเคียงของยา โดย 5 รายมีระดับยาที่สูงเกินกว่าระดับที่เหมาะสม จากข้อมูลดังกล่าวบ่งชี้ว่าแพทย์ควรพิจารณาอย่างระมัดระวังถึงข้อบ่งชี้ในการรักษาผู้ป่วยโดยการให้ยาพีในโตอินทางหลอดเลือดดำ

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