THREE-DAY PHENYTOIN PROPHYLAXIS IS ADEQUATE AFTER SUBARACHNOID HEMORRHAGE

Sorayouth Chumnanvej, M.D.

Department of Neurosurgery, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts

Ian F. Dunn, M.D.

Department of Neurosurgery, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts

Dong H. Kim, M.D.

Department of Neurosurgery, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts

Reprint requests:
Dong H. Kim, M.D., Department of Neurosurgery, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115.
Email: dkim7@partners.org

Received, May 26, 2006.
Accepted, September 8, 2006.

OBJECTIVE: Phenytoin (PHT) is widely administered after subarachnoid hemorrhage, often for several weeks or months. In addition to known side effects, PHT use has been correlated with cognitive disability and poor outcome. To reduce the rate of PHT complications, we converted from a multi-week prophylactic regimen to a 3-day course of treatment. This study evaluates the changes in seizure rates and adverse events.

METHODS: From July 1998 to June 2002, 453 patients with spontaneous subarachnoid hemorrhage were treated. In the first 9 months, 79 patients were administered PHT until discharged from the hospital, unless a drug reaction occurred first. In the last 39 months, PHT was discontinued 3 days after admission (370 patients), unless there was a history of epilepsy (four patients). This study represents a retrospective analysis of prospectively collected data, with follow-up periods of 3 to 12 months after discharge.

RESULTS: The 3-day PHT regimen produced a statistically significant reduction ($P = 0.002$) in the rate of PHT complications. In the first period, seven (8.8%) out of 79 patients experienced a hypersensitivity reaction, compared with two (0.5%) out of 370 patients in the second period. The percentage of patients having seizures, both short- and long-term, did not change significantly. In the first period, the seizure rate during hospitalization was 1.3%; in the second period, it was 1.9% ($P = 0.603$). At an average follow-up period of 6.7 months, three (5.7%) out of 53 survivors in the first period experienced a seizure (including those who had a seizure during hospitalization). In the second period, 12 (4.6%) out of 261 survivors experienced a seizure at an average follow-up period of 5.4 months ($P = 0.573$).

CONCLUSION: A 3-day regimen of PHT prophylaxis is adequate to prevent seizures in subarachnoid hemorrhage patients. Drug reactions are significantly reduced, but seizure rates do not change. Short-term PHT administration may be a superior treatment paradigm.

KEY WORDS: Anticonvulsant, Arteriovenous malformation, Intracranial aneurysm, Phenytoin, Seizure, Subarachnoid hemorrhage

Neurosurgery 60:99-103, 2007 DOI: 10.1227/01.NEU.0000249207.66225.D9 www.neurosurgery-online.com

Up to 10% of patients have a seizure after subarachnoid hemorrhage (SAH) (8, 21). Seizures can increase intracranial pressure, cause hemodynamic instability, and diminish oxygen delivery (20). These are potentially harmful effects, particularly in the acute period. For these reasons, most neurosurgeons administer anticonvulsants after SAH, and many continue prophylaxis for weeks and even months (7, 12, 16, 22).

In the setting of SAH, phenytoin (PHT) is the preferred agent because it can be loaded intravenously. PHT use, however, is associated with adverse effects, such as fever or rash. Serious, life-threatening complications also occur. Examples include Stevens-Johnson syndrome, pancreatitis, hepatitis, leukopenia, and thrombocytopenia (2, 9, 13, 18). With prolonged use, a majority of patients will develop a side effect (19); up to 15% will develop a serious complication (14).

Recently, Naidech et al. (15) sought to correlate the amount of PHT exposure with outcome after SAH. They defined the "PHT burden" as the average serum PHT level multiplied by the number of days between the first and last measurements, up to a maximum of 14 days. In a series of 527 patients, the PHT burden was correlated with outcome after SAH using a multivariate model. They found a strong association between greater PHT exposure and poor neurological and cognitive outcome. They concluded that the PHT burden was an independent predictor of poor outcome.

Because of these findings, it may be better to limit anticonvulsant prophylaxis to a necessary minimum, especially because

most seizures occur with the ictus (7, 11, 20). To our knowledge, only one group has published results following a limited anticonvulsant protocol. In an article published in 1995, Baker et al. (1) classified patients with ruptured or unruptured cerebral aneurysms into categories of seizure risk. The "high-risk" patient had a previous seizure history, pre- or postoperative ischemic infarction, parenchymal clot, postoperative hematoma, or concomitant arteriovenous malformation resection. These patients received prolonged anticonvulsant prophylaxis. All other patients were "low-risk" and were treated for an average of 5.3 days after surgery. At an average follow-up period of 2.4 years, only 5.4% of patients in the low-risk group had experienced a seizure. Their recommendation was that "all low-risk patients with aneurysms receive no more than 7 days of anticonvulsant therapy, beginning with the loading dose the day before surgery." Furthermore, they questioned whether "this degree of anticonvulsant prophylaxis is even necessary."

When we began a neurovascular database in July 1998, we were able to systematically follow both patient outcomes and complications. After several months, it became evident that PHT toxicity was a major problem on our service. Because of the findings reported by Baker et al. (1), we altered our treatment protocol. In April 1999, we began to use PHT for a total of 3 days after admission in patients with SAH. We did not distinguish between high- and low-risk groups. Even patients who had experienced a seizure after SAH remained on this protocol. The only exceptions were patients with known epilepsy who were already on anticonvulsants. This report details our subsequent experience.

PATIENTS AND METHODS

Patient Population

From July 1998 to June 2002, 453 patients with spontaneous SAH, including those with associated intracranial hematomas, were treated by the senior author (DHK) at the University of Texas Health Science Center in Houston, Texas. Patients with traumatic SAH were excluded. The cause of SAH was mostly aneurysm rupture. A small number of patients had an arteriovenous malformation or no defined etiology. Only nine patients did not complete a follow-up visit 3 to 12 months after discharge.

For each patient, data were prospectively gathered by a research nurse or physician assistant. Demographic information, medical comorbidities, the nature of hemorrhage, noted vascular lesions, the timing and type of repair, and medical and surgical complications were noted and entered into a database in an ongoing manner. This study represents a retrospective analysis of prospectively collected data.

For this cohort, the average age was 54.3 years; 68.9% of patients were women. The ethnic backgrounds were as follows: 59.1% Caucasian, 17.8% African-American, 19.3% Hispanic, and 3.8% Asian. The average length of hospital stay was 13.3 days.

TABLE 1. Patient demographics for the two treatment periods[a]

	7/98–3/99	4/99–6/02
No. of patients	79	374
Age (yr)	53.2	54.4
Female (%)	67.9	69.2
Hypertension (%)	39.7	46.2
Cardiac disease (%)	16.6	13.8
Smoking history (%)	25.6	34.1
AN size (mm)	9.4	9.0
>20 mm (%)	11.8	12.0
Post. circulation (%)	10.4	10.6
H-H Grade 1,2	39.1%	32.6%
H-H Grade 3	31.9%	29.0%
H-H Grade 4	17.4%	20.8%
H-H Grade 5	11.6%	16.6%

[a] AN, aneurysm; Post, posterior; H-H, Hunt and Hess.

Period I: PHT Use during the Entire Hospitalization

In Period I, 79 patients were treated between July 1998 and March 1999. PHT was started or continued on admission. After loading with 1000 mg, the dosage was set at 100 mg three times per day and continued until discharge from the hospital or until a contraindication developed (allergic reaction or fevers of unknown etiology). In such instances, carbamazepine was administered instead of PHT. One patient with a history of epilepsy was already on anticonvulsants.

Period II: 3-Day Use of PHT

In Period II, 374 patients were treated between April 1999 and June 2002. After loading with PHT at admission (1000 mg), each patient received 100 mg three times per day for 3 days only. PHT was discontinued after 3 days and no anticonvulsant was administered unless the patient experienced a subsequent seizure. PHT dosages in both periods were maintained at 100 mg three times a day, and serum levels were not checked. Four patients in Period II had a history of epilepsy and were maintained on their baseline medication.

Statistical Analysis

The patient demographics for the two treatment groups were compared with analysis of variance. With α at 0.05, we calculated the power to detect a 5 or 10% difference in several demographic characteristics: age, male-to-female ratio, risk factors, such as smoking history and hypertension, and SAH severity as defined by the Hunt and Hess scale. Fisher's exact test or the χ^2 test was used to compare the rates of drug reaction, seizures, and mortality in the two treatment periods.

RESULTS

Table 1 shows the demographic comparison between the two groups. The average age, male-to-female ratio, and aneurysm

size were almost identical. In addition, the rates of comorbidities were similar. In Period I, 39.7% of patients had known hypertension and 16.6% of patients had cardiac disease; these rates were 46.2% and 13.8%, respectively, in Period II. The numbers of patients smoking was slightly higher in Period II (34.1 versus 25.6%). Similarly, the severity of SAH as defined by the Hunt and Hess grade was somewhat higher in the second group (note that this group had the shorter duration of PHT prophylaxis). Analysis of variance did not note statistically significant demographic differences in the two treatment groups. For the several factors tested, the power to detect a 5% difference was calculated to be a minimum of 74%; the power to detect a 10% difference was a minimum of 91%.

When the patient had an aneurysm in Period I, it was repaired with surgical clipping in 65 patients (82.3%) and endovascular coiling in five patients (6.3%). In Period II, the aneurysm was repaired by clipping in 306 patients (81.6%) and coiling in 41 patients (11.0%). For both periods, more than 95% of patients had aneurysm repair within 3 days of admission. The rate of surgical complications is noted in *Table 2*.

A statistically significant reduction ($P = 0.002$) was noted in the rate of drug reaction from the first period (seven out of 79 patients, 8.8%) to the second period (two out of 370 patients, 0.5%). These numbers only reflect patients with a hypersensitivity reaction, not drug intolerance. In the first period, four patients developed a rash and one patient developed hepatotoxicity. In two other patients, there were severe drug reactions (pancreatitis and leukopenia) with significant morbidity and prolonged hospitalization.

An additional 23 patients were switched to carbamazepine in Period I, usually because of persistent fevers without other etiologies (we had prospectively collected data on patients switched to other anticonvulsants but did not note the specific reason if a drug reaction was not the cause). Although some of these patients may have had a central fever, their temperatures often normalized 1 to 2 days after stopping PHT. Because we did not prospectively collect these data, we cannot comment on whether or not a higher percentage of patients had unexplained fevers in the first period. Anecdotally, the incidence of fevers seemed much lower once a short course of PHT was adopted.

The number of patients experiencing seizures did not change significantly (*Table 3*). In Period I, the seizure rate during hospitalization was 1.3%; in Period II, it was 1.9% ($P = 0.603$). Follow-up periods ranged from 3 to 12 months; the average was 6.7 months in Period I and 5.4 months in Period II. At the time of the follow-up examination, three (5.7%) out of 53 survivors in Period I had experienced a seizure (including those who had a seizure during the hospitalization). In Period II, 12 (4.6%) out of 261 survivors experienced a seizure ($P = 0.573$).

Overall mortality in this series was 30.7% at the time of the last follow-up visit. The mortality in Period I was 32.9% (26 deaths) and it was 30.2% (113 deaths) in Period II. Similarly, there was a slight decrease in the length of stay from Period I (14.17 d) to Period II (13.12 d). In either case, the difference did not reach statistical significance.

TABLE 2. Surgical complications[a]

	7/98–3/99	4/99–6/02
No. of patients	65	306
Infarct	2 (3%)	10 (3.3%)
CN palsy	3 (4.6%)	3 (1%)
ICH/contusion	1 (1.5%)	2 (0.7%)
SDH/EDH	2 (3%)	4 (1.3%)
CSF leak	1 (1.5%)	2 (0.7%)
Wound infection	0	2 (0.7%)

[a] CN, cranial nerve; ICH, intracerebral hematoma; SDH, subdural hematoma; EDH, extradural hematoma; CSF, cerebrospinal fluid.

TABLE 3. Rates of seizure and hypersensitivity reaction in the two treatment periods[a]

	7/98–3/99	4/99–6/02
No. of patients	79	370
PHT hypersensitivity	7/79 (8.8%)	2/370 (0.5%)
Seizures during hospitalization	1/79 (1.3%)	7/370 (1.9%)
Seizures at follow-up (survivors only)	3/53 (5.7%)	12/261 (4.6%)
Hospital length of stay (d)	14.2	13.1

[a] PHT, phenytoin.

DISCUSSION

In this study, we retrospectively reviewed prospectively collected data comparing two periods before and after a change in PHT regimen after SAH. We found that a statistically significant decrease in drug complications was achieved without an increase in seizure rates if prophylaxis was shortened to 3 days.

To our knowledge, this article represents the second report, from a different neurovascular center, noting that a short course of anticonvulsant prophylaxis is adequate after SAH. Compared with the regimen reported by Baker et al. (1), there was an important difference. In our series, we did not classify patients as being high- or low-risk; all patients in Period II received a short course of PHT treatment. The only exceptions were the four patients with a history of epilepsy. These data show that even patients with an associated hematoma or concomitant arteriovenous malformations may not need prolonged seizure prophylaxis.

After SAH, the incidence of seizures can be high, but most of these seizures occur with the ictus or within a few hours of the hemorrhage (7, 11, 20, 21). After that initial period, the incidence of seizures is low. Even with only 3 days of PHT prophylaxis, only 1.9% of patients experienced a seizure during the hospitalization in this series, despite the fact that 80% of these patients had aneurysm repair by craniotomy. The incidence of delayed seizures also did not change. These data are similar to those noted for patients with traumatic closed head injury in whom early anticonvulsant use did not change the incidence of delayed epilepsy (6, 23, 24).

Because of these findings, it is clear that prolonged anticonvulsant use is not necessary after SAH. It may even be that anticonvulsant use is not indicated after SAH, although we do not present data supporting this possibility.

We find that most of our patients who arrive by transfer have already been loaded with PHT. In addition, some members of our own department prefer PHT use in SAH patients. For these reasons, we recommend a short course of anticonvulsant use, and we suggest that 3 days of treatment is adequate. Such a protocol will dramatically reduce the incidence of drug reaction, and decreasing the exposure to PHT may have other benefits. Several lines of evidence suggest that PHT use can harm the injured brain, even in the absence of a hypersensitivity reaction. For example, PHT exposure in animal models of ischemic stroke leads to worse recovery (4, 5). Furthermore, PHT often causes fever, which is independently associated with worse outcome after neural injury (3, 10, 16, 17). Finally, as noted, the "PHT burden" may be correlated with worsening cognitive deficit (15).

CONCLUSION

Our study shows that 3 days of anticonvulsant treatment is adequate for seizure prophylaxis after SAH. The rate of drug reaction decreased significantly when PHT was stopped at 3 days, declining from 8.8% with longer use to 0.5% ($P = 0.002$). Furthermore, the rate of seizures during the hospitalization and at the time of follow-up did not increase.

REFERENCES

1. Baker CJ, Prestigiacomo CJ, Solomon RA: Short-term perioperative anticonvulsant prophylaxis for the surgical treatment of low-risk patients with intracranial aneurysms. **Neurosurgery** 37:863–870, 1995.
2. Beenen LF, Lindeboom J, Kasteleijn-Nolst Trenite DG, Heimans JJ, Snoek FJ, Touw DJ, Ader HJ, van Alphen HA: Comparative double blind clinical trial of phenytoin and sodium valproate as anticonvulsant prophylaxis after craniotomy: Efficacy, tolerability, and cognitive effects. **J Neurol Neurosurg Psychiatry** 67:474–480, 1999.
3. Commichau C, Scarmeas N, Mayer SA: Risk factors for fever in the neurologic intensive care unit. **Neurology** 60:837–841, 2003.
4. Goldstein LB: Common drugs may influence motor recovery after stroke: The Sygen In Acute Stroke Study Investigators. **Neurology** 45:865–871, 1995.
5. Goldstein LB: Potential effects of common drugs on stroke recovery. **Arch Neurol** 55:454–456, 1998.
6. Haltiner AM, Newell DW, Temkin NR, Dikmen SS, Winn HR: Side effects and mortality associated with use of phenytoin for early post-traumatic seizure prophylaxis. **J Neurosurg** 91:588–592, 1999.
7. Hart RG, Byer JA, Slaughter JR, Hewett JE, Easton JD: Occurrence and implications of seizures in subarachnoid hemorrhage due to ruptured intracranial aneurysms. **Neurosurgery** 8:417–421, 1981.
8. Hasan D, Schonck RS, Avezaat CJ, Tanghe HL, van Gijn J, van der Lugt PJ: Epileptic seizures after subarachnoid hemorrhage. **Ann Neurol** 33:286–291, 1993.
9. Jones AL, Proudfoot AT: Features and management of poisoning with modern drugs used to treat epilepsy. **QJM** 91:325–332, 1998.
10. Kreiter KT, Commichau C, Kowalski RG, Ostapkovich N, Huddleston D, Fitzsimmons BF, Parra A, Connolly ES Jr, Mayer SA: Fever burden and cognitive outcome after subarachnoid hemorrhage. **Neurology** 60:A230, 2003 (abstr).
11. Lin CL, Dumont AS, Lieu AS, Yen CP, Hwang SL, Kwan AL, Kassell NF, Howng SL: Characterization of perioperative seizures and epilepsy following aneurysmal subarachnoid hemorrhage. **J Neurosurg** 99:978–985, 2003.
12. Manaka S, Ishijima B, Mayanagi Y: Postoperative seizures: epidemiology, pathology, and prophylaxis. **Neurol Med Chir (Tokyo)** 43:589–600, 2003.
13. Manon-Espaillat R, Burnstine TH, Remler B, Reed RC, Osorio I: Antiepileptic drug intoxication: Factors and their significance. **Epilepsia** 32:96–100, 1991.
14. Mattson RH, Cramer JA, Collins JF, Smith DB, Delgado-Escueta AV, Browne TR, Williamson PD, Treiman DM, McNamara JO, McCutchen CB, Homan RW, Crill WE, Lubozynski M, Rosenthal NP, Mayersdorf A: Comparison of carbamazepine, phenobarbital, phenytoin, and primidone in partial and secondarily generalized tonic-clonic seizures. **N Engl J Med** 313:145–151, 1985.
15. Naidech AM, Kreiter KT, Janjua N, Ostapkovich N, Parra A, Commichau C, Connolly ES, Mayer SA, Fitzsimmons BF: Phenytoin exposure is associated with functional and cognitive disability after subarachnoid hemorrhage. **Stroke** 36:583–587, 2005.
16. North JB: Anticonvulsant prophylaxis in neurosurgery. **Br J Neurosurg** 3:425–427, 1989.
17. Oliveira-Filho J, Ezzeddine MA, Segal AZ, Buonanno FS, Chang Y, Ogilvy CS, Rordorf G, Schwamm LH, Koroshetz WJ, McDonald CT: Fever in subarachnoid hemorrhage: Relationship to vasospasm and outcome. **Neurology** 56:1299–1304, 2001.
18. Perucca E: An introduction to antiepileptic drugs. **Epilepsia** 46 [Suppl 4]: 31–37, 2005.
19. Rabinowicz AL, Ginsburg DL, DeGiorgio CM, Gott PS, Giannotta SL: Unruptured intracranial aneurysms: Seizures and antiepileptic drug treatment following surgery. **J Neurosurg** 75:371–373, 1991.
20. Rhoney DH, Tipps LB, Murry KR, Basham MC, Michael DB, Coplin WM: Anticonvulsant prophylaxis and timing of seizures after aneurysmal subarachnoid hemorrhage. **Neurology** 55:258–265, 2000.
21. Rose FC, Sarner M: Epilepsy after ruptured intracranial aneurysm. **Br Med J** 5416:18–21, 1965.
22. Temkin NR: Prophylactic anticonvulsants after neurosurgery. **Epilepsy Curr** 2:105–107, 2002.
23. Temkin NR, Dikmen SS, Wilensky AJ, Keihm J, Chabal S, Winn HR: A randomized, double-blind study of phenytoin for the prevention of post-traumatic seizures. **N Engl J Med** 323:497–502, 1990.
24. Young B, Rapp RP, Norton JA, Haack D, Tibbs PA, Bean JR: Failure of prophylactically administered phenytoin to prevent late posttraumatic seizures. **J Neurosurg** 58:236–241, 1983.

Acknowledgment

The authors have no personal or institutional financial interest in the drugs, materials, or devices mentioned in this article.

COMMENTS

The study clearly demonstrates that seizure rates after subarachnoid hemorrhage (SAH) in the 3-day phenytoin group did not show any significant difference compared with the group that received phenytoin throughout their hospital stay. This is an important observation and raises an important question: Is phenytoin prophylaxis necessary at all after SAH? This could be a subject for a future study.

Gopalan Umashankar
Hans Luders
Neurologists
Cleveland, Ohio

The authors provide a retrospective comparison of two regimens of anticonvulsant coverage after aneurysmal SAH applied during sequential epochs in a single practice setting (prolonged phenytoin versus 3-day prophylaxis, except in cases with previous epilepsy or subsequent documented seizures). The volume of cases in each cohort is large, and the case mix and other treatment paradigms, including aneurysm size and location, clinical grade, fraction of cases treated with surgery, and surgical complication rates, seem similar during the two epochs. Drug reactions were significantly reduced in the second cohort, without significant increase of seizure prevalence.

We concur with the authors' conclusion that the 3-day prophylaxis regimen was safer, and equally effective, in comparison with arbitrary longer-term phenytoin coverage. This conclusion seems justified, even if other factors of patient management were unknowingly introduced in the second epoch that may have reduced epileptogenic risks. The seizure breakthrough rate was low, leading the authors to suggest that risk stratification may not be necessary in determining anticonvulsant coverage, except for the maintenance of anticonvulsants in patients with subsequent overt seizures.

The results are compelling but may not be generalizeable to high-grade patients (37–39% of their patients were Grade 4–5) or those with associated intracerebral hemorrhage or infarcts. The two cohorts may not have included sufficient cases in various risk strata. Occult nonconvulsive status epilepticus has been reported in a high fraction of unconscious patients after SAH, hence the regime of anticonvulsant coverage must be balanced against the vigilance of electroencephalographic screening in comatose patients or those with suspected ongoing seizures.

The authors acknowledge that their results do not address the question of whether or not the 3-day anticonvulsant prophylaxis is even necessary. We agree that it is often difficult to rule out an acute seizure in association with the ictus of SAH. Altered consciousness or awareness is common, and the possibility of seizure cannot easily be excluded during acute resuscitation, especially at outlying facilities before transfer of the patient to a neurovascular center for definitive aneurysm management. And, too often there is the scenario of a patient arriving to a neurovascular center in a poorer grade than "advertised" or with rebleeding and seizure, which are often reported in association with clinical deterioration. It is impossible to exclude seizure as a cause or effect of such acute deterioration. Until an aneurysm is clipped or coiled, even a rare seizure may be catastrophic, predisposing to rebleeding. Early postoperative or postcoiling complications, even if uncommon, are often associated with seizures, and an epileptogenic cause may be difficult to exclude. For all of these reasons, we continue to support a practice similar to the authors' in which we institute anticonvulsant prophylaxis in the acute state (even loading patients with fosphenytoin before transfer from another facility), and we discontinue use soon after definitive aneurysm treatment, except in comatose patients and other cases in which ongoing seizures are suspected. We acknowledge the controversy regarding such hyperacute usage, but we do not think that there is sufficient controlled safety data in the literature to justify withholding anticonvulsants altogether in the acute state.

Of course, anticonvulsant prophylaxis is changing with the advent of likely equally effective agents such as levetiracetam (Keppra; UCB, Inc., Smyrna, GA), with a much safer profile and less serious complications than phenytoin. Until this publication, Keppra has not been available for intravenous loading in the United States, so we often bridge patients from phenytoin to Keppra during the first 3 days if we anticipate longer-term use, so as to avoid phenytoin complications and cumulative sequelae. The risk-benefit considerations will likely be revisited with safer agents, especially for hyperacute coverage before the aneurysm is secured in comatose patients and those with suspected ongoing seizures.

Issam A. Awad
Evanston, Illinois

The necessity of prophylactic antiepileptic treatment after spontaneous SAH is still a matter of debate. The authors undertook a clinical study, evaluating multiweek treatment against a 3-day course, with respect to seizure rates and adverse events. Four hundred fifty-three patients were included in the study. The results demonstrated that there was no significant difference with respect to seizure rates in both groups. Drug reactions (e.g., rash, hepatotoxicity, pancreatitis, and leukopenia) were significantly reduced.

The presented investigation addresses an important aspect of prophylactic antiepileptic treatment in a certain neurosurgical patient group. It is still not clear which patients are prone for seizure development. As long as we cannot predict the occurrence of ictus after SAH, the 3-day treatment might be a suitable method to follow. However, whether or not prophylactic antiepileptic treatment has to be applied at all should also be considered. In our hands, SAH patients do not receive antiepileptic drugs on a routine basis. They are only treated if they develop repeated seizures.

Gabriele Schackert
Dresden, Germany

Chumnanvej et al. have demonstrated that, by limiting the duration of phenytoin administration after SAH, the incidence of significant side effects can be greatly reduced without a concomitant increase in the risks of seizures. Strikingly, this effect was seen in all patients (except those with a preexisting seizure disorder) regardless of clinical grade, radiographic evidence of brain injury, or intraparenchymal hemorrhage. Because this duration of dosage represents roughly a 50% reduction of that previously recommended by the Columbia group without evidence of increased seizure incidence, one wonders if limiting anticonvulsant administration to the initial 24 hours after SAH might be equally effective.

Duke Samson
Dallas, Texas