Relation of prophylactic medication to the occurrence of early seizures following craniocerebral trauma

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In a series of 1614 cases of combat head injury incurred in Vietnam between 1967 and 1970, 70% received prophylactic anticonvulsant medication (diphenylhydantoin, 300 to 400 mg/day); 36 developed fits in the first week following injury. The prophylactic regimen had no recognizable effect. Therapeutic serum levels of anticonvulsants are not achieved for 2 or 3 weeks. Usefulness of dexamethasone in controlling brain swelling may be seriously impaired by diphenylhydantoin. Thus prophylaxis against early posttraumatic fits may not be practical or desirable.

KEY WORDS: brain injury · Vietnam · diphenylhydantoin · dexamethasone · early epilepsy · war wounds · head injury

THIS study evaluates the use of prophylactic anticonvulsant medication in the treatment of head injuries sustained in military combat.

Analysis of Cases

Selection of Patients

A Registry for Head and Spinal Cord Injuries, as they occurred in military combat in Vietnam, was developed by one of us (W.F.C.) at the request of the Surgeon General of the Navy, and was implemented with the cooperation of the Surgeons General of the Army and Air Force. The reports from the field neurosurgeons, from January, 1967, to August, 1970, were screened for legibility and completeness, and 1614 were then processed for this report. Supplemental data were obtained directly from the surgeons in regard to their use of anticonvulsant prophylaxis and the occurrence of early fits.

Prophylaxis

Of the 1614 patients, 1136 (70%) received routine anticonvulsant therapy, 465 (29%) received no prophylactic regimen, and in 13 cases (1%) the presence or absence of a prophylactic regimen was unknown. The anticonvulsants were included in the postoperative orders, which in more than half the cases were established within 6 hours of injury; 93% of the prophylactic regimen consisted of diphenylhydantoin, 300 to 400 mg daily. Phenobarbital alone was employed in 4% of the cases, and the combination of diphenylhydantoin and phenobarbital in 3%. The usual route of administration was intramuscular, progressing to oral as tolerated (Fig. 1).

Occurrence of “Early Epilepsy”

Reports vary in their definition of early traumatic epilepsy, but there is general agreement that this represents a distinct clinical entity. Although the occurrence of early traumatic fits increases the chance for the appearance of late traumatic epilepsy, the former is more likely to be self-limited than
The regional distribution of injuries in the seizure cases was as follows: frontal 9; parietal 20 (including frontoparietal, temporoparietal, and occipitoparietal); temporal and frontotemporal 5; occipital 3, and suboccipital 1. Twenty-five of these were on the right side of the head and 13 on the left.

Loss or alteration in consciousness occurred in 89% of the seizure group, in contrast to 63% of the total series. When the groups of patients responding only to painful stimuli on the initial examination are compared, the seizure group included 24/36 or 68% in contrast to 483/1614 or 30% in the total series. This difference is significant at the 2% level (Fig. 3).

The incidence of seizures within the prophylactically treated group was 18/1136 or 1.6% compared to 17/465 or 3.7% within the untreated group. This difference (7% level) is not statistically significant (Fig. 4).

Discussion

The effectiveness of the prophylactic regimen cannot be reliably judged by the number of fits that developed in the first week. It may even have been nil. Studies of the development of therapeutic serum levels of diphenylhydantoin, or phenobarbital, by Buchthal and Svensmark indicate a time lapse of between 1 and 2 weeks before an effective level can be achieved. This was true for both oral and intramuscular administration, the latter being the slower route. The heroic regimen devised by Wallis, et al., provides an immediate serum level within the usual therapeutic range, + 20 μg/ml, by the administration of 1000 mg of diphenylhydantoin intrave-
Prophylactic therapy for traumatic epilepsy

nously and 500 mg intramuscularly at the outset with a 300 to 500 mg daily maintenance dose orally thereafter. This procedure requires repeated serum level determinations and careful attention to adverse effects on the cardiovascular system, and is not thought to be practical for most acute missile injuries.

A further important consideration is the effect of diphenylhydantoin on the metabolism of dexamethasone. Haque, et al., have recently demonstrated that diphenylhydantoin markedly hastens the removal of dexamethasone from plasma mainly by hepatic conversion to metabolites that can be removed in the urine. The mean increase in metabolic clearance rate was +140%. In cases in which it is imperative to control brain swelling, it would be unwise to impair the effectiveness of such an agent as dexamethasone by the prophylactic use of diphenylhydantoin.

The prognostic significance of seizures in the first week has been emphasized by those who have studied the natural history of post-traumatic epilepsy. Jennett and Lewin point out that fits occurring in cases with cortical damage and prolonged coma carry a high probability (47%) of subsequent seizures. Weiss and Caveness indicate that more than one seizure episode in the first week raises the probability from 18% to 44% that the attacks will persist into the fourth year. Most authors agree that early focal, and focal to general, seizures are more likely to persist than general attacks.

In this series, 10 patients had cortical damage and prolonged coma, 11 had multiple attacks, and 21 had focal attacks.

The prophylactic use of anticonvulsants in combat head injuries needs to be reconsidered on the basis of the knowledge and techniques now available. Thought should be given to postponement of efforts to establish an adequate plasma level until after the 7- to 14-day period of acute reaction to injury. This attitude is reinforced by the realization that less than 4% develop fits, and that there is practical difficulty in protecting the majority of these since they occur in the first 4 days, before an adequate serum level can be established.

References

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