Necropsy revealed normal heart, brain and lungs, except for aspiration of stomach contents. There was no evidence of an overdose, anticonvulsant levels of the previous month, or any other drug. Abrupt withdrawal of parathemadine is not associated with serious adverse effects, such as autonomic epilepsy,7–9 although withdrawal of a related oxazolidine, trimethadione may precipitate fits.21 However, carbamazepine is known to affect the myocardium in pharmacological studies and to cause Stokes-Adams attacks and conduction block in clinical practice.

Carbamazepine is a group IA antiarrhythmic which blocks the fast inward sodium current during the depolarisation of the cardiac membrane.22 It increases atrioventricular conduction time in vivo and depresses ventricular automaticity in vitro, by reducing the rate of phase 4 depolarisation.23 There are nine reported cases of carbamazepine causing atrioventricular conduction block or bradycardia when taken in therapeutic dosage.24–29 Stokes-Adams attacks occurred in two patients.24–25 Complete heart block in five.24–26–28 and bradycardia in two other patients.29–30 In all cases, sinus rhythm was re-established after withdrawal of the drug.

In the five cases which were specially monitored, the conduction block reappeared on restarting carbamazepine.24 25 28 29 Six of the nine cases had previous ECGs available for analysis; left anterior hemiblock was present in two cases and no abnormality in three cases. There appeared to be no relation between these pre-morbid traces, the severity of the later conduction block or the dose of carbamazepine. In fact, a daily dose of only 200 mg produced Stokes-Adams attack in one patient with a previously normal ECG.24 Nonetheless, it has reasonably been suggested that a latent defective conduction system might be a necessary pre-requisite for the induction of atrio-ventricular block.26 Some support for this comes from a small pilot study on patients with pre-existing block whose ventricular standstill time, or pre-automatic pause, was significantly prolonged when carbamazepine was administered. It should also be noted that heart block may intervene after many years of carbamazepine therapy24 and that it may last for three or four days.31 It has thus been

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Syncope and sudden unexpected death attributed to carbamazepine in a 20-year-old epileptic

Sir: Carbamazepine is known to cause atrioventricular conduction block but has not yet been implicated in sudden unexpected death in epilepsy. We report one such death which, we suggest, may have resulted from ventricular arrest induced by carbamazepine.

A 20-year-old student teacher presented for routine review with a 7 year history of intractable petit-mal but with well controlled grand-mal epilepsy. She was taking valproate 400 mg tds and paramethadione 300 mg bd. Troxide and ethosuximide had failed to control her petit-mal. A fresh history elicited features of temporal lobe epilepsy coinciding with her absences, namely deja-vu, jamais-vu, and amnesic spells. There were prodromal symptoms (strange epigastric sensations, extreme pallor) and postictal features (headache, unsteadiness). A review of her EEGs showed excess slow wave activity in the right fronto temporal region in 1978 and in repeat EEGs in 1979, 1980 with a normal CT brain scan. The diagnosis was changed to temporal lobe epilepsy. Paramethadione was withdrawn and carbamazepine was started 200 mg bd. After 3 days, her mother reported that she began to suffer syncopal episodes within a few hours of starting treatment. These were different from any previous seizures, lasted a few minutes, were preceded by lightheadedness, and were followed by total recovery. Her family doctor visited and witnessed a typical attack. She became pulseless with no heart sounds. Resuscitation was unsuccessful
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recommended that, in elderly patients at least, it would be prudent to perform an ECG prior to starting carbamazepine therapy.31

All nine cases described so far, have been elderly and only one patient has had epilepsy. No fatalities have been reported, and in the two detailed post-mortem studies on sudden death in epileptics,8,9 only one was taking carbamazepine, but not in the therapeutic dosage.8 We suggest, however, that carbamazepine was responsible both for the syncopal attacks and the death of our young epileptic probably by causing ventricular asystole.

The lesson to be drawn would seem to be that any patient on carbamazepine, for whatever reason, who complains of syncope or a change in seizure type, should be admitted for investigation of this atrio-ventricular conduction system.

The differentiation of cardiac and epileptic loss of consciousness can often be difficult and the temptation to increase the dose of carbamazepine in an epileptic who complains of loss of consciousness should be resisted until assessment of their cardiovascular status is complete. If in doubt, it is probably best to stop the drug and substitute an alternative. It may be prudent to perform an ECG in the elderly, before commencing treatment with carbamazepine but, in the absence of further data on death related to the drug, no further precautions can be justified.

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Correction


Notice

The Upjohn Prize for Neurosurgical Research

The European Association of Neurosurgical Societies awards annually a prize of $3,000 provided by the Upjohn Company. Applicants must be either a member of one of the national societies of the EANS or should be supported by such a member. Details of the regulations concerning the prize can be obtained from secretaries of the national societies or from Professor F Cohadon, Hospital Pellegrin, Place A, Raba Leon, 33076 Bordeaux, France.
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