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Use of mefloquine in epileptic patients

Sir: I consider the following observation to be of particular interest.

A 38 year old man began to have complex partial seizures when aged 15 years. No cause was found to explain this epilepsy. Treatment with carbamazepine (1·2 g/day) and sodium valproate (1 g/day), reduced the frequency of his seizures to about three per month. Plasma levels of anti-epileptic drugs confirmed compliance (carbamazepine: 6·2 g/l and sodium valproate: 82 g/l, on the 22 June 1987.

Having planned to spend his holidays in Kenya, he was advised to take mefloquine to prevent malaria (250 mg tablet per week).

The day after he took the first dose (26 June), he had three partial seizures. Twenty-four to 72 hours after he took the other regular doses of mefloquine, several partial seizures and three generalised seizures occurred. He was hospitalised before taking the last dose (on 20 August). We observed then three partial seizures on the same morning, needing IV injection of clonazepam.

Epileptic seizures, or the aggravation of known epilepsy, have never been reported with this dose by the manufacturers as a side effect of treatment of mefloquine;[1] only one case has been reported (1 000 mg/dose) with an acute brain syndrome.[2]

During hospitalisation, we studied the kinetics of anti-epileptic drugs after the patient took his last dose of mefloquine. We observed a reduction of biological half-life of sodium valproate (5·65, normal: 8–20 hours),[3] though that of carbamazepine was unchanged. Consequently, it is possible mefloquine accelerated sodium valproate metabolism, both having the same hepatic metabolism. This observation should lead to a careful administration of mefloquine to epileptic patients, especially when they are treated by sodium valproate.

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Midazolam in the treatment of epileptic seizures

Sir: Midazolam (Dormicum) is a benzodiazepine used for the premedication and induction of anaesthesia. Its diazepine nucleus is fused with a nucleus of the imidazol group having a basic azote in position 2, which allows the formation of water soluble salts. Its antiepileptic properties have been most recently studied on interictal spikes[1] and on status epilepticus.[2]

Fourteen patients, nine females and five males, from 19 to 72 years old, suffering from subsequent repeated epileptic seizures were treated with 0·2 mg/kg intramuscular midazolam. We performed 18 interventions: three for complex partial seizures, nine for tonic-clonic seizures, two for myoclonic, one for tonic, one for atonic seizures, and two for partial motor prolonged seizures. The clinical status (heart and respiratory rate, blood pressure, waking state and clinical evolution of seizures) was followed during one hour after the injection. In nine cases, classical EEG was recorded for the whole of this period.

A slight decrease of blood pressure (15%) was noted in only three cases with a slower heart rate (10%) in one of them. The disappearance of the epileptic seizures was observed in all cases, 5 to 10 minutes after the injection. This response was complete in 15 interventions and partial in three.

On the nine recorded EEGs, the epileptiform activities had disappeared in 10 min in five cases, but reappeared at the end of the recording in one of them. They diminished significantly in three cases and remained unchanged in one case. The EEG changes were concomitant with the clinical improvement. The response to this treatment was stable in all but four cases, who presented with a relapse within the first 24 hours after the injection (two after 3 hours, one after 4 hours and one after 18 hours), two of which were then treated by a second injection of midazolam and responded very well.

Our results are comparable with those of Egli and Albani[1] and Jawad *et al*,[2] reporting respectively 12 complete clinical responses on 15 cases of tonic-clonic and complex partial seizures, and 21 complete responses on 26 cases. In our study, the mean of complete clinical responses reached 82%.

Compared with other benzodiazepines used in emergency for iterative epileptic seizures, midazolam offers two advantages. First, its action is rapid and effective by the intramuscular route. Jawad *et al*[3] have compared intramuscular midazolam with intramuscular and intravenous diazepam on the ability to reduce interictal spikes. It appears that 10 or 15 mg intramuscular midazolam is as effective as 20 mg intravenous diazepam, while 10 or 15 mg intramuscular midazolam is more effective than 10 mg diazepam administered, intramuscularly or intravenously. The second advantage of midazolam is its short half life (1 to 2 hours), as compared with diazepam, lorazepam and clonazepam which have values from 15 to 31 hours. This short half life allows us to exclude from the number of relapses the case who presented with a seizure after 18 hours, as we consider this seizure as a new event.

In conclusion, these results indicate that midazolam is an effective treatment of repeated epileptic seizures. In addition, this drug may be easily and safely administrated by the intramuscular route.

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