REVIEW ARTICLE

Management of Status Epilepticus

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ABSTRACT: The pharmacologic management of major motor status epilepticus is summarized. When general anesthesia is required, the electroencephalogram (EEG) is used for monitoring the adequacy of treatment. The EEG findings may also be important in recognizing status epilepticus and monitoring its response to treatment when this is clinically difficult, as when it occurs in comatose or pharmacologically paralyzed patients or in the context of severe brain damage. Finally, the EEG helps to clarify the nature of motor activities of uncertain basis in patients in the intensive care unit and has indicated that non-convulsive seizures or status are more common than clinically suspected in such patients.

RÉSUMÉ: Études électrophysiologiques à l'unité de soins intensifs. Nous résumons le traitement pharmacologique de l'état de mal épileptique moteur. Quand une anesthésie générale est nécessaire, l'électroencéphalogramme (EEG) est utilisé pour vérifier si le traitement est adéquat. Les observations EEG peuvent également être importantes pour reconnaître l'état de mal épileptique et pour surveiller la réponse au traitement quand cette surveillance est difficile à faire cliniquement, comme dans le cas de patients comateux ou paralysés pharmacologiquement, ou quand les dommages cérébraux sont importants. L'EEG aide également à clarifier la nature des activités motrices dont la base est incertaine chez les patients admis à l'unité de soins intensifs et nous a permis de constater que les crises éplileptiques non convulsives ou l'état de mal épileptique sont plus fréquents que la clinique ne le laisse soupçonner chez ces patents.

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Status epilepticus is becoming increasingly common, poses difficult management problems, and sometimes has a fatal outcome. Major motor status epilepticus may occur in known epileptics or in patients without previous seizures, and arises for many different reasons.[1] Prognosis depends on the time required to control seizures: as this increases, and particularly when this exceeds 2 hours, the outlook for survival or recovery without sequelae diminishes significantly. Effective treatment must generally be instituted before the cause of the status is known.

Initial management (Table) is with intravenous diazepam (10-20 mg) or lorazepam (4-8 mg), which often controls seizures temporarily. Long-lasting control requires intravenous phenytoin (18 mg/kg at 50 mg/min); this is best administered as fosphenytoin sodium, the dose of which is expressed as phenytoin equivalents (PE). Fosphenytoin is water soluble, can be infused in saline or dextrose, and is better tolerated at the infusion site than phenytoin. It is converted in the body to phenytoin and is administered in a dose of 18 mg PE per kg infused at a rate of 150 mg PE per minute. Additional phenytoin or fosphenytoin can be given if seizures continue (Table). Alternatively, phenobarbital (15 mg/kg at 100 mg/min) can be infused intravenously. The side effects of phenytoin or phenobarbital include hypotension, respiratory depression, and cardiac arrhythmias. If these measures fail, the patient is paralyzed pharmacologically, ventilated, and transferred to the intensive care unit (ICU) to be treated by pentobarbital- or midazolam-induced anesthesia. The electroencephalogram (EEG) is used for monitoring control of seizures and level of anesthesia. The aim is to suppress electrographic seizures and epileptiform activity, and usually to obtain a burst-suppression pattern, but it is unclear whether inducing a burst-suppression pattern provides any added advantage if seizures are controlled with lower levels of medication.

Pentobarbital is given in an intravenous loading dose of 15 mg/kg over 1 hour, followed by maintenance doses of 0.5 mg/kg/hour; higher doses are used depending on the clinical and EEG response.[2] With midazolam, a loading bolus of 200 μg/kg is followed by continuous intravenous infusion of 0.75 to 10 μg/kg/min.[3] In either case, hypotension may occur and is treated by pressor agents and intravenous fluids. The pentobarbital or midazolam is stopped after 12 hours but restarted for a further 12 to 24 hours (or longer) if seizures recur; it may have to be continued for several days. Prognosis depends on the cause of status and condition of patients. A poor prognosis is associated with advancing age and the occurrence of hypotension or multiorgan failure.[4]

Development of status epilepticus may be difficult to recognize in comatose or pharmacologically paralyzed patients already in the ICU, or when severe brain damage restricts the clinical manifestations of convulsions to, for example, the extraocular muscles. The EEG findings may then be definitive, especially when they consist of repeated electrographic seizures or continuous spike-wave activity. The significance of a burst-suppression pattern or periodic spiking is less clear. In a personal series of 10 patients in electrographic status epilepticus with

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Table: Management of Convulsive Status Epilepticus in Adults.

	Time/Procedure	Drug	Dose (intravenous)	Comment
Step 1	Immediate	Diazepam or Lorazepam	10 mg 0.1 mg/kg or 4 mg	Give over 2 min; repeat once if necessary
	Monitor vital signs			
	Insert intravenous catheter; draw venous blood for laboratory studies; commence infusion with N saline; give 50 ml of 50% dextrose and thiamine (250 mg)			
Step 2	Concurrent with or immediately after Step 1	Phenytoin plus	18 mg/kg 5 mg/kg if needed	Infuse at 50 mg/min
		or		
		Fosphenytoin plus	18 mg PE/kg 5 mg PE/kg if needed	Infuse at 150 mg PE/min
Step 3	Immediately after conclusion of Step 2, if seizures continue	Phenobarbital	15 mg/kg	Infuse at 50-100 mg/min
Step 4	Proceed immediately after Step 3 if seizures continue. Transfer patient to ICU Paralyze with a short-acting neuromuscular blocker, and ventilate mechanically	Midazolam plus or Pentobarbital plus	0.2 mg/kg 0.75-10 μg/kg/min 15 mg/kg 0.5-4 mg/kg/hr	Intubation and ventilatory support required. Stop after 12 hrs; if seizures recur, reintroduce for a further 12 hrs. Repeat every 12-24 hrs for as long as necessary.
	Monitor EEG for seizures and level of anesthesia			
	Treat hypotension with low-dose dopamine infusion			

only minor motor accompaniments following cerebral anoxia, 7 had spontaneous repetitive eye movements. Similar ocular movements were seen in 2 other patients without electrographic status; there was a lateralized burst-suppression pattern in one and pseudoperiodic spiking in the other.[5] Among these 12 patients, 4 had associated movements of the eyelids, tongue, or mouth. The absence of limb movements presumably reflected the severity of brain damage.

We recently evaluated 47 comatose patients in an ICU who were in clinical or electrographic status epilepticus.[6] In 5 patients there was electrographic but not clinical status, emphasizing that clinically unsuspected seizures or status may confound patient management. Among 42 patients with clinically-evident status, the EEG showed repetitive seizures or continuous spike-wave activity in 33; by contrast, it was nonspecifically abnormal in 9, possibly because severe cortical dysfunction or the distant origin of seizures prevented EEG detection of seizures. Thus, when status is suspected clinically in ICU patients, the lack of supportive EEG findings does not necessarily exclude the diagnosis. However, in ICU patients with motor activities (such as tremors, shivering, or posturing) that could be, but probably do not represent clinical manifestations of seizures, the absence of ictal EEG accompaniments provides support for a probable non-epileptic basis for them.

Alterations in mental status of patients in the ICU are commonly attributed to metabolic, toxic, or septic encephalopathy. EEGs (routine recordings or continuous monitoring) suggest, however, that nonconvulsive seizures and status are more common than clinically suspected, especially in patients with acute cerebral dysfunction or recent craniotomy.[7] Delay in diagnosis affects outcome significantly, especially in such patients. The EEG typically shows continuous spike-wave activity, repeated partial (focal or lateralized) seizures, or some combination of these findings. Recent studies show that, in nonconvulsive status epilepticus occurring in the ICU, seizure duration is strongly associated with mortality, regardless of etiology.[8]

The EEG thus has an important role in evaluating the adequacy of treatment of convulsive status by barbiturates- or midazolam-induced anesthesia. It is essential for the recognition of status epilepticus with minor or no motor manifestations, and in monitoring its response to treatment. Finally, the EEG is important in clarifying the nature of certain motor and behavioral disturbances, especially in ICU patients, and showing that they do not relate to seizure activity.

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