Emergency control of convulsions

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The authors discuss various concepts of treatment for major status epilepticus. An evaluation of drugs as well as general anesthesia and curarization as methods of control are presented.

The anesthetist is occasionally called to stop convulsions. This is akin to cardiopulmonary resuscitation, in the sense that there is an initial emergency phase, nonspecific in nature, and directed solely toward the restoration of vital functions. A rapid acting anticonvulsant drug, usually a benzodiazepine or a barbiturate, is administered intravenously. Respiratory support is often required after seizures are controlled, and arterial hypotension may occur. The concepts of treatment are usually simple, and a routinized approach can easily be adopted.

Our experience in dealing with seizure states has not, however, been uniformly satisfactory. In a few instances, the selected drug did not stop the convulsions at all; in other cases, dosage requirements were raised to the point where postictal depression was severe. Follow-up medications were not always judiciously chosen, and seizures recurred. On "staffing" some of these cases, we soon recognized that our errors were due mainly to insufficient background knowledge concerning central hyperirritability. Also we noted a paucity of information concerning seizure states in the literature of anesthesiology.

This review is drawn largely from neurological sources, where most pertinent discussions are found under the topic, status epilepticus. Its principal value may be to epitomize some primary reference sources from which the anesthetist can gain further information concerning the etiology, pathogenesis, diagnosis, and treatment of seizure states.

Major status epilepticus is defined as a continuous tonic-clonic (grand mal) seizure lasting longer than 30 minutes, or a series of two or more major convulsions occurring without intervening recovery of consciousness. It is a serious medical emergency, with mortality as high as 21%, even with prompt treatment. The mortality rate before adequate treatment was available was from 30-50%. When immediate control is achieved, virtually all the mortality in adults can be attributed to the underlying pathology rather than to the convulsive episode itself. In children under the age of ten, there is urgent need for prompt treatment, since permanent neurological sequelae occur in 57% of cases following an episode of status. In a study of 239 children with status epilepticus, about half the mortality was due to underlying pathology while the other half was due to the seizure itself. Status epilepticus was the first manifestation of epilepsy in 77%
of these cases. It is important, therefore, to initiate prompt, effective treatment, to prevent subsequent neurologic deficits.

Causes of status epilepticus

The cause of the seizure state is not a prime concern during the immediate treatment period, but lasting control can be achieved only if the causal factor can be identified and removed. The most common causes in adults include brain tumors, cerebrovascular disease, trauma, infectious diseases, metabolic disturbances, congenital brain defects, and surgical frontal lobe damage. Perhaps the most common cause of status epilepticus in adults is withdrawal of anticonvulsant drugs in chronic epileptics.

Status epilepticus in infants and children is commonly associated with infectious diseases such as meningitis or encephalitis, or metabolic disorders such as hypocalcemia. Seizures occur in conjunction with a febrile state in about 3% of all infants and children. In over 50% of cases of childhood status, there is no cause found.

Management

Adequate respiratory exchange must be maintained, and this may be difficult during the seizure itself. A plastic Ber- man oral airway is useful, since it cannot be compressed and offers some protection to the teeth. Endotracheal intubation is occasionally indicated; if it becomes necessary, the tube should be introduced during an interictal or postictal period. Once convulsions are adequately controlled by incremental doses of drugs, ventilation often returns to normal. Drugs used in treating status can cause respiratory depression and ventilatory insufficiency. If ventilation is not adequate, due either to drug therapy or postictal depression, intubation and mechanical ventilation are required. Suction equipment should be readily available to prevent aspiration of gastric contents.

The convulsing patient should be protected from physical injury. Padding should be applied to prevent fractures or soft tissue contusions.

An intravenous catheter should be inserted as soon as an adequate airway has been established so that proper airway can be instituted immediately. Rarely is a convulsion so severe that venipuncture is impossible. Drugs can be given intramuscularly, but their effects are delayed and unpredictable.

Drug treatment

Benzodiazepines. Diazepam continues to be the emergency drug of choice for major status epilepticus in both adults and children. In a series of 188 cases, diazepam gave lasting control in 68%, temporary control in 20%, and was ineffective in 12%. Lasting control was defined as a 24-hour period with no convulsions requiring three or fewer injections. Temporary control was defined as 24-hour control requiring more than 3 injections.

In treating adults, approximately 10 mg should be given intravenously over a 2-minute period. The initial dose in children should be 0.2 mg/kg with a maximum single dose of 10 mg, given over a two-minute period. If the initial dose does not control the seizures, a second dose can be given after 10 minutes, or a continuous infusion of 100 mg diazepam in 500 ml of 5% dextrose can be started at a maximum rate of 3 mg/kg/24 hours. A continuous infusion is safer than repeated bolus administration, in terms of minimizing respiratory and circulatory depression.

Administration of diazepam is often accompanied by transient hypotension and bradycardia. More serious side effects seen with large dosages include respiratory depression, severe hypotension, and cardiac arrest. These problems are magnified if the patient has received phenobarbital.

Intramuscular diazepam should not be used in the treatment of status epilepticus. Due to its limited water solubility, the drug is absorbed slowly and unpre-
dictably from intramuscular sites, and the peak concentration may not be reached until two to three hours after injection.\textsuperscript{12} Repeated doses of diazepam then accumulate and increase the potential toxicity of subsequent drugs given.\textsuperscript{1} Diazepam taken orally is more quickly and predictably absorbed than by the intramuscular route.

As soon as the seizure is controlled by diazepam, a longer acting anticonvulsant should be administered.\textsuperscript{8}

According to some researchers, clonazepam (Clonospin\textsuperscript{®}) is more effective than diazepam in treating all types of status epilepticus. No direct comparisons between the two drugs have been performed to date. In one study, clonazepam was effective in 38 out of 39 cases.\textsuperscript{18} It also appears to be effective in treating diazepam-refractory status epilepticus.\textsuperscript{13}

Clonazepam is approximately 10 times as potent as diazepam. In the treatment of major status epilepticus in adults, 1 mg is infused intravenously\textsuperscript{6}; up to 8 mg has been given safely via slow infusion.\textsuperscript{18} The manufacturer advises that 3 mg in 250 ml of normal saline or glucose be given slowly intravenously.\textsuperscript{9} The side effects of clonazepam are similar to those of diazepam, although one author claims that clonazepam in comparable doses has a greater cardiorespiratory depressant effect than diazepam.\textsuperscript{15} In the series of 39 cases of status epilepticus just cited, no unfavorable side effects were noted.\textsuperscript{13} Clonazepam may be harder to titrate due to its higher potency. After control has been achieved with clonazepam, a longer acting anticonvulsant should be given.

Barbiturates. Intravenous thiopental is effective in controlling major status epilepticus. In a study of 117 patients, thiopental was successful in controlling all but 2 cases within 72 hours.\textsuperscript{16} The average dose needed to achieve definitive control was found to be less than the sleep dose, so that some patients did not lose consciousness.

The recommended initial dose is 25-100 mg given intravenously, followed by an infusion of 2 gm dissolved in 1 liter of lactated Ringer's solution given at 1 ml/minute. It must be remembered that the action of thiopental is largely terminated by redistribution to fat and other tissue compartments. Prolonged depression may result if a large total dose is administered, due to storage and subsequent release. The depressant effect on respiration will summate with the postictal depression. When using thiopental (or any barbiturate), one should be prepared to intubate and provide ventilatory assistance.

Other barbiturates, such as amobarbital, pentobarbital or hexobarbital can be used to terminate status epilepticus.\textsuperscript{1} Amobarbital is given in a 50 mg bolus; this can be repeated up to a total dose of 200 mg.\textsuperscript{17} Amobarbital may achieve control for as long as 12 hours, compared to approximately 1 hour with a therapeutic bolus of diazepam. Pentobarbital can be given intravenously in 300-500 mg doses to adults.

Phenobarbital is the most consistently effective anticonvulsant known. Because of its slow distribution to the brain it is not practicable for immediate treatment of status epilepticus. Intravenous phenobarbital requires approximately 15 minutes to equilibrate with the brain, once therapeutic levels have been reached in the plasma. There is thus a danger of overdosage if enough phenobarbital is given initially to terminate convulsions, because the brain concentration will continue to rise. Phenobarbital is, however, a preferred drug for long term control after seizures have been stopped with shorter acting agents. A continuous intravenous infusion can be administered within the dose range of 400-4000 mg/24 hours.\textsuperscript{6} Again it should be mentioned that phenobarbital may augment the depressant effects of diazepam on circulation and respiration.\textsuperscript{11}

Phenytoin. Phenytoin (diphenylhydantoine) injected slowly intravenously at a
rate of 50 mg/minute up to 1000 mg has been employed for treatment of status epilepticus. In one series, 114 out of 121 cases were treated successfully, with no significant respiratory depression. It is no longer considered the drug of choice due to its delayed onset, but it is valuable for maintenance of long term control. Phenytoin can be infused at a rate of 300-500 mg/24 hours once initial control is achieved. Since the drug is poorly soluble in water, intramuscular administration is ineffective due to poor absorption and local tissue irritation.

Common side effects include cardiac conduction depression and hypotension. Continuous ECG monitoring should be routine when phenytoin is to be given parenterally. ECG changes include widening of the QRS complex, prolongation of the P-R or Q-T intervals, and T wave depression.

Chlormethiazole. Chlormethiazole (Heminevrin®) is not clinically available in the United States. It is a sedative-hypnotic and anticonvulsant drug that causes little respiratory depression or hypotension. Intravenous chlormethiazole was reported effective in 8 cases of major status epilepticus that were refractory to diazepam and paraldehyde. The drug is poorly soluble in pure water; the proprietary solution contains 8 mg/ml dissolved in water containing 40 mg/ml glucose and 30 mMol/L of sodium hydroxide. Approximately 500 ml of this mixture can be given over a six-hour period at a constant infusion rate. The drug may cause hypotension at higher dose levels, or if given as a bolus injection. Transient thrombophlebitis may occur at the infusion site. Although probably inferior to diazepam as a first line drug, chlormethiazole does appear to be valuable as a second anticonvulsant in diazepam-refractory major status epilepticus.

Muscle relaxants. Myoneural blocking agents may be used to control tonic or clonic seizure activity. Since they do not suppress the causal cerebral dysrhythmia, it is necessary to employ EEG monitoring, and to administer an anticonvulsant drug to suppress the electrical discharge. The effects of allowing dysrhythmias to continue in adequately oxygenated adults are unknown, but this is definitely harmful in children. Prolonged dysrhythmia in children can result in sclerosis of Ammon’s horn of the temporal lobe and recurring epilepsy of the psychomotor type. In severe seizure states, relaxant drugs may be necessary in order to achieve control of ventilation, and to prevent musculoskeletal injury. Intubation and mechanical ventilation are, of course, necessary if continuous control is to be achieved.

Lidocaine. This drug has been recommended as a trial agent before initiating general anesthesia to control severe refractory seizures. In one case refractory to diazepam, phenobarbital, and phenytoin, a 30 mg bolus given intravenously was successful in stopping the convulsions. Continuous ECG monitoring is mandatory. Resuscitative equipment must be available, since convulsions and vasomotor collapse are manifestations of lidocaine toxicity.

General anesthesia. General anesthesia with curarization can be used when intravenous therapy has failed. Once anesthesia has been induced, EEG monitoring should be maintained continuously.

Diagnosis. While definitive diagnosis may be deferred until after emergency control has been achieved, some basic tests can be done to aid in formulating the treatment plan. Blood samples should be drawn as soon as feasible. Electrolyte levels should be measured; hypocalcemia and hypomagnesemia can thus be identified. Glucose determinations will reveal the presence of hypoglycemia. A high proportion of seizures in children are caused by metabolic disturbances. Temperature should be monitored in children, since febrile convulsions are commonly encountered.

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Blood samples should also be drawn for determinations of serum levels of oral anticonvulsant drugs, since cessation of medication in chronic epileptics is a common cause of major status epilepticus.

A spinal tap may be done in the immediate post-acute period, particularly for CSF culture to identify infectious causes for the convulsions.

REFERENCES

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