www.jmscr.igmpublication.org

Impact Factor 3.79
Index Copernicus Value: 5.88
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: http://dx.doi.org/10.18535/jmscr/v3i12.03

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Management of Status Epilepticus (SE) – Recent Trend

Authors
Dr Arata Kumar Swain[1], Dr Pradipta Kumar Patel[2]
[1]MD, Fellowship in Critical Care Medicine, Assistant Professor, Dept. of Anaesthesiology, VIMSAR, BURLA
[2]Associate Professor, Anaesthesiology, VIMSAR, BURLA

Abstract
Status Epilepticus is a Medical emergency associated with high morbidity and mortality.SE as a seizure that lasts for 20-30 minutes. Prolonged seizures produce CNS damage. Continued epileptic activity may lead to relative cerebral hypoxia and hypoglycemia. The most important factor deciding outcome in SE is the underlying etiology SE should be identified early and treatment initiated as soon as it is clear that a seizure has lasted 5-10 minutes; out-of-hospital administration of intramuscular midazolam or rectal diazepam by paramedics transporting the patient could shorten the duration of SE and hospital stay. Airway, breathing and circulation should be assessed in the emergency department and adequate steps initiated to correct any abnormalities.

INTRODUCTION

Status Epilepticus is a Medical emergency associated with high morbidity and mortality. The etiology varies among the different age groups, being more common at the extremes of ages. The outcome depends to a great extent on the underlying etiology and the presence of additional medical conditions. Outcome also depends on the rapidity of diagnosis and initiation of appropriate therapy. The goals of therapy include rapid termination of clinical and electrical ictal activity, prevention of aspiration pneumonia, and treatment of complications in anticipation. Every hospital needs to manage SE on the basis of established protocols, and an early decision regarding artificial ventilation.

DEFINITION

SE is defined as "a seizure that persists for a sufficient length of time or is a repeated frequency enough that the recovery between attacks does not ococur. This definition difficult to use in clinical practice because lacks of specific duration and more recent publications have tried to remedy this by defining SE as a seizure that lasts for 20-30 minutes. (1) This time frame is based on an estimate of duration necessary to cause damage to cerebral neurons (1). Therefore an operational definition that either continuous seizure lasting at least 5 minutes or two or more discrete seizures between which there is incomplete recovery of consciousness (2)

Clinical Features

The most common potentially and dangerous forms of status epilepticus are described below.

1. **Generalized convulsive status epilepticus** is the most common form of status epilepticus. Despite treatment, the mortality associated with this type of

status epilepticus is 20%-27% [3]. After about 30 minutes, generalized convulsive status epilepticus can degenerate to non-convulsive status.

2. **Non-convulsive generalized status epilepticus** (subtle status epilepticus) is associated with minimal or no motor activity and requires electroencephalo-graphy for diagnosis. As many as 25% of cases of status epilepticus are nonconvulsive, and this condition is responsible for 8% of cases of unexplained coma [4]. In fact, the most common seizure recorded during electroencephalographic monitoring of patients with altered mental status is non-convulsive [5]. Non-convulsive seizures are often refractory to therapy, and are associated with a 65% mortality [3].
3. **Refractory status epilepticus** is a seizure that lasts more than 1 or 2 hours or is refractory to therapy with 2 or 3 anticonvulsant agents [6]. Almost one-third of cases of status epilepticus are refractory [6].
4. **Myoclonic status epilepticus** can occur in up to one third of patients with persistent coma following out-of-hospital cardiac arrest. This condition is characterized by sound-induced or spontaneous irregular and repetitive movements of the face and extremities [7]. When it persists for 24 hours following resuscitation, myoclonic status is a sign of devastating neurological damage.

Etiologies

New-onset seizures can be the result of a drug intoxication (e.g. theophyhlline), drug withdrawal (e.g., thanol), infections (e.g., meningoencephali-tes, abscess), head trauma, ischemic injury (e.g., focal or diffuse), space-occupying lesions (e.g., tumor of hemorrhage), or systemic metabolic derangements (e.g., hepatic or uremic encephalopathy, sepsis, hypoglycemia, hyponatremia, or hypocalcemia). In one survey of new-onset seizures in ICU patients, the most common causes were sedative or opioid withdrawal (33%), severe metabolic abnormalities (33%), and drug intoxication (15%. The drugs most likely to cause seizures in ICU patients are listed in Table 1.

TABLE-1

Drug-Related Seazures in the ICU

Drug Intoxication	**Drug Withdrawal**
Pharmaceuticals:	**Barbiturates**
Ciprofloxacin	**Benzodiazepines**
Imipenem	**Ethanol**
Isoniazid	**Opiates**
Lidocaine	
Meperidine	
Penicillins	
Theophylline	
Tricyclics	
Drugs of Abuse:	
Amphetamines	
Cocaine	
Phencyclidine	

(Lancet-1998;352:383-390.)

Pathophysiology

Isolated seizures occur due to the generation and spread of abnormal electrical activity among neuronal networks; the networks are probably abnormal to start with. But several mechanisms come into play with the onset of a seizure, which work to terminate the attack. SE is believed to be due to the failure of these seizure abortive mechanisms.

It is now believed that loss of GABA-mediated inhibitory synaptic transmission in the hippocampus is critical for the emergence of SE, and excitatory synaptic transmission is important in sustaining SE.(8) Experimental studies in rats have shown that the sensitivity of GABA-A receptor to benzodiazepines, and other allosteric modulators decreases over time as SE continues. [(8)] This may be one of the reasons for the failure3 of the inhibitory mechanisms.

Prolonged seizures produce CNS damage. The physiologic consequences of SE, such as elevation of body temperature, transient metabolic acidosis, and elevation of hormonal concentrations (such as epinephrine in the arrhythmic range) add to the injury.

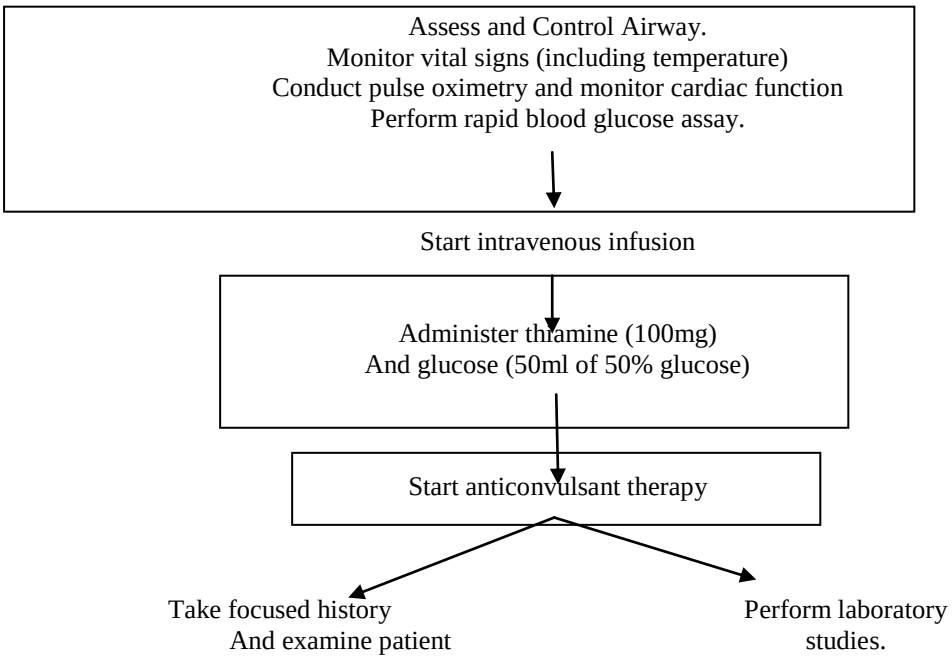
Marked rise in pressure in the systemic as well as the pulmonary circulation may have deleterious effects, such as by causing pulmonary edema. [(9)] Prolonged and repeated seizures themselves cause damage to limbic structures like the hippocampus. This damage is partly due to glutamate-mediated excitotoxicity, and not merely because of increased metabolic demands of repetitive neuronal firing. Continued epileptic activity may lead to relative cerebral hypoxia and hypoglycemia. The seizures compromise cerebral vascular auto-regulation, which in turn compromises hypothalamic autonomic regulation, and intra-cranial hypertension may then supervene.[(36)] Complications such as cardiovascular collapse, arrhythmias, aspiration pneumonia, acute lung injury, and pulmonary hypertension may further compromise cerebral oxygen delivery. Cerebral and systemic hypoxia and acidosis, hyperthermia, rhabdomyolysis, and DIC may then lead to multiple organ failure and death.

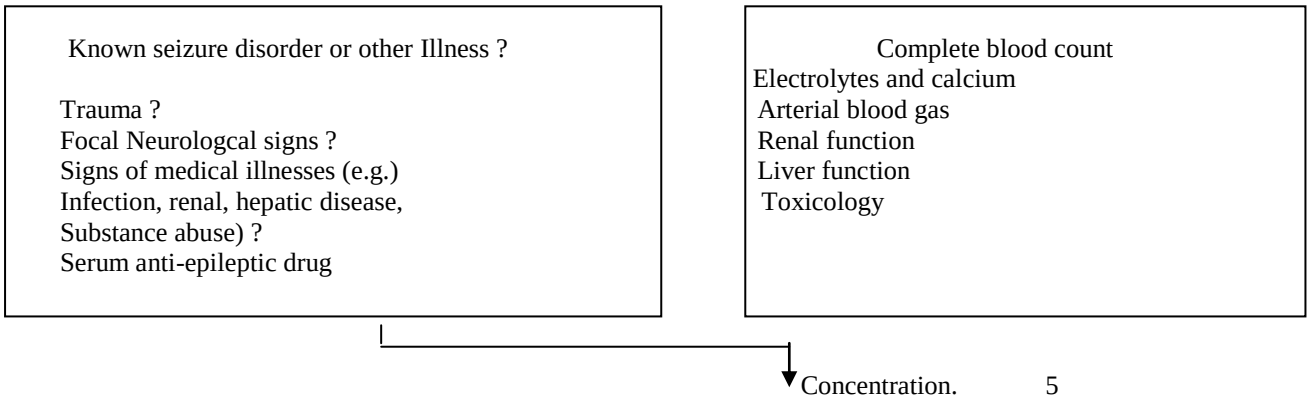
Management

The management of the patient with SE should normally occur at two levels.

1. Management of the seizures themselves.
2. General medical management.

Figure 1 provides the algorithm for the general management of SE presenting to the Emergency Room.





Manage other medical problems.

The patient should be placed in a position to minimize trauma to convulsing limbs from neighbouring hard objects and surfaces. Frequent oro-pharyngeal suctioning may be required. Attempts to prevent tongue bites by placing handkerchiefs and other objects in the mouth between the teeth, have led to choking and death; a towel, folded cylindrically and placed sideways in the mouth may be far safer.

The immediate assessment of breathing and securing the airway is of paramount importance in the actively convulsing patients, as they are highly prone to develop aspiration and all the attendant complications. During the tonic-clonic phase of the convulsion, the patient may stop breathing and become cyanosed; however this is generally short-lasting, and does not create a problem, unless the airway is blocked. Administration of 100% oxygen is usually sufficient, but the airway patency should be secured with an oral or nasopharyngeal airway tube. If there is respiratory compromise, an emergent intubation may be called for; if neuromuscular blockade is deemed necessary to perform the procedure, then a short-acting agent like 0.1mg/kg of vecuronium should be employed, thereby ensuring that ongoing seizures are not missed by the attending physician. Alcohol ingestion is a common cause of presentation in the emergency with SE; prompt administration of thiamine is therefore essential, often before it can be ascertained that alcohol has been consumed . Similarly, immediate blood sugar measurement is now routine, and even when initially normal, 100-200ml of 25% glucose are administered in actively convulsing patients, as blood sugar levels tend to fall, and hypoglycemia can add to the complications.

Hyperthermia and metabolic acidosis occur relatively frequently in SE; together with the peripheral blood leucocytosis, they may suggest an infection and lead to the inappropriate use of antibiotics. Later on the patient may actually develop aspiration pneumonia, for which antibiotics may become necessary. On the other hand, the classical symptoms and signs of acute bacterial meningitis may be absent in convulsive SE with fever; a high index of suspicion for acute bacterial meningitis is therefore of paramount importancde. The most appropriate management is early parenteral antibiotics and lumbar puncture if there are no contraindications. [(11)]. Metabolic acidosis gets corrected once the seizures are controlled. Hyperthermia should be managed emergently with anti-pyretics and colling blankets, as continued high fever can have deleterious effects on the central nervous system.

Control of Seizures

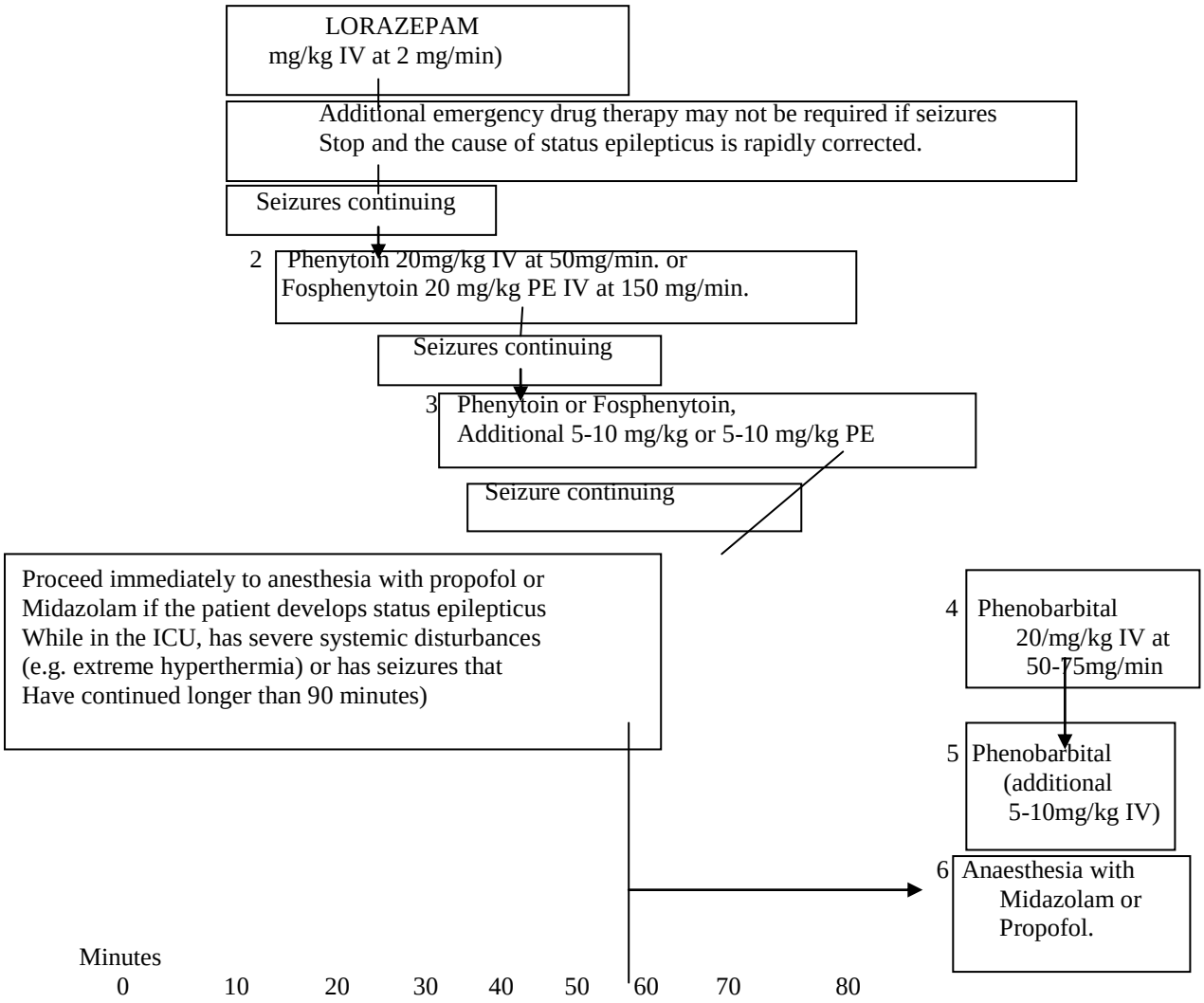
Drug Therapy

In the management of SE, the response to treatment and the ultimate outcome are very much dependent on the duration of the status before effective anti-epileptic medications are administered. This was amply demonstrated in the study in San Francisco in the 1980s, where the authors found that if the AED was administered within 30 minutes of the onset of SE, the response

rate was as high as 80%, whereas in those treated after the 30 minutes period, the response rate fell to 40%. Rapid functional plasticity of $GABA_A$ receptors has been demonstated to occur during SE in rats with a substantial reduction of diazepam potency for termination of the seizures, especially as the duration of electrographic seizures increases. [12].

The ideal drug to control status should be easy to administer, should produce the effect immediately, have long-lasting effect, and at the same time should not depress cardio-respiratory function or the consciousness. Benzodiazepines like diazepam and barbiturates carry the risk of respiratory depression and also depress consciousness in a dose-dependant manner. Phenytoin and fosphenytoin can cause hypotension and cardiac arrhythmias if administered too fast; this can be a limiting factor when attempting rapid seizure control, though in practice this is seldom the reason for failing to control seizures. The Figure 2 gives an algorithm for the management of SE in adults and older children that is followed all over the world ; the choic of drugs is based on the rapidity of action of the drugs and the duration of action. Lorazepam has an extremely rapid onset oft action; in a retrospective analysis comparing the treatment of SE with diazepam and lorazepam, both were found to be equally effective, but there were fewer recurrences with lorazepam, and fewer repeat doses were required. Based on this the authors recommended that lorazepam should be the drug of first choice.

Fig-2- Algorithm for management of status Epilepticus in adults & older children.



Phenytoin has the advantages of the availability of an inject able preparation, and till recently was the only other anti-epileptic drug whose plasma levels could be rapidly brought to the therapeutic range. In addition it has a long duration of action. In a five- year randomized, double-blind trial comparing the efficacy of lorazsepam alone, phenytoin alone, diazepam with phenytoin, and Phenobarbital alone for the treatment of generalized SE, the treatments were equally effective, except that lorazepam alone was more effective than phenytoin alone, when seizures were assessed 20 minutes after the administration began. In the algorithm, lorazepam is followed by Phenytoin if the seizures are not controlled, and this is preferred by neurologists and epileptologists the world over. When the cause of the SE is a reversible one, such as sub-therapeutic drug concentration or an acute metabolic process, then lorazaepam alone may be sufficient and obviate the need for phenytoin or Fosphenytoin.

Pharmacologic Therapy

Benzodiazepines

Intravenous benzodiazepines will terminate 65-80% of convulsive seizures within 2 to 3 minutes. Lorazepam in a dose of 0.1mg/kg. IV or diazepam in a dose of 0.15mg/kg IV is equally effectivfe in aborting a generalized seizure. However, the anticonvulsant effects of lorazepam lasts longer than those of diazepam (12-24 hours vs. 15-30 minutes, respectively), so recurrent seizures are less likely following lorazepam. Because of its prolonged effect, lorazepam is the initial agent of choice for treatment of convulsive seizures. If diazepam is used, it should be followed immediately by phenytoin to prevent seizure recurrence.

Phynytoins

Intravenous phenytoin has been widely used to treat seizures since 1956. The standard intravenous dose is 20mg / kg in adults; a smaller dose of 15mg/kg is recommended in the elderly . A maximum infusion rate of 50mg/min is advised to reduce the risk for cardiovascular depression (which is due to the drug itself and the propylene glycol diluents used in intravenous preparation) . If the initial dose of phenytoin is unsuccessful, additional doses can be given to a total cumulative dose of 30mg/kg . The therapeutic serum level for phenytoin is 10 to 20 microgram/mL.

Phenytoin should not be given in dextrose-containing solutions because it can precipitate, and tissue extravasation must be avoided because the highly alkaline pH of 12 can cause tissue necrosis.

Fosphenytoin is a pre-drug that may be preferred to phenytoin because [(1)] it can be infused faster than phenytoin, [(2)] it does not contain propylene glycol (which contributes to cardiovascular depression), 3) it is compatible with dextrose-containing solutions, and 4) drug extravasation does not cause skin necrosis [(18)]. Fosphenytoin is rapidly converted to phenytoin (half life is 7-15 minutes), and the therapeutic doses are the same as those recommended for phenytoin. However, the maximum allowable infusion rate for fosphenytoin is 150 mg/min, which is three times faster than phenytoin, so fosphenytoin could produce more rapid suppression of seizures than phenytoin.

Phenobarbital

The combination of benzodiazepines and phenytoin will control seizures in 60-90% of cases of convulsive status epilepticus. In refractory cases, intravenous Phenobarbital can be effective when given in a dose of 50-75mg/min. until seizures are controlled or a maximum of 20mg/kg is achieved. The therapeutic serum level for Phenobarbital is 20 to 40microgram/mL. Common side effects include hypotension (usually responsive to IV fluids), respiratory depression, and prolonged sedation (at the higher dose range) Phenobarbital is also the most effective agent available for the initial treatment of nonconvulsive seizures.

Anticonvulsant hypersensitivity syndrome is an uncommon (incidence 1:1,000 to 1:10,000) idiosyncratic reaction to phenytoin or Phenobarbital (cross-reactivity is 50%) associated

with the triad of fever, rash, and lymphadenopathy. Elevated liver enzymes and lymphocytosis occur in up to two-thirds of cases. Treatment involves immediate withdrawal of the offending agent and seizure control with diazepam at 0.05-0.4mg/kg. /hr.

Treatment of Refractory SE (RSE)

When SE does not respond to standard treatment with benzodiazepine, phenytoin, and Phenobarbital, then it is considered to be refractory, requiring aggressive management. Patients generally need to be in the intensive care unit, and most require intubation to prevent aspiration and mechanical ventilation.

This therapy requires a team approach, with the anaethesiology and intensivist playing vital roles . Infusions with anesthetic doses of midazolam or propofol are usually required. EEG monitoring is generally necessary, and the aim is suppression of epileptic spikes; the end point is burst-suppression, though occasionally, fall in Blood pressure becomes a limiting factor, especially when propofol is used. Midazolam is given in a bolus dose of 0.2 mg/kg slow intravenous push, followed by 0.75 to 10 microgram/kg per minute. Alternatively, propofol at a dose of 1 to 2 mg per kilogram intravenous followed by 2 to 10mg/kg/hr may be used. It directly activates $GABA_A$ receptors. In addition, propofol inhibits the NMDA receptor and modulates calcium influx through slow calcium ion channels. Propofol has a rapid onset of action with a dose-related hypnotic effect; and recovery is rapid even after prolonged use. Propofol decreases cerebral oxygen consumption, reduces intracranial pressure and has potent anti-convulsant properties. It is a potent antioxidant, has anti-inflammatory properties and is a bronchodilator. As a consequence of these properties propofol is being increasingly used in the management of traumatic head injury, SE, delirium tremens, status asthmaticus and in critically ill septic patients. [13] Propofol has a remarkable safety profile; dose dependent hypotension is the commonest complication, particularly in patients who are volume-depleted, or have limited cardiac reserve. Hypertriglyceridemia and pancreatitis are uncommon complications. [13] High dose propofol infusions have been associated with the “propofol syndrome”; this is a potentially fatal complication characterized by severe metabolic acidosis and circulatory collapse. [13] A smaller proportion of patients respond to propofol, than to barbiturates, but the response appears much earlier (2.6 min versus 123 min with barbiturate coma). The plasma concentrations of propofol associated with control of SE were 14 microgram / ml+ 4 (25.5 microgram/ml). Recurrent seizures are common when propofol infusions are suddenly discontinued but not when the infusions are gradually tapered Continuous electroencephalo-graphic monitoring is necessary. The duration of treatment is never certain, but usually, a seizure-free period of about 24 hours is sufficient, and the agent can be gradually tapered thereafter, unless further seizures supervene. Recovery usually takes a long time, depending on the duration of infusion, occasionally taking as long as 36-72 hours. More recently a meta-analysis of 22 studies with original data on the use of propofol in SE, has raised serious doubts about the safety of propofol in refractory SE, because two non-randomized studies and several case reports show an increased risk of mortality. The authors of this meta-analysis advise that guidelines should not recommend the use of propofol as a routine treatment in refractory SE before a proper randomized trial has been performed. Midazolam, on the other hand, appears safer; in a recent report of the treatment of 27 pediatric patients with refractory generalized convulsive SE, midazolam infusion at a rate of 3.1 μ/kg/min was found to be effective and safe in 26, without adverse effects such as hypotension, bradycardia or respiratory depression. In a randomized open-label study in children at the PGIMER, Chandigarh, comparing the efficacy of midazolam and diazepam in refractory SE, both were found to be equally effective, with median time to seizure control of 16 minutes; however in the midazolam group, seizures recurred in more children (57% versus

16% in diazepam group; P<0.05) and the mortality was higher in the midazolam group (38%) as compared to the diazepam group (10.5%), P<0.1>0.05). The maximum dose (mean ±SD) of midazolam and diazepam required was 5.3± 2.6 μg/kg/min and 0.04± 2.6mg/kg/min respectively. Thus the experience with midazolam also is varied and mixed, though overall it appears to be equally effective and marginally safer.

Benzodiazepines and barbiturates enhance GABAA receptor-mediated inhibition. However, patients often become refractory to benzodiazepines when seizures are prolonged, and barbiturates are often then used for these refractory cases of SE.[8] RSE has been treated conventionally with high-dose intravenous barbiturate coma; pentobarbital coma (PBC) was evaluated in a small series of 17 patients with RSE.[14] Seizures were aborted in 16 of 17 patients, but vasopressors were required in 11 for severe hypotension; nine of them died, and among these, new-onset epilepsy, multiorgan failure before or during PBC, age>40 years, and hypotension requiring vasopressors during PBC were the causes identified. In a meta-analysis of twenty-eight studies describing a total of 193 patients comparing the efficacy of midazolam (MDL), propofol (PRO), and pentobarbital (PTB) for terminating seizures and improving outcome in RSE patients, PTB treatment was associated with a lower frequency of short-term treatment failure (8 vs. 23% ; P<0.01), break through seizures (12 vs. 42%; p<0.001) and a higher frequency of hypotension (systolic blood pressure <100mmHg; 77 vs 34%; P<0.001). The conclusion is that though PB is more effective, midazolam is both safe and effective.

Sodium Valproate

Although sodium valproate is not approved by the US FDA for treatment of SE, it was found to have an overall efficacy of 63.3% in a study in which 63 patients were given a median dose of 31.5 mg/kg of IV valproate. In a multicenter, open-label, prospective, dose-escalation study of IV sodium valproate administered to patients with epilepsy, rates of infusion of upto 6 mg/kg/minute and doses of upto 30 mg/kg were well tolerated, with no clinically significant negative effects on blood pressure and pulse rate and caused only mild-to-moderate, reversible adverse events, even among unstable SE patients with hypotension.

Topiramate

Topiramate is an anticonvulsant with multiple activities at receptors and ion channels that may be more effective than conventional anticonvulsants in treating RSE. Like phenytoin, topiramate exhibits voltage-sensitive, use-dependent, sodium-channel blockade and may have an additive effect at this site. Topiramate potentiates GABA inhibition independently of the benzodiazepine site on the GABAA receptor and significantly elevates brain GABA levels; this more likely underlies its effectiveness in RSE. . Another action of topiramate is its ability to antagonize excitatory glutamatergic transmission, providing a mechanism for termination of seizure discharges in RSE. [15] Topiramate has been shown to reduce neuronal injury after prolonged SE and may prevent delayed neuronal death. In a series of six cases, topiramate effectively terminated RSE in a variety of clinical settings[16]. In cases of RSE unresponsive to sequential trials of multiple agents, a suspension of topiramate administered via nasogastric tube was effective in aborting RSE; effective dosages ranges from 300 to 1,600 mg/d, Except for lethargy, no adverse events were reported.[16]

Surgery for SE

Patients with RSE of focal origin may be potentially amenable to respective surgery. The literature is limited to isolated case reports or small case series involving multiple subpial transections, cortical resection, corpus callosotomy, or implantation of a vagus nerve stimulator. At the Jefferson Comprehensive Epilepsy Center, patients with medically intractable SE who fail to respond to three courses of cedrebral suppressant therapy for approximately 2 weeks are considered for surgical

treatment in the absence of any known remitting etiology. When structural or functional neuroimaging shows a focal lesion, or the EEG displays focal changes, they prefer focal resection and/or subpial transaction. Corpus callosotomy is used for patients with generalized or non-localizable intractaqble SE. Bingaman and colleagues at the Cleveland Clinic performed respective surgery in the acute setting for refractory SE in 10 patients with focal epileptogenesis when High Dose Supressive Therapy (HDST) failed; 7(10%) became seizure-free, and 3(30%) had significant improvement in epilepsy.

Pre-hospital treatment

SE frequently occurs or is identified in settings where it may not be fesible to administer intravenous drugs; in these settings, rectal diazepam, especially in children, and intramuscular midazolam can be used. Rectal diazepam is very easy to administer ; a starting dose of 0.5 mg/kg is recommended, with a maximum of 20mg per single dose, this is effective in 67% within 15 minutes. A gel formulation for rectal administration of diazepam is under study for rapid out-of-hospital control of SE. After intramuscular administration midazolam is rapidly absorbed (mean time to peak serum concentrations 25 min), and seizures are controlled within 10 minutes.

The mean absolute bioavailability of intramuscular midazolam is 87% and after intramuscular administration, sedation is slower (2-30 min versus less than 1-2 min with the intravenous preparation) and persists for a longer period (20-120 min versus 7-75 min).

Diazepam is administered to children in SE by paramedics in many Emergency Medical Services systems throughout the United States despite the lack of clear evidence that this therapy is safe and effective when employed in the pre-hospital environment. In a retrospective review, published in 1995, (17) pre-hospital diazepam therapy was associated with SE of shorter duration (32 min vs. 60 min; P=0.007) and a reduced likelihood of recurrent seizures in the emergency department (58% vs. 85%; P=0.045). Though these data suggest that pre-hospital administration of diazepam may shorten the duration of SE in children and simplify the subsequent management of these patients in the emergency department, data concerning the safety of such treatment are scanty. Possibly, rectal diazepam or intramuscular midazolam may be considered relatively safe and effective in this setting.

Outcome in SE

The most important factor deciding outcome in SE is the underlying etiology. In the Scan Francisco study, the best response to anticonvulsants occurred in patients with SE related to tumor, anticonvulsant drug withdrawal, or refractory epilepsy. [18] The poor responders in this study had anoxia, drug toxicity, CNS infection, or other metabolic abnormalities. Aminoff et al found that the outcome of SE worsened with an increase in the duration of status.. Towne et al also found that the group with SE lasting <1 h had a lower mortality as compared with seizure duration one hour or more. Hyperthermia, peripheral leucocytosis and CSF pleocytosis are common accompaniments of SE, and even systemic acidosis may occur in a few patients, without necessarily portending a worse outcome. The overall mortality among adults with SE is 20% , and those with first-time episodes of SE are at substantial risk for more such episodes and for the development of chronic epilepsy. [17] When SE is related to an acute medical problem such as renal failure, sepsis, electrolyte abnormality, CNS infections, stroke, head trauma, drug toxicity, or hypoxia, seizures are especially difficult to control and associated with a higher mortality.[18,19]. The best example of this is the elderly patient who has survived as episode of cerebral hypoxia, and has developed myoclonic SE, which carries a grave prognosis. In a recent study evaluating variables affecting outcome in children with SE, no deaths were due to SE itself; [20] symptomatic etiology (acute or remote) and refractory SE were associated with adverse outcomes, and age <12

months at development of SE, and duration of SE>60 minutes tended to be more frequent among those who developed adverse outcome.[20]

CONCLUSION

SE should be identified early and treatment initiated as soon as it is clear that a seizure has lasted 5-10 minutes; out-of-hospital administration of intramuscular midazolam or rectal diazepam by paramedics transporting the patient could shorten the duration of SE and hospital stay. Airway, breathing and circulation should be assessed in the emergency department and adequate steps initiated to correct any abnormalities. The appropriate drug in correct doses should be administered; every hospital needs to follow the treatment based on established protocols, and an early decision to paralyze and ventilate the patient in preparation for continuous midazolam or propofol administration should be taken. With the available drugs and the facilities to manage complications, the morbidity and mortality associated with SE can be minimized.

REFERENCES

1. Bleck TP.Convulsive disorders: Status epilepticus. Clin Neuropharmacol 1991;14:191-08.
2. Treiman DM, meyer PD, Walton NY, et al.A comparison of four treatments for generalized convulsive status epilepticus: Veterans Affairs Status Epilepticus Cooperative Study Group. Neurology 2000;54:340-345.
3. Towne AR, Waterhouse EJ, Boggs JG, et al. Prevalence of nonconvulsive status epilepticus in comatose patients. Neurology 2000;54:340-345.
4. Claassen J, Mayer SA, Kowalski RG, et al. Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. Neurology 2004;62:1743-1748.
5. Mayer SA,Claasen J,Lokin J, et al. Refractory status epilepticus: frequency, risk factors, and impact on out come.Arch Neurol 2002;54:340-345.
6. Wijdicks EF, Parisi JE, Sharbrough FW. Prognostic value of myoclonus status in comatose survivors of cardiac arrest. Ann Neurol 1994;64:267-268.
7. Macdonald RL,Kapur J.Acute cellular alterations in the pippocampus after status epilepticus.Epilepsia 1999;40:S9-20;discussion S21-2.
8. Meldrum BS, Vigouroux RA, Brierley JB. Systemic factors and epileptic brain damage: Prolonged seizures in paralyzed, artificially ventilated baboons.Arch Neurol 1973;29:82-07
9. Hillbom M,pieninkeroinen l,Leone M.Seizures in alcohol-de-pendent patients: Epidemiology, pathophysiology & management CNS.Drugs 2003;17:1013-30.
10. Chin RFM, Neville BGR,Scott RC.Meningitis is a common cause of convulsive status epilepticus with fever. Arch Dis Child 2005;90:66-9.
11. Walton NY, Treiman DM. Response of status epilepticus induced by lithium and pilocarpine to treatment with diazepam.Exp Neurol 1988;101:267-75.
12. Marik PE,Propofol:Therapeutic indications & side-effect.Currpharm Des 2004;10:3639-49.
page-16
13. Yaffe K, Lowenstein DH. Prognostic factors of pentobarbital therapy for refractory generalized status epilepticus. Neurology 1993;43:895-900.
14. Gibbs JW, Sombati S,Delorenzo RJ, Coulter DA. Cellular actions of topiramate: Blockade of kainite-evoked inward currents in cultured hippocampal neurons.Epilepsia 2000;41:S10-6.
15. Towne AR, Garnet LK, Waterhouse EJ, Morton LD, DeLorenzo RJ.The use of topiramate in refractory status epilepticus. Neurology 2003;60:332-4.(Page-16)
16. Alexopoulos A, Lachhwani DK, Gupta A, Kotagal P, Harrison AM, Bingaman W, et al. Resective surgery to treat refractory

status epilepticus in children with focal epileptogenesis. Neurology 2005;64:567-70.

17. Chin RF,Nevile BG, Scott RC. A systematic review of the epidemiology of status epilepticus.Eur J Neurol 2004;11:800-10.
18. Singhi S,Singhi P,Dass R.Status epilepticus:Emergency man agement. Indian J Pediatr 2003;70:S17-22.
19. Hui AC,Joint GM, Li H,Wong KS. Status epilepticus in Hong Kong Chinese:Etiology,outcome and predictors of death and morbidity.Seizure 2003;12:478-82.
20. Kwong KL,Chang K,Lam SY. Features predicting adverse outcomes of status epilepticus in childhood.Hong Kong Med: J 2004;10:156-9.