TABLE 3

Primary Headache Disorders

Headache features	Tension-type headache	Migraine headache	Trigeminal autonomic cephalalgias and cluster headache
Characteristics	No nausea and 2 or more of the following: Bilateral location Nonpulsatile pain (usually pressing, tightening) Mild to moderate intensity Not exacerbated by activity	At least 1 of the following: Nausea or vomiting Photophobia or phonophobia And 2 or more of the following: Unilateral location Pulsatile pain Moderate to severe intensity Exacerbated with activity	Unilateral (usually recurs on the same side) Severe orbital, supraorbital, or temporal pain And 1 or more of the following ipsilateral features: Conjunctival erythema or lacrimation Rhinorrhea Forehead or facial diaphoresis Upper eyelid ptosis or constricted pupil
Other symptoms	With or without pericranial tenderness	With or without aura	Restlessness or agitation
Duration	30 minutes to 7 days	4 to 72 hours	15 minutes to < 3 hours
Frequency	At least 10 attacks in a lifetime	At least 5 attacks in a lifetime	At least 5 attacks in a lifetime Each cluster attack occurs from every other day to 8 per day Cluster attacks cycle between remission periods of a few months
Chronic type diagnosis requirement	Symptoms ≥ 15 days per month for > 3 months	Symptoms ≥ 15 days per month for > 3 months	Remission interval < 3 months, or attacks occur for ≥ 1 year without remission

Information from references 1, 5, and 8.

If the patient has a prolonged (>5-10 min.) seizure or repetitive (3 or more/hr) seizures without recovery between episodes, he is considered to be in SE and the Rx protocol initiated.

The term “prolonged” was previously used to refer to seizures lasting 30 minutes or longer; this interval has been shortened to 5-10 min. for several reasons:

1. almost all convulsive seizures in adults cease in less than 5 minutes without treatment; seizures lasting longer than this are more likely to be self-sustained and to require intervention.

2. the longer seizures persist, the harder they are to terminate pharmacologically, due to down-regulation of inhibitory GABA receptors

3. outcome tends to correlate with seizure duration even after controlling for other important factors, such as age and cause of SE.

The annual incidence of generalised tonic-clonic convulsive SE is estimated to be 18–28 cases per 100 000 persons.

Acute seizures account for 1% of adult and 2% of pediatric emergency department visits– 6% of these are in SE. Higher in developing countries.

SE occurs most commonly in children, the mentally handicapped, and in those with structural cerebral pathology especially in the frontal lobes.

About 5% of all adult patients attending an epilepsy clinic will have at least one episode of status in the course of their epilepsy; in children the proportion is between 10–25%.

Most episodes of status develop in patients without a prior history of epilepsy

Common causes are cerebral infection, trauma, cerebrovascular disease, cerebral tumour, acute toxic or metabolic disturbances, or anoxic encephalopathy. This group of patients have a worse outcome.

In patients with pre-existing epilepsy, status can be precipitated by drug withdrawal, intercurrent illness or metabolic disturbance, or the progression of the underlying disease, and is more common in symptomatic than in idiopathic epilepsy.

Stages os SE

Premonitory SE	Increased frequency or severity of seizures over hours to days, can be a warning of impending SE
Early SE	Up to 30 minutes continuous seizures (or recurrent seizures with no recovery between)
Established SE	More than 30 minutes continuous seizures
Refractory SE	More than 30-60 minutes continuous seizures, despite adequate AED treatment

The approach to the patient with SE should proceed along four overlapping, often concurrent, lines:

(1) terminate SE,

(2) prevent its recurrence,

(3) treat its complications, and

(4) determine and manage its etiology

Risk factors for refractory SE:

1...Underlying acute brain insult etiology– in particular, acute encephalitis but also stroke, trauma.

2....Lack of pre-existing epilepsy.

3....focal neurological signs/seizures at onset.

General Management - In Parallel to Drug Management

General Medical Measures

Secure airway and resuscitate

Administer oxygen

Assess cardiorespiratory function

Establish intravenous access (large veins if possible)

Measure capillary blood glucose and immediately correct hypoglycaemia.

- Give 75 mL 20% glucose intravenously over 5 minutes
- If no intravenous access 1 mg intramuscular glucagon
- Re-check blood glucose after 15 minutes

Check temperature

Check blood gases

If poor nutrition/alcohol abuse suspected give:

Pabrinex® (thiamine, riboflavin, pyridoxine, ascorbic acid, nicotinamide) ONE PAIR intravenously over 10 minutes

OR

Thiamine 100 mg intravenously in 100 mL 0.9% sodium chloride over 30 minutes

If woman of child bearing age—consider pregnancy test

Take blood for:

- electrolytes
- glucose
- calcium
- magnesium
- full blood count
- liver function tests and INR
- anti-epileptic drug levels
- creatine kinase
- alcohol and toxicology screen
- culture as appropriate

CAUTION: Not all seizures are epileptic

In psychogenic non-epileptic seizures 'pseudostatus' **OR**, treatment with sedation or anti-epileptic drugs is not indicated

Consider urgent EEG and seek senior opinion

In-Hospital **Emergency** Drug Management of Convulsive Status Epilepticus in Adults

See page 2 for essential parallel general measures

STEP 1:
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ve if fitting for
> 5 min

First choice:

- **Intravenous lorazepam:** Usual dose bolus **2 to 4 mg** (maximum rate 2 mg/min). If necessary repeat up to a total maximum dose of 0.1 mg/kg.

OR Intravenous diazepam: Usual dose **5 to 10 mg** titrate for effect, up to 20 mg if necessary. Do not gi too fast to avoid respiratory depression (maximum rate 5 mg/min).
Diazepam is rapidly redistributed and may accumulate with repeated dosing.

OR Intravenous clonazepam: Usual dose 1 mg, if necessary repeat 1 mg dose after 5 minutes (maximum rate 0.5 mg/min).

If intravenous is difficult or not possible:

- **Buccal midazolam:** Usual dose **10 mg** (caution: Give 5 mg in the elderly or patients less than 50 kg Repeat dose once after 10 minutes if necessary.[1]
  If buccal preparation not available, use 10 mg/2 mL injection via buccal route.

OR Intramuscular midazolam: Usual dose 10 mg (Caution: Give 5 mg in the elderly or patients weighin less than 50 kg). Repeat dose once after 10 minutes if necessary.

If intravenous, buccal and intramuscular are not possible:

- **Rectal diazepam:** Usual dose **10 mg** (caution: give 5 mg in elderly patients or patients weighing less than 50 kg). Repeat dose once after 10 minutes if necessary.

If seizures stop, the recurrence rate is high; most patients need an intravenous stage 2 anti-epileptic drug (see below for doses) to prevent further seizures

STEP 2:
If no response to step 1 WITHIN 10 min, give stage 2 agent and INFORM NEURO-INTENSIVIST or EXPERIENCED ANAESTHETIST

Second stage antiepileptic drug given **intravenously and inform neurointensivist or experienced anaesthetist**

See loading dose proformas for administration guidance

If there is no specific contraindication or a clear preference for alternative:

Phenytoin; 18 mg/kg (range 15–20); **maximum rate 50 mg/min**. Infuse into large or central vein via filter with ECG and blood pressure monitoring (caution **hypotension, bradycardia)**. Check concomitant drugs (phenytoin is an enzyme inducer—its effect on the half-life of affected drugs is not immediate). For patients already on phenytoin, see note on page 2* before administering.

OR

Levetiracetam; 30 mg/kg (range 20–70); **infuse over 10 minutes**; no interactions; good side effect profile in this setting but comparative efficacy remains to be established; renal excretion.[2,3]

OR

Sodium Valproate; 30 mg/kg (range 15–30); **infuse over 5 minutes**

Contraindicated in mitochondrial disease. Avoid in status of unknown cause in young people. Caution: in pregnancy or acute liver failure, where an alternative is preferable. Check concomitant drugs (valproate is an enzyme inhibitor, with immediate effect on half-life of affected drugs).[4,5]

OR

Phenobarbital; 10 mg/kg (range 10–15); **maximum rate 100 mg/min.** Monitor blood pressure, ECG and respiratory function (Caution: **respiratory depression** may occur—only give if ventilatory support can be provided). Check concomitant drugs (phenobarbital is an enzyme inducer—its effect on the half-life of affected drugs is not immediate).

CAUTION: Not all seizures are epileptic

In psychogenic non-epileptic seizures 'pseudostatus' **OR**, treatment with sedation or anti-epileptic drugs is not indicated

Consider urgent EEG and seek senior opinion

Mandatory Seizure Related Measures

- Investigate the cause of status and treat accordingly
- Consider reinstating any recently withdrawn anti-epileptic drug
- Continue existing anti-epileptic drugs
- Start maintenance anti-epileptic drug therapy promptly
- Refer to local specialist services

*For those on phenytoin, full loading is not appropriate but 'top-up' dose is given as per **clinical decision or** using the following formula:

DOSE = (target level (mg/L) – actual level obtained urgently (mg/L)) × 0.7 × weight in kg

Example: If desired level is 20 mg/L, actual level is 5 mg/L and weight is 70 kg, then
Dose = 20 – 5 = 15; 15 × 0.7 × 70 = 735 mg, rounded up to 750 mg

STEP 3:
If no response to step 2 within 30 minutes of onset anaesthesia and ICU admission

General anaesthesia with intubation and ventilation

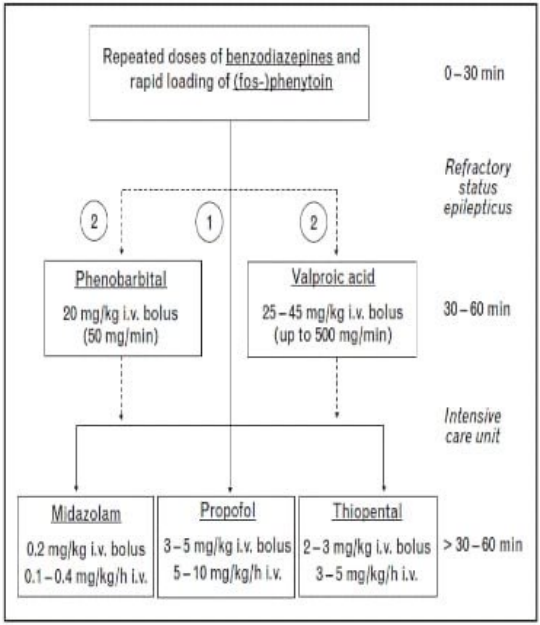
Consider if haemodynamically unstable at any stage or if respiratory support is needed

- These drugs must be **administered by a neurointensivist/experienced anaesthetist in an intensive care unit (ICU) setting** as per local protocols to control clinical/EEG seizures
- *Induction*: usually propofol (1.5–3 mg/kg bolus); caution: hypotension, bradycardia **OR**
  - thiopentone (usually 3–5 mg/kg bolus, additional boluses of 50 mg every 3 minutes until seizures terminated may be given if blood pressure remains stable)
- *Maintenance*: Propofol 1–5 mg/kg/hour titrated to effect; prolonged use may lead to propofol infusion syndrome **OR**
  - midazolam if patient already ventilated, initial bolus 1 mg intravenously and titrate to effect then 0.05–0.20 mg/kg/hour titrated to effect **OR** consider propofol with midazolam **OR**
  - thiopentone 3–5 mg/kg/hour titrated to effect. Caution: hypotension, cardiac suppression, immunosuppression, hypokalaemia, pancreatitis and drug accumulation
- **EEG monitoring is indicated (continuous or minimum every 24 hours) to assess level of anaesthesia and abolition of ictal discharges.**

Over next 24-48 hours, optimise doses and levels of non-anaesthetic anti-epileptic drugs and, if no electrical or clinical evidence of ongoing seizures, withdraw anaesthesia to assess response.

Figure 1 Treatment algorithm for refractory status epilepticus

Pharmacological treatment after failure of first and second-line anticonvulsants. In generalized convulsive status epilepticus, rapid administration of intravenous (i.v.) anaesthetics is recommended (treatment pathway 1) but some centres at first prefer a third nonanaesthetic such as phenobarbital or valproic acid before induction of pharmacological coma (treatment pathway 2). In nonconvulsive status epilepticus, pathway 2 is recommended and anaesthetics are preferably avoided.



Super-refractory (malignant) SE

- SE that continues or recurs 24 h or more after the onset of anaesthetic therapy, including those cases where SE recurs on the reduction or withdrawal of anaesthesia.
- It is an uncommon but important clinical problem with high mortality and morbidity rates.
- New-Onset Refractory SE (NORSE) has a very aggressive course with very high mortality– underlying encephalitis (viral or immune-mediated most likely cause, based on CSF lymphocytosis).

Errors in Management causing poor outcomes

- Inadequate anticonvulsant dosage
- Delay in switching to another drug
- Wrong route of administration (intramuscular phenytoin)
- Delay or failure in initiating maintenance anticonvulsants
- Missing and not treating the precipitating and underlying causes and complications
- Delay in providing cardiorespiratory support such as intubation and vasopressor administration.

Psychogenic Non-Epileptic Status (PNES)

- PNES is characterized by generalized motor activity and no response to tactile and verbal stimuli that continue after intravenous benzodiazepines and I.V. phenytoin.
- It is as common as "true" refractory convulsive SE .
- The vast majority of patients with PNES are misdiagnosed and mistreated for refractory SE including the administration of intravenous anaesthetics
- This aggressive treatment may be associated with serious side effects; morbidity and mortality in PNES are exclusively iatrogenic.

Table 2 Differences between clinical features of true status epilepticus and psychogenic status epilepticus

Clinical features	True status epilepticus	Psychogenic status epilepticus
Sex	Occurs in both male and female patients	Observed in a higher proportion of female patients[20]
Psychiatric history	History of abuse is as prevalent as in other medical disorders	Prevalence of abuse, traumatic life events, comorbid psychiatric disorders and treatment is higher than that observed in patients with epilepsy[20]
Onset	Sudden	Gradual
Motor activity	Tonic–clonic limb jerking	Preparatory movements, body stiffening, thrashing, pelvic thrusting, back arching and head rolling
Progression of motor activity	Initially well-defined or continuous episode; limb movements are usually synchronous; in prolonged status, subtle limb movements, epileptic nystagmus and focal twitching may be observed	Stopping and restarting of motor activity; out-of-phase, asynchronous limb movements; non-physiological progression of activity is more common; subtle eye movements are rare
Vocalisation	At the start of seizure	In the middle of seizure; sobbing, crying and shouting are frequent
Eye open or closed	Forceful eye closure is uncommon	Eyes held shut, resisting passive lid opening
Ocular deviation	Upward or to one side, where present	Geotrophic eye movement; patients tend to look away from the examiner
Pupillary light reaction	Poorly reactive	Briskly reactive
Tongue biting	On the side of the tongue	On the tip of the tongue
Cyanosis	Frequent	Uncommon
Responsiveness during episode	Usually motor activity is not modified by outside stimuli; no withdrawal response to painful stimuli noted	When restrained by examiner, modification of activity with more vigorous and violent movements observed; limb withdrawal to painful stimuli more commonly observed
Consistency of seizure pattern	Usually stereotyped	Variable
Recovery	Clinical and EEG recovery is gradual; organic amnesia for the episode observed after recovery	Prompt clinical and EEG recovery; non-organic amnesia observed
Episodes in sleep	Can occur	Uncommon; to exclude feigned sleep with EEG monitoring
Avoidance testing manoeuvres	On releasing the patient's hand over face, no attempt observed at self-protection; (care should be taken not to cause trauma to patient)	Active resistance of hand falling over face or termination of activity
Induction by suggestion and saline injection in the follow-up clinic after recovery	Controlled induction of seizure is unusual; however, caution should be exercised not to trick the patient	Creating a permissive setting to bring on a typical episode and evaluation with EEG monitoring enables better characterisation of the spell

EEG, electroencephalographic.

Portrait of a Neurology Lesson at the Salpêtrière, Paris-1887 .
Charcot and his resident Babinski are demonstrating the case of young lady with a pseudoseizure