CLINICAL PRACTICE GUIDELINES

Management of Epilepsy

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1. Introduction

Epilepsy is defined as a neurological condition characterized by recurrent seizures. A seizure is the clinical manifestation of an abnormal and excessive discharge of a set of neurons in the brain. Epilepsy should be viewed as a symptom of an underlying neurological disorder and not as a single disease entity.

Epilepsy is the commonest chronic disabling neurological condition. The incidence is about 50 per 100,000 per annum. The incidence is high in childhood, decreases in adulthood and rises again in older people. In the different areas of Sri Lanka, the crude prevalence figure for active epilepsy ranges from 9 -11 cases per 1,000.

The majority with epilepsy does not have any identifiable aetiology; vascular disease and tumor are the commonest. Clinical presentation depends predominantly on the site of origin and pattern of spread of the epileptic discharges within the brain. Epilepsy is primarily a clinical diagnosis, based on detailed description of the events before, during and after the seizure.

Of the patients with epilepsy two thirds have focal or secondarily generalized seizures and one third have generalized tonic-clonic seizures. Most (70%) will enter into remission (free of seizures for five years), but the rest develop chronic epilepsy.

The mainstay of treatment of epilepsy is antiepileptic drug therapy. Surgery is now an option for refractory epilepsy. Due to the social stigma associated with epilepsy, patients commonly encounter problems in education; employment and inter-personal relationships, resulting in significant psychosocial disability. Hence, it is vital to ensure the provision of appropriate information to people with epilepsy and their carers.

This guideline is not intended to serve as a standard of medical care. Adherence to the guidelines,

will ensure a successful outcome in the majority of cases, however, there will be instances where other methods of care may be deemed necessary. The ultimate judgment regarding the management plan must be made by the doctor. However, it is advised that significant departures from the national guideline should be documented in the patient's case notes at the time the relevant decisions are taken.
This guideline will provide evidence based recommendations (where available) on the diagnosis and treatment of epilepsy.

2. Diagnosis of epilepsy

A correct diagnosis of epilepsy is important because it carries major health, educational and psychosocial implications. However, establishing the diagnosis of epilepsy can be difficult. Misdiagnosis is frequent especially if made by a non Specialist. It is therefore crucial that Specialists are involved in the diagnosis of epilepsy.

Recommendations

- The diagnosis of epilepsy should be suspected by all doctors when confronted with a patient presenting with an episodic disturbance of the level of consciousness or an episodic motor, sensory or psychic disturbance.

- All individuals with suspected seizures should be seen early (within 4 weeks) by a Specialist. A Specialist being preferably a Consultant Neurologist, or when not available, a Consultant Physician.
- The name of the Specialist who establishes the diagnosis should be stated in the patient's notes.

The specialist should make every effort to obtain a detailed history from the patient and the eye witnesses to the attack, to determine whether or not a seizure is likely to have occurred. The presence of more than one of the following positive features will support a diagnosis of a seizure.

- Abnormal sensation of taste and smell, rising epigastric discomfort or Déjà vu or Jamais vu phenomena prior to the episode
- Early or late head turn or unusual posturing of limbs during the episode
- Tonic clonic movements during the episode
- Tongue biting during the episode
- Burns, fractures or dislocations sustained during an episode
- Passage of urine or stools, without the patient's knowledge
- Headache, confusion and amnesia following an episode
- Episodes occurring during sleep

Recommendation

- Diagnosis should be collectively based on the description of an episode and the positive features.
- Diagnosis should not be based on the presence or absence of a single feature.

The differential diagnosis of seizures will vary depending on the presenting episodic symptom.

1. Differential diagnosis of an episode of loss of awareness

Patients often present with blackouts and may have amnesia of both the event and its exact circumstances. When confronted with such a patient, in addition to epilepsy, the following diagnoses need consideration.

- Vaso-vagal syncope
- Cardiac arrhythmias
- Transient cerebral ischaemic attacks
- Hypoglycaemic attacks
- Panic attacks
- Non - epileptic attack disorder NEAD

However, syncope is the commonest cause of an episode of loss of awareness. The differentiation from epilepsy could be difficult and needs great skill and judgment. A wrong diagnosis can be made in as high as 25% of patients.

The following features, if present, support a diagnosis of syncope:

- Evidence of a precipitating factor
  - attack brought on by standing quickly, or sitting or standing for prolonged periods.
  - attack triggered by coughing, urination, defecation, fright, shock, unpleasant scene or painful procedure.
- Attack preceded by light-headedness, dizziness, nausea, bilateral visual loss.
- Attack associated with pallor and sweating.

2. Differential diagnosis of generalized convulsive movements

Although this symptom is the commonest epileptic phenomenon, the following conditions may lead to diagnostic confusion.

- Convulsive syncope (convulsive movements can sometimes occur in syncope)
- Primary cardio-respiratory arrest manifesting with secondary anoxic seizures
- Episodic involuntary movement disorders like paroxysmal kinesogenic dyskinesia
- Non epileptic attack disorders (NEAD)

The differentiation of Non epileptic attack disorders (NEAD), previously known as pseudoseizures, from epilepsy, can be extremely difficult. No single feature typifies NEAD. If in doubt, referral to a Tertiary care centre should be made for further evaluation.

The following features if present support a diagnosis of NEAD:

- Attacks triggered by external event or stress
- Suggestible or inducible attacks, or which resolves on distraction
- An attack that builds up slowly and have fluctuating intensity and severity
- Bilateral motor phenomena with preserved consciousness
- Side to side rolling, pelvic thrusting, wild movements and directed violence
- A patient who resists examination and screws up eyes
- Absence of stereotypy

3. Differential diagnosis of drop attacks

Epilepsy may present as a sudden collapse or drop attack. The other causes of that need to be considered include

- Vasovagal syncope
- Cardiac arrhythmia
- Transient ischaemic attacks
- Parkinson's plus syndromes
- Cataplexy
- NEAD
- Idiopathic

4. Differential diagnosis of episodic phenomena in sleep

Attacks occurring in sleep present particular diagnostic difficulty because they are often poorly witnessed and the patient may have little or no recall of the event.

- Normal physiological movements e.g. whole body (hypnic) jerks
- Frontal lobe epilepsy (FLE)
- Parasomnias
- Restless leg syndrome

Some cases of frontal lobe epilepsy (FLE) may be misdiagnosed as NEAD. FLE patients may display frequent, bizarre brief attacks which may be restricted to sleep.

Once the diagnosis is made, a complete physical examination should be carried out. Although often epilepsy is idiopathic, it is important to attempt to identify aetiological factors (Annexure 1).

Recommendation

- A complete neurological examination should be done, though on most occasions the findings will be normal.

3. Classification of epilepsy

3.1 Classification of epilepsy according to seizure type

The International League Against Epilepsy (ILAE) in 1981 proposed this classification based on clinical features and EEG findings. Accordingly, seizures can be classified into 3 main groups, namely partial, generalized and unclassified.

1. Partial seizures

They arise from a focal cortical lesion, most commonly in the temporal lobe.

A. Simple partial seizures (consciousness is not impaired during the episode)

1. with motor manifestations : focal motor (jerking) with or without a march.
2. with somatosensory or special sensory manifestations: somatosensory (tingling, numbness), visual (flashing lights), auditory (buzzing), olfactory & gustatory hallucinations.
3. with autonomic manifestations: changes in blood pressure, heart rate, piloerection.
4. with psychic manifestations: dysphasic (speech arrest, vocalization), dysmnestic (déjà vu, jamais vu), affective (fear), illusions (macropsia, micropsia).

The symptoms and signs depend on the region of the brain where the epileptic discharge originates.

B. Complex partial seizures (consciousness is impaired during the episode)

1. Simple partial seizures followed by impairment of consciousness
2. With impairment of consciousness at onset

C. Partial seizures evolving to secondarily generalized seizures (generalized tonic-clonic, tonic, or clonic)

2. Generalized seizures

They are produced by epileptic discharges that affect both hemispheres simultaneously. Consciousness is almost invariably impaired from the onset of the attack. The seizures may be convulsive or non-convulsive.

A. Typical absence seizures (petit mal seizures) comprise sudden brief episodes of loss of consciousness with cessation of all motor activity. Patient is unaware and appears vacant, but the tone is usually preserved and there is no fall. There may be eyelid twitching during the attack. The attacks end abruptly within seconds.

B. Atypical absence seizures differ from above as the duration is longer, loss of awareness is incomplete, tone changes are more pronounced, and onset / cessation of attacks are not as abrupt.

C. Myoclonic seizures are characterized by sudden brief shock like contractions of muscle groups that cause mild to severe, focal or generalized jerks, singly or in clusters, with usually unaltered consciousness.

D. Clonic seizures take the form of repetitive clonic jerks, often asymmetrical and irregular.

E. Tonic seizures take the form of tonic muscle spasms with altered consciousness without a clonic phase.

F. Tonic-clonic seizures (grand mal seizures) is initiated by loss of consciousness and sometimes by an epileptic cry, followed by a fall. There is a period of tonicity with eyes rolled up and jaw clamped shut, and respiration ceases. This stage is followed by a clonic phase with convulsive movements of all four limbs, jaw and facial muscles, and saliva may froth. There may be incontinence. The final phase is characterized by flaccidity, post ictal confusion and deep sleep.

G. Atonic seizures occur abruptly and result from a sudden loss or reduction of postural tone, which may be limited to a part, but can involve the whole body resulting in a fall. The seizures are short and are followed by immediate recovery.

3. Unclassified seizures

When seizures do not conform to the typical patterns described above or when adequate description or a witness account is not available

3.2 Classification according to epilepsies and epileptic syndromes

In 1989, the ILAE proposed this classification based on age of onset, clinical features, etiology, familial predisposition and response to medication. This classification has the advantage that it provides a guide to appropriate investigations, treatment, and prognosis. Though this is more comprehensive, it is practically more difficult to use and many of the epilepsies remain unclassified. However, all attempts should be made to classify epilepsy using this classification (Annexure 2).

Attempt should at least be made to identify certain syndromes, whenever possible. It will be apparent, that many adults presenting with epileptic seizures will be found to have symptomatic localization related epilepsy. Juvenile Myoclonic Epilepsy should always be considered in young adults presenting with one or more generalized tonic clonic seizures.

4. Investigations

4.1 Electroencephalography (EEG)

A standard EEG should use the 10-20 system for electrode location, and contain at least bipolar montages with longitudinal and transverse chains. Artifacts of eye movement should be excluded using eye-opening, eye-closing, and blink procedures. Provocation techniques like photic stimulation and hyperventilation should be included.

4.1.1 What is the role of EEG in establishing a diagnosis of epilepsy?

Although the diagnosis of epilepsy is essentially a clinical one, the EEG can add powerful supporting information. However, its application is misused in many instances.

Epileptiform abnormalities may be seen in the EEG in about 50% of patients with epilepsy and also in 1% of the normal population. Therefore, the EEG should not be used in isolation to make a diagnosis of epilepsy.

EEG should not be performed when the clinical presentation supports a diagnosis of a non-epileptic event. Similarly, the lack of EEG abnormalities, does not exclude the diagnosis of epilepsy.

The distribution of the epileptiform discharges on the EEG will usually allow a confident distinction between generalized and focal epilepsy.

Recommendations

- An EEG should be performed only to support a diagnosis of epilepsy in patients in whom the clinical history suggests that the attack is likely to be epileptic in origin.
- In all suspected cases of epilepsy, an EEG should preferably be performed after a first seizure; but definitely after a second seizure.

- Individuals requiring an EEG should have the test performed as soon as possible, ideally within 4 weeks.
- Repeated EEGs may be helpful when the diagnosis of the epilepsy or the syndrome is unclear. However, if the diagnosis has been established, repeated EEGs are not likely to be helpful

- When a standard EEG has not contributed to diagnosis or classification a sleep EEG should be performed. Repeated standard EEGs should not be used in preference to sleep or sleep-deprived EEGs.

4.1.2 What is the role of long-term video-EEG?

- Video EEG is useful when faced with diagnostic difficulties, and it can help classify seizure type and syndrome, and help differentiate between epileptic and non-epileptic attacks.

4.2 Neuroimaging

Neuroimaging is useful in the evaluation of patients with seizures, especially to identify structural abnormalities that cause certain epilepsies.

Recommendations

- MRI should be performed in all patients in whom a focal onset of seizure is suggested on the history, examination or EEG.
- MRI is should be performed if the diagnosis of Mesial Temporal Sclerosis (MTS) is considered.
- MRI/CT should be performed if seizures continue despite optimal medication or in the event of recent deterioration in seizure control without apparent reason.

- Neuroimaging should not be routinely requested when a diagnosis of idiopathic generalised epilepsy has been made.

- CT is used to identify an underlying gross lesion, if MRI is not available or is contraindicated.
- CT may be used in an acute situation, to determine whether a seizure has been caused by an acute neurological lesion or illness.

- MRI is the imaging investigation of choice in individuals with epilepsy.
- MRI should be performed in all those who develop late onset epilepsy (over 25 years of age)

4.3 Other tests

Recommendations

- A serum biochemical profile (including plasma electrolytes, renal and liver function, glucose, calcium, magnesium) is essential.
- A 12 lead ECG should be performed as disorders of cardiac rhythm may simulate epilepsy. Twenty four hour ambulatory ECG may also be helpful. In case of diagnostic uncertainty, a referral to a cardiologist should be considered.

- Further investigation of metabolic or biochemical disturbance is indicated if there is any abnormality in the screening test or on clinical evaluation.

4.4 Neuropsychological assessment

Neuropsychological assessment is required in individuals with learning disabilities and cognitive dysfunction, particularly in regard to language and memory.

5. Management of epilepsy

A comprehensive care plan for the management of epilepsy must be drawn up when initiating therapy. This should include the drug choices and dosage, possible side effects, and the plan of action if problems with therapy arise or seizures persist. The patient and family should be fully informed about this plan to ensure good compliance. This should ideally be done by the Epilepsy specialist nurses, who should be appointed to be an integral part of the Epilepsy care team.

Recommendations

- The comprehensive care plan should be drawn up by the specialist.

- Epilepsy Specialist Nurses should be appointed to all Specialists in charge of Neurology units in the health sector.

The goal of therapy is to achieve complete seizure control with minimal antiepileptic drugs, without adverse effects.

5.1 Initiation of pharmacological treatment

Pharmacological therapy will need to be initiated in a majority of patients with epilepsy, and this should be commenced without delay.

Recommendations

- AED therapy should be commenced on the recommendation of a Specialist.
- Therapy should only be initiated once the diagnosis of epilepsy is confirmed.
- Therapy should generally be commenced after the second seizure.

- It maybe considered after the first seizure if the:
  - patient has a neurological deficit
  - EEG shows unequivocal epileptic activity
  - patient and family consider the risk of having a further seizure unacceptable
  - brain imaging shows a structural abnormality.
- It should be commenced only after a full discussion with the patient of the risks and benefits of treatment.
- AED therapy should be individualized according to the seizure type and syndrome, co-medication and co-morbidity, the patient's lifestyle and preferences of the patient and family.
- AED therapy should always be commenced with a single drug.

- AED therapy may be commenced in exceptional circumstances even when epilepsy is still not confirmed, but strongly suspected. This is done when the specialist considers the risk of recurrence of seizure unacceptable.

5.2 Choice of pharmacological treatment

5.2.1 What factors determining the choice of AED therapy?

- seizure type and syndrome
- potential interactions with other drugs
- potential contraindications and adverse effects
- availability and cost of the drug
- co-morbidity
- women of child bearing potential
- patient preferences

5.2.2 What are the available AEDs and their side effects?

Conventional AED – carbamazepine, sodium valproate, phenytoin, phenobarbitone, clonazepam, clobazam

Newer AED - topiramate, gabapentin, vigabatrin, lamotrigine, ethosuximide
Please refer Annexure 3 for common side effects of AEDs.

5.2.3 How would you select the monotherapy?

Most of the conventional AEDs still remain the first choice drugs for the treatment of epilepsy, while the newer drugs are used mainly as add on therapy.

Table : AEDs therapy for different seizure types

Seizure type	First choice	Second choice	Third choice or Add on therapy
Partial seizures (simple & complex)	Carbamazepine	Valproate, phenytoin	Lamotrigine, topiramate, clobazam
Generalised seizures Second choice depends on the seizure type	Valproate		
• Tonic clonic/ clonic		Carbamazepine, phenytoin	Topiramate, lamotrigine, clobazam, phenobarbitone
• Absence seizures		Ethosuximide	Lamotrigine, clobazam, clonazepam
• Myoclonic seizures		Clonazepam	Topiramate, lamotrigine
Unclassified seizures			
• Under the age of 25 years	Valproate		
• Over the age of 25 years	Carbamazepine		

5.2.4 How should monotherapy be commenced?

Recommendations

- The first choice AED therapy should be commenced at a low dose.
- If the first choice cannot be used, the second choice should be used.
- Gradual dose increments (to prevent adverse effects, especially with drugs like carbamazepine) should be made up to the optimal dose for seizure control.

5.3 Continuation of pharmacological therapy

5.3.1 How should AED therapy be continued?

Continuation of therapy should be done by the Specialist, or at the primary care level if the management is straightforward and the local circumstances are favourable.

Recommendations

- If seizures continue despite optimal dosage, it should be built up to a maximum tolerated dosage unless side effects occur.
- The patient should be reviewed every 3 - 6 months, but the frequency of review should be determined by the patient's epilepsy and wishes.
- Specific investigations (eg liver profile) maybe required if side effects are suspected.

- The plan for continuation of therapy should be drawn up by the Specialist and discussed with the patient for good compliance.

5.3.2 What should be done if the first monotherapy fails?

If seizures continue despite the maximally tolerated dose of the first AED,

- review the diagnosis
- review the seizure type / syndrome
- review dosage and frequency of administration
- review compliance

If the first monotherapy fails, it is always essential to try the patients on the second choice AED as monotherapy.

Recommendations

- If the initial AED has failed or has to be withdrawn due to adverse effects, then monotherapy using the second choice AED may be tried. Caution is needed during the changeover period.
- The second drug should be built up to an optimal dose and then the initial drug should be tapered off slowly.
- All attempts should be made to control the epilepsy on monotherapy.
- At least two attempts at monotherapy should be tried before considering a combination therapy.

5.3.3 What should be done if attempts at monotherapy fail?

Combination therapy should be tried, and there is a 10-15% chance of duo therapy controlling the seizures.

Recommendations

- If symptoms are not adequately controlled on monotherapy, an appropriate second choice AED should be added.
- If the added second drug is unhelpful, it should be gradually withdrawn, and another AED should be gradually commenced.

- If the second drug is also only partially helpful, either the first or second drug may be tailed off, depending on the relative efficacy, side effects and tolerance, and another drug tried.
- If symptoms are not adequately controlled on several attempts with two drug combinations, a third AED may be added.
- The aim of treatment is to maintain the patient on the minimum number of drugs required to achieve adequate symptom control.
- If trials of combination therapy do not bring about worthwhile benefit, treatment should revert to the regimen (monotherapy or combination therapy) that has proved most acceptable to the patient (considering seizure frequency and tolerability of side effects).

5.3.4 What AEDs could be used for combination therapy?

When two or more AEDs are combined, pharmacokinetic interactions may affect drug efficacy or result in adverse effects. However, certain combinations may result in synergistic antiepileptic effects without concomitant adverse effects so giving rise to an increase in therapeutic efficacy.

Recommendations

- It is beneficial to combine two AEDs that have differing modes of action, ie the mode of action of the second drug should be complimentary to the first AED.
- Avoid combinations of AEDs with similar adverse effect profile.

Acceptable combinations of AEDs

- Carbamazepine and valproate (leads to an enhanced therapeutic efficacy).
- Valproate and ethosuximide (controls absences in some patients who are not controlled by either drug alone).
- Valproate and clonazepam (combination useful for control of myoclonic seizures)

Combinations of AEDs that should preferably be avoided

- Carbamazepine and phenytoin (enzyme inducers causes reduced drug level of each drug).
- Carbamazepine and lamotrigine (enhances each others side effect profile).

5.3.5. When should blood levels of AEDs be monitored?

- to detect non-adherence to medication
- when toxicity is suspected
- to adjust the dose of phenytoin
- in specific conditions: status epilepticus, organ failure, pregnancy.

Regular monitoring of blood levels of AEDs is not routinely recommended. Measurement of blood levels of valproate is of little use in management.

5.4 Withdrawal of treatment

Withdrawal of anti-epileptic drug treatment should be considered only after a seizure free period of at least 3 years. Due consideration should be given to the following factors which predict increased seizure recurrence following withdrawal of therapy - age over 16 years, seizures requiring more than one AED for control, recurrence of seizures after starting antiepileptic treatment, presence of multiple seizure types, presence of an underlying neurological disorder, persistence of an abnormal EEG, and a longer period of active disease prior to seizure control.

Recommendations

- Withdrawal of AED therapy should be considered in patients who have been seizure free for at least 3 years.
- The seizure free period, prior to withdrawal of AED therapy should be longer in high risk patients.
- Decision to continue or withdraw medication should be made after a full discussion of the risks and benefits of withdrawal. The discussion should take into account the epilepsy syndrome, prognosis and patient's lifestyle. It should also consider the patient's fear of having recurrence of seizures and attitude toward prolonged AED treatment.
- When AED treatment is being discontinued, it should be done slowly (at least over 2-3 months) and one drug should be withdrawn at a time.
- Care should be taken when withdrawing benzodiazepines and barbiturates because of a higher risk of seizure recurrence during withdrawal. The aim is to extend withdrawal to a minimum of six months per AED, with dosage being reduced at 4 week intervals.
- Patients should be advised that if seizures recur, they should reverse the last dose reduction and seek medical advice.

- Withdrawal of AEDs must be managed by, or done under the guidance of, a specialist.

5.5 Risk of relapse on withdrawal of therapy

Eighty percent of relapses occur during the first year and the majority of these relapses occur during the withdrawal phase.

Recommendations

- In the event of seizure recurrence following withdrawal of AEDs the patient should be referred to a specialist.

- AED therapy must be recommenced in accordance with the principles of initiating treatment.
- AED therapy must be continued again for at least three years or longer.

6. Management of Medically Refractory and Complex Epilepsy

About 15% of patients with epilepsy have poorly controlled epilepsy where the seizures are difficult to control with currently available AED therapy. Such patients should benefit from referral to a tertiary centre and further assessment, which may include assessment for epilepsy surgery.

Recommendation

- All individuals with epilepsy should have access via their specialist to a tertiary service when circumstances require.

6.1 What are the components of a tertiary service?

The tertiary service should include a multidisciplinary team, experienced in the assessment of individuals with poorly controlled epilepsy, and have adequate access to investigations and treatment by both medical and surgical means.

The multidisciplinary team should include a neurologist, neurosurgeon, psychologist, psychiatrist, neuroradiologist, epilepsy specialist nurses, social worker, occupational therapists and physiotherapists. The teams should have MRI and video telemetry facilities available to them.

6.2 When should you refer patients to a tertiary service?

If seizures are not controlled and/or there is diagnostic uncertainty or treatment failure, individuals should be referred early to a tertiary service for further assessment.

Recommendations

Referral should be considered when one or more of the following are present:

- epilepsy is not controlled with appropriate medication within 2 years
- management is unsuccessful after combination of two AEDs
- presence of unacceptable drug side effects
- presence of a structural brain lesion
- when there is doubt as to the seizures type and/or seizure syndrome
- presence of behavioral or developmental regression, or psychiatric co-morbidity
- presence of specific conditions like Sturge-Weber syndrome, Rasmussen's encephalitis and hypothalamic hamartoma

6.3 What is the role of non-drug treatments in the management of the epilepsy?

Although the mainstay of treatment for epilepsy is pharmacological, non-drug treatments may be used.

- Psychological interventions such as relaxation therapy, cognitive behavior therapy and bio-feedback have been used alone or in combination.
- Ketogenic diet which is a high in fat and low in carbohydrate can be used mainly as an adjunctive treatment for children.
- Vagus nerve stimulation (VNS) may be used as an adjunctive treatment in drug resistant epilepsy patients who are unsuitable for surgery.

6.4 What is the role of epilepsy surgery?

All patients with medically refractory seizures must be evaluated by a Neurologist, so that those suitable are offered surgery. Surgery is a desirable option for treatment of certain forms of refractory epilepsy, especially temporal lobe epilepsy due to Mesial Temporal Sclerosis. Surgery has a high chance of controlling epilepsy in these patients, allowing them to complete their education, integrate socially, obtain employment and avoid a lifetime of antiepileptic drugs and hospital attendance.

Epilepsy surgery is underused as a treatment modality as suitable individuals are not being referred to a tertiary centre.

Recommendation

- Every patient with refractory temporal lobe epilepsy should be referred to a tertiary centre for evaluation for surgery.

7. Management of Status Epilepticus

Status epilepticus is a state in which epileptic activity persists for 30 minutes or more, and may take the form of continuing seizures or repetitive attacks of seizures without regaining consciousness in-between. It generally refers to convulsive or tonic clonic status. Non convulsive status epilepticus is a state in which continuing seizure discharges on EEG may not be accompanied by convulsive movements.

It is important to look for any causes of precipitation of status which include structural cerebral pathology, cerebral infections, trauma, cerebrovascular disease, neoplasm, acute toxic or metabolic disturbances and sudden AED withdrawal.

The aims of management are,

- Recognition of status or its premonitory stage.
- Maintain vital functions: airway, breathing and circulation.
- Arrest seizure activity: treat promptly, appropriate to stage of status.
- Recognize any underlying precipitating causes.
- Start concurrent regular maintenance AED therapy.
- Anticipate complications.
- Adjust treatment protocols to suit local conditions.

Recommendations

Management will depend on stage of status epilepticus.

1. **Premonitory stage:** Stage of increased epileptic activity (serial or prolonged seizures) which may indicate impending status epilepticus.

General measures

- Secure airway and administer oxygen
- Assess cardiorespiratory function (pulse, blood pressure, oxygen saturation, ECG)
- Establish intravenous access

Emergency medication

- Lorazepam iv: 4mg (0.07mg/kg up to 4 mg), rate of injection is not crucial or
- Diazepam iv: 10 mg (0.2mg/kg up to 10mg), rate not exceeding 5mg/min or
- Diazepam rectally: 10 -30 mg or
- Midazolam: buccal: 10 mg, instilled into sublingual area.

If at home, give diazepam rectally (10-30mg), and admit to nearest hospital.

2. Early status: first 30 minutes

General measures

- Monitor cardiorespiratory function.
- Do urgent blood sugar, serum electrolytes, blood urea, liver function, calcium and magnesium, full blood count and clotting screen.
- Give 50 ml of 50% dextrose with iv thiamine (250 mg) if suggestion of alcohol abuse
- Treat acidosis if severe.
- Consider possibility of non- epileptic status.

Emergency medication

- Lorazepam iv (0.1mg/kg, usually a 4mg bolus), rate of infusion is not critical, is drug of first choice or
- Midazolam iv (0.1-0.3mg/kg), rate at less than 4mg/minute or
- Diazepam iv (0.2 mg/kg, usually 10 mg), rate not exceeding 5mg/min.

  May be repeated once should seizures recur within 10-15 minutes.
- Regular AED therapy to be started or upgraded at this stage.
- Infusions of diazepam (recommended previously) is discouraged as there is likely to be a sharp rise in blood levels following saturation of adipose tissue, with resultant respiratory depression and hypotension.

3. Established status: next 30 to 60 minutes or where early treatment has failed. It is also safe to assume this stage, if no accurate estimation of duration of status can be made.

General measures

- Request for ICU bed and inform anaesthetist
- Search for metabolic complications such as acidosis and electrolyte disturbance.
- May need circulatory support (iv fluids and presser therapy)
- Perform concurrent investigations to detect possible precipitating causes.

Emergency medication

- Fosphenytoin iv (prodrug of phenytoin) if available would be drug of first choice. Dosage calculated in phenytoin equivalent (PE) units - 15mgPE/kg iv given at rate of 100mgPE/min (7-10 min) or
- Phenytoin iv infusion -15mg/kg iv given at rate of 50 mg/min (15- 20min) and /or
- Phenobarbitone iv bolus – 10 mg/kg iv at 100 mg/min. (usually 5-7 minutes)

Following intravenous loading, therapeutic levels should be maintained with oral or intravenous supplementation of above medication.

- ECG monitoring is essential. Risk of respiratory depression is higher after long acting benzodiazepines. Patients should be managed in an ICU setting.

4. Refractory status: Once status has continued for 60-90 min with previous therapy.

General measures

- ICU setting is mandatory
- EEG monitoring
- Long term AED therapy should be started if already not initiated.

Emergency Medication

Essentially require general anaesthesia and ventilation. Three drugs are commonly used.

- Propofol (1-2mg/kg bolus, then 2-10mg/kg/hour) titrated to effect or
- Thiopentone – 3-5mg/kg bolus (usually 250 mg) with further 50mg boluses every 2-3 minutes till seizures are controlled, followed by iv infusion (3-5mg/kg/hour), titrated to effect or
- Midazolam – bolus 0.1-0.3mg/kg iv given at less than 4mg/min, followed by iv infusion at 0.05-0.5mg/kg/hour titrated to effect.

Depth of anaesthesia should be titrated to achieve suppression of epileptic activity or achieve a burst suppression pattern on EEG. Anaesthetic medication is continued for 12-24 hours after last clinical or EEG seizure and slowly withdrawn, provided adequate levels of regular AED' therapy have been built up.

8. Women of childbearing age with epilepsy

Women with epilepsy face special problems with regard to contraception, pregnancy and breastfeeding.

8.1 Contraception

Women with epilepsy should be informed of the risks and benefits of the different contraceptives.

Recommendations

- If a woman taking enzyme-inducing AEDs (phenytoin, carbamazepine, phenobarbitone, topiramate) chooses to take a combined oral contraceptive pill, a minimum initial dose of 50 mcgs per day of oestrogen is recommended. If breakthrough bleeding occurs, the dose should be increased to 75 to 100 mcgs.

- Women taking enzyme-inducing AEDs who choose to use depot injections of progesterone should be informed that a shorter repeat injection interval is recommended (10 weeks instead of 12 weeks).
- The progesterone-only pill and the progesterone implant are not recommended as reliable contraception in women taking enzyme-inducing AEDs.

8.2 Preconception

The preconception period should be utilised to identify and correct the risk factors for the fetus and mother, and also to take action to prevent an increase of seizures during pregnancy.

Recommendations

- All women should be advised at the very first clinic visit, about the need for a planned pregnancy.

- Pregnancies in women with epilepsy should be planned well in advance, following consultation with a specialist.
- Patients should be discouraged to alter or stop medication without medical advice when they discover that they are pregnant.
- Supplemental folic acid (0.5mg per day) is advised from before conception as it results in a significant reduction in the risk of neural tube defects.

- Patients should be evaluated for the possibility of withdrawal of AEDs before they become pregnant.
- If further therapy is required, the AED may be modified so as to use the least teratogenic drug e.g. carbamazepine. Sodium valproate carries a more teratogenic risk and should be withdrawn, where possible.
- Attempt should be made to decrease AEDs from polytherapy to monotherapy. Polytherapy should be avoided as this confers the highest teratogenic risk to the foetus.
- The therapy should be adjusted so that the patient receives the lowest possible dose, which is sufficient to control seizures.
- Genetic counselling may be required for certain patients.

8.3 Pregnancy

It is important to reassure that most women with epilepsy will have no problems with pregnancy and the postpartum period. The frequency of their seizures often remains unchanged, and in more than 90% they have a normal baby. Injury to foetus can occur during generalised tonic clonic seizures in pregnancy. Thus, good seizure control is very important.

Recommendations

- All women with epilepsy planning a pregnancy should be seen by a specialist and the care should be shared with the obstetrician.

- Pregnant women who are taking AEDs should be offered a high resolution ultrasound scan to screen for structural anomalies. Maternal alpha-fetoprotein levels may need to be checked.
- The risk of seizures during labor is low, but delivery should take place in an obstetric unit with facilities for maternal and neonatal resuscitation and treating maternal seizures.
- All women taking enzyme-inducing AEDs should 10mg of vitamin K parenterally during labour. All children born to mothers should be given 1 mg of vitamin K parenterally at delivery.

8.4 Breast Feeding

Breastfeeding for most women taking AEDs is generally safe and should be encouraged. Most AEDs pass into breast milk only in low concentrations. The benefits of breast-feeding usually out weigh any hazard to the baby.

9. Psychosocial aspects of Epilepsy

A diagnosis of epilepsy is a very traumatic event and has far reaching consequences not only to the patient, but to society as a whole. Misconceptions abound regarding the true nature of epilepsy, underlying aetiology and treatability, and the ability of the patient to lead a normal and productive life. This leads to a significant treatment gap and delay that needs to be urgently addressed.

Epilepsy patients face a multitude of problems which include a very high school drop out rate, difficulties with obtaining employment, reduced marriage prospects, problems regarding pregnancy and the inability to integrate and be accepted in society. It needs to be appreciated that in the management of epilepsy, education of the patient, caregivers, family, school teachers, medical practitioners and the society as a whole is as important, as its treatment. Therefore, all of these groups need to be made aware of the following recommendations.

Recommendations

- The 5th of July is the National Epilepsy day, which is a pivotal event in the epilepsy calendar. This day is followed by an awareness week during which all concerned need to conduct and /or participate in awareness and health educational programs on epilepsy.
- Patients and their family should be given appropriate information before they make important decisions (eg: marriage, family planning, pregnancy).
- Patients and their family must be counselled about marriage and childbearing, and be advised that there is no contraindication to marriage or pregnancy.
- It is important to advocate an independent life style as possible, and discuss leisure and social issues (including recreational drugs, alcohol, sexual activity and sleep deprivation).

- Patients must be advised about the occupations that are considered unsafe and the importance of disclosing epilepsy at work. Insurance issues should be discussed.

- Every Specialist, in each of the provinces, along with the Epilepsy specialist nurse must ensure that they devote adequate time for community education programs. They could use educational materials available at a national level or develop suitable alternative material for distribution.
- The information should be provided in suitable formats and languages. Consideration should be given to the patient's age, gender, culture and any specific needs.
- The educational programs and material should encompass the following aspects
    - epilepsy in general
    - diagnosis and treatment options
    - medication and side effects
    - seizure type(s), triggers and seizure control
    - first aid, safety and injury prevention at home and work
    - road safety and driving regulations
    - prognosis
    - sudden death in epilepsy (SUDEP)
    - status epilepticus
- In the out patient clinic setup, adequate time should be set aside in the consultation to provide information, which should be revisited on subsequent consultations.
- Checklists should be used to remind healthcare professionals about information that should be discussed during consultations.
- A named individual should be responsible for ensuring that the information needs of the patient and family are met.

- The specialist must address any psychological issues, refer the patient to other relevant specialists as necessary, and involve social services in the management.
- Patients must be made aware of the available voluntary organizations, support groups and charitable organizations, and how to contact them.

Annexure 1

Aetiology of epilepsy

1. Post traumatic epilepsy
2. Cardiovascular disease
3. Primary cerebral degenerative disorders
4. Epilepsy due to alcohol, drugs and metabolic disturbances
5. Epilepsy following infection
6. Cerebral tumour
7. Congenital or perinatal causes
8. Genetic causes
9. Epilepsy after neurosurgery
10. Reflex epilepsy
11. Cryptogenic epilepsy

Annexure 2

Classification of adult epilepsies and epileptic syndromes

1. Localisation related epilepsies

A Idiopathic (common – Rolandic epilepsy, rare – primary reading epilepsy, benign occipital epilepsy)

B Symptomatic (most commonly temporal lobe epilepsies, but also frontal, parietal or occipital epilepsies)

2. Generalised epilepsies

A Idiopathic
- juvenile absence epilepsy
- juvenile myoclonic epilepsy
- epilepsy with tonic clonic seizures on awakening
- epilepsies with seizures precipitated by specific modes of activation

B Cryptogenic or Symptomatic - epilepsy with myoclonic absences

C Symptomatic - inherited metabolic or congenital disorders

3. Epilepsies undetermined whether focal or generalised

4. Situation related

seizures occurring only when there is an acute metabolic or toxic event – alcohol, drugs, non ketotic hyperglycaemia.

Annexure 3

Common side effects of AEDs

1) Carbamazepine – skin reactions, drowsiness, nausea, vomiting, blurred vision, diplopia, and ataxia, hyponatraemia.
2) Valproate – nausea, weight gain, tremor, hair loss, liver impairment, blood dyscrasias, menstrual disturbances.
3) Phenytoin – hypersensitivity reactions, drowsiness, ataxia, slurred speech, coarsening of facial features, gingival hyperplasia, hirsuitism, haemopoetic complications, hepatitis.
4) Phenobarbitone – drowsiness, lethargy, mental depression.
5) Topiramate – somnolence, weight loss, difficulty with memory, depression.
6) Lamotrigine – skin rash, drowsiness, diplopia, ataxia, nausea, vomiting
7) Clobazam – drowsiness, blurred vision, withdrawal symptoms
8) Clonazepam – sedation, ataxia, withdrawal symptoms

MANAGEMENT GUIDELINES FOR AN ACUTE TONIC CLONIC CONVULSION INCLUDING ESTABLISHED CONVULSIVE STATUS