Making Sure Everything Fits

A rational, individualised approach to patients with seizures - GS Baron

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Curriculum vitae

Geoff Baron obtained the MBChB at UCT in 1985. He completed his internship at Groote Schuur Hospital and then did two years of National Service in the SADF. He has since completed the Vocational Training rotation at Frere Hospital and is registered at MEDUNSA as a part time student for the MPrax Med degree. His interests include Health Resource utlisation and patients' perceptions of quality of care. He is married to Ceri and they have two children.

Summary

Most articles on epilepsy deal mainly with the pharmacology of anti-convulsant drugs. This article also helps with basic aspects like a differential diagnosis, the investigation, the choice of drugs and drug interaction, treatment failure etc. But throughout the whole process it evaluates the ideal situation of the GP to offer comprehensive care to patients who suffer seizures. Optimal bio-scientific knowledge is obviously essential and a treatment protocol in this context is a safety net, but the GP's intimate knowledge of his patient as a person will help to individualize the treatment - and this far exceeds the possibilities offered by other "protocols".

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Epilepsy; Drug Therapy; Physicians, Family; Physician-Patient Relations.

Introduction

There have been a number of articles in the medical literature recently about the treatment of epilepsy.[1-3] These dealt mainly with the pharmacology of anticonvulsant drugs (ACDs) and treatment of the "disease".

This article attempts to look at patients with seizures in a broader perspective and to offer some thoughts on how to deal with the patients as individuals.

Seizures - Some Basics

Bioscientifically a seizure can be defined as "a brief disturbance of behaviour, emotion, motor function or sensation which on clinical evidence results from cortical neuronal discharge".[4] The diagnosis is thus a clinical one and based on a detailed description of events by the patient before, during and after the seizure, or, better still, by an eye witness.

It is of the utmost importance to distinguish a seizure from other causes of intermittent neurological dysfunction. This differentiation often depends entirely on the medical history. Care must be taken to ascertain whether there was a loss of consciousness involved.

A detailed account of three distinct phases should be sought:[5]

1. Events preceding the episode (aura)
2. The episode itself (period of unconsciousness)
3. The period after the episode (post ictal)

The presence of unilateral neurological symptoms such as muscle twitching, parasthesia or altered sensory perception suggests that the loss of consciousness results from a seizure and also suggests the region of the brain from which the problem originates. Seizures may occur during sleep while, with the exception of Stokes-Adams attacks, cardiac causes of syncope do not.

Not all generalised seizures result in loss of consciousness. Simple partial seizures result when the seizure focus remains localised and the manifestations reflect the location of

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the focus. It is often difficult to distinguish these from transient ischaemic attacks (TIAs). As a guide, seizures tend to give rise to positive symptoms whereas TIAs give rise to negative ones. So if the same motor area was to be involved, a seizure would cause abnormal movement and a TIA paralysis.

Psychogenic attacks such as panic attacks are usually precipitated by specific circumstances and there is usually no loss of memory for the event. Pseudoseizures tend to occur with an audience, self injury is rare and the descriptions of the event often bizarre.

Not all generalized seizures result in loss of consciousness

The diagnosis of epilepsy means that the afflicted patient has a continuing tendency to attacks of seizures. In view of the stigma attached to a diagnosis of epilepsy, care must be taken not to make the diagnosis and apply the label incorrectly.

It is obviously important to consider diagnoses other than seizures in a patient in whom the diagnosis is not clear cut. Table 1 lists the common alternative possibilities.[4]

So far we have concentrated on a narrower view of seizures. If we were to attempt to view seizures from a more holistic point of view, the following could emerge.

Brain: Electrical Discharge
? Scarring
? Lesion
? Infection

Body: Motor disorder
Sensory disorder
Risk of injury

Person: Insecurity
Diminished prospects of employment
Diminished self esteem
Sick role

Family: Overprotective, Uncaring

Community: Stigma
Helpful/caring
Chances of employment
Possible severe stigmatization (patient bewitched etc)

Table 1. Differential Diagnosis of Seizures

Syncope – (associated with light-headedness, pallor, nausea, sweating) – consciousness returns quickly, unlike post ictal drowsiness	
Reflex syncope	Postural "Psychogenic" Micturition syncope Cough syncope Valsalva
Cardiac syncope	Dysrhythmias Valvular disease (especially aortic stenosis) Cardiomyopathies Shunts
Perfusion failure	Hypovolaemia Autonomic failure
Psychogenic attacks precipitated by specific circumstances	
Pseudoseizures	usually occur with an audience, self injury rare
Panic attacks	Hyperventilation
Transient ischaemic attacks	
Migraine	
Narcolepsy	
Hypoglycaemia	associated with headache, sweating, anxiety, confusion.

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Accepting that the practitioner needs this type of perspective in mind, it is important to make sure that there is no treatable cause of the seizure.

Treatable causes

Metabolic disturbances
- Hyper/hypoglycemia
- Hyponatremia
- Renal failure
- etc

Pyrexia
Alcohol
Meningitis
Fatigue/stress
Focal lesion eg abscess, tumour
Head injury (acute)
Neurocysticercosis

Non Treatable

Old head injury
Birth trauma/hypoxia
Atrophic focal neurological lesions eg infarcts

Seizures are an all-or-nothing phenomenon

Once the practitioner is satisfied that:

1. The patient has had a seizure
2. There is no immediate treatable cause for it

He then has two dilemmas:

1. How to investigate the patient
2. Who to treat.

Investigation

Both university teaching[6] and our hospital handbook[7] suggest that patients with unprovoked seizures undergo a "recipe" of investigations, viz:

- Random blood glucose
- VDRL (or equivalent)
- Biochemical panel
- Full blood count and ESR
- Skull and chest X-ray

The use of a CT scan and EEG in this setting is not as clearly defined.

Obviously a rational approach is required – what is the doctor looking for, why is he looking for it, and will he be able to offer any sort of intervention on the basis of the investigation? A British study surveyed 408 patients after a first seizure and found no evidence to support the routine use of EEG after an initial seizure. They also found no reliable clinical method of determining who would need CT scanning and did not recommend routine CT scanning.[8] However, Van Donselaar et al prospectively studied 165 patients referred with seizures and felt that routine CT scanning was worthwhile.[9]

The 1st year of treatment is crucial for the long term prognosis

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Cysticercosis is regarded as a common cause of seizures locally in both adults and children. Campbell and Farrell showed that 50% of their series of new epileptics are due to neurocysticercosis and 10% are due to active lesions.[10] This study also showed that with traditional chest, skull and thigh radiographs, a large proportion of cases will be missed. Naidoo found an incidence of cysticercosis of 30% of a random sample of epileptics.[11] Cysticercosis is endemic in the Ciskei/Transkei/East London area and is considered one of the regions major health hazards.[12]

In practical terms the above will be irrelevant for most patients with seizures in our country and the rest of the developing world due to a lack of sophisticated resources. Once the doctor is satisfied that the patient is not hypoglycemic at the time of the seizure, a thorough history and examination should suffice in most cases.

Who To Treat

Conventional wisdom is that patients should not be subjected to long term therapy with ACDs until they have had at least two seizures. The risk of seizure recurrence after a single unprovoked seizure was not thought to be sufficiently high to warrant the potential hazards of therapy.

However there are some problems concerning the research methodology in some of the studies from which the above conclusion was drawn. Since fully 40% of recurrent seizures occur within two months of the initial seizure[13, 14], a delay between the initial seizure and the study entry excludes many single seizure patients as they have already thus experienced two seizures by the time that they would be entered in the study.

For many patients, seizures are controlled with levels below the therapeutic range

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Hopkins et al studied 408 patients with an initial seizure and found a high rate of recurrence after a single seizure in adult life - at least 52% at three years.[8] They were unable to define any clinical factors which characterised patients at particular risk of relapse and also found the EEG to be of little use in predicting recurrence.

However, van Donselaar et al, whose overall recurrence rate in 165 patients was 40% at two years (cf Hopkins 45% at two years) found that the risk of recurrence was 81% in patients with epileptic discharges on a standard or partial sleep deprivation EEG. They concluded that the decision to initiate or delay treatment should be based on EEG findings.[9]

The first year of treatment is crucial for the long term prognosis.[15] If all patients are treated immediately after their first seizure, intractability might be prevented in some patients. Elwes et al found that the interval between untreated seizures decreased successively and that the number of seizures before treatment was started correlated with the outcome of treatment.[16]

> If the treatment is not working, the patient's life circumstances may provide the clue

Where does all this leave the South African practitioner and his (her) patient who has had a seizure? I believe that while all of the above must be borne in mind, a thorough knowledge of the individual patient and his circumstances will allow treatment to be used rationally at an individual level. It would be wise to consider treatment before the "mandatory" two seizures have

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Treatment – What, When and How Much?

The relevance of tailoring drug treatment to the type of seizure has been briefly dealt with above. There are also some important "seizure hygiene" measures to be applied. These involve the removal or dealing with triggering factors. Factors such as:

- Excessive alcohol intake
- Fatigue
- Tricyclic drugs
- Phenothiazines
- Photostimuli
- Glucose control

may play an important role and correcting these may suffice to prevent further seizures. The removal or diminishing of stress is a difficult thing to measure, however some form of psycho-, marital- or family therapy may be appropriate in some cases.

Choosing a Front Line Agent

Once the decision has been made to treat a patient with seizures and the seizure type/classification has been determined as far as possible, a front line single ACD should be chosen. Anticonvulsant polypharmacy confers no advantage over monotherapy in 90% of patients.[3]

The choice of drug is made by taking into account:

- Seizure type
- Cost
- Side effect profile
- Dosage regime/compliance
- Availability
- Individual patient's needs

All ACDs can adversely affect psychomotor and cognitive function.[3] There is also, now, mounting evidence that a reduction in polypharmacy can often improve wellbeing and quality of life without any decrease in seizure control.[17]

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Therapeutic Half Life		Side Effects		
Range	*(Average)*	*Idiosyncratic*	*Toxic*	*Chronic*
40-80 mmol/l	24 hours	Rash Blood dyscrasia (BD)	Sedation Nausea Unsteadiness Headache Behavioural changes	Sedation Intellectual blunting Mood changes Hirsutism Gum hypertrophy Metabolic bone disease (MBD) Folate def. Acne Cerebellar syndrome
15-50 mmol/l	12 hours	Rash (in 5-10%) BD	Diplopia Nausea Drowsiness Unsteadiness	Hyponatremia Drowsiness (less than others)
60-180 mmol/l	96 hours	Rash BD	Sedation Headache Unsteadiness Nausea	Sedation Behavioural changes Intellectual blunting Connective tissue disorder MBD
not helpful	8 hours	Rash BD Hepatic failure Pancreatitis Thrombocytopenia	Sedation Unsteady Behaviour changes	Nausea/vomiting Sedation Tremor Hair loss Weight gain Behaviour change Bleeding disorder
200 - 600 mmol/l	40 hours	Rash BD	Headache Ataxia Nausea Behaviour change	Headache Behaviour change Nausea/vomiting Psychosis
not helpful	30 hours	Rash Thrombocytopenia	Dizziness Sedation Ataxia	Fatigue Weight gain Psychosis
not helpful	30 hours		Occasional idiopathic hyperkinesia/ aggression	

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condition, such as a tumor, may underly the condition.

4. There may be problems with the patient's lifestyle (eg alcohol abuse) which were not previously recognised.

If none of the above apply and seizure control remains poor at the highest tolerated dose, another front line ACD may be substituted. Abrupt withdrawal of the first drug while initiating therapy with the second may precipitate withdrawal seizures or leave the patient without protection while the second drug is building up to a steady state. In practice it is, therefore, safer to add the second drug at a suitable dose and allow it to reach a steady state before beginning to slowly withdraw the first drug. This process is complicated by the fact that most ACDs interact with one another (enzyme induction etc) and serum levels and dosages at these times may be unpredictable and require diligent monitoring.

Numerous drug interactions to be considered when using ACDs

Once all reasonable monotherapy options have been exhausted, it is time to add a second first line drug or possibly clobazam. There do not appear to be studies looking at the additive and synergistic effects between pairs of anticonvulsants.

Only when all these measures have failed, can the patient be truly diagnosed as having refractory epilepsy. In such patients the practitioner would do well to remember the law of diminishing returns as he tries to balance optimal seizure control with quality of life. It is of paramount importance to treat the *patient* rather than the *disease*. A thorough knowledge of a patient and his (her) life circumstances may provide the clue as to why the treatment is not working.

There is no reason for the family practitioner to feel that specialist intervention is warranted without a specific indication for it. Indeed, if one buys the concept of patient-centredness, it must be strongly argued that the family practitioner is best placed to help the patient.

Stopping Treatment

Most ACDs have significant toxic side effect profiles and it is worth exploring the possibility of drug withdrawal in patients who achieve remissions lasting upwards of two years. The danger of such a policy is that of seizure recurrence which may have major implications for self esteem and employment.

There appears to be no good study on this subject, but overall it appears that approximately 30% of patients achieving a two or three year remission will have a recurrence on withdrawal of anticonvulsant drugs. Almost all these recurrences will occur either during the period of withdrawal or within six to twelve months of stopping.[4]

Factors that influence the outcome of treatment withdrawal are similar to those that determine whether a patient initially achieves a two to three year remission. The duration of the epilepsy and its severity (as judged by the number and frequency of seizures before remission) are directly related to the likelihood of a relapse. The type of seizure (according to International classification) is also important in assessing the risk.

Table 5. Stopping Epileptic Treatment[4]

Absolute requirements	Factors in favour	Factors against
2-3 years free of seizures	Childhood epilepsy	Late onset epilepsy
Patient's informed consent	Primary generalised epilepsy	Partial epilepsy
	Absence of cerebral disorder	Cerebral disorder
	Short duration of epilepsy	Long duration of epilepsy
	Normal EEG	Abnormal EEG
	Non driver	Driver
		Juvenile myoclonic epilepsy

When withdrawal is indicated, it is sensible to proceed slowly with dosage decrements over 3 – 6 months.

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Drug Interactions with ACDs[1]

1. Enzyme Inhibition. May Result in Toxicity

Serum levels of carbamazepine increased by:
- cimetidine
- diltiazem
- isoniazid
- verapamil

Serum levels of phenytoin increased by:
- barbiturates
- ethosuximide
- isoniazid
- imipramine
- prochlorperazine
- chlorpromazine

2. Enzyme Induction: Efficacy of the Interacting Drug is Reduced

Serum levels of carbamazepine reduced by:
- barbiturates
- phenytoin

Serum levels of phenytoin reduced by:
- barbiturates
- benzodiazepines
- carbamazepine
- folate
- valproate

Both phenytoin and carbamazepine reduce the efficacy of:
- oral contraceptives
- warfarin

Phenytoin reduces the serum levels of:
- steroids
- nortryptyline

Mutual inhibition of serum levels with:
- barbiturates
- phenytoin

It can be seen from the above that there are numerous drug interactions to be considered when using ACDs. It is wise to monitor serum levels closely in the event of ACD polypharmacy until stable levels are achieved.

Social and Psychological Support for Patients with Seizures

Psychological and social problems are common in patients with seizures.[1] some of the common possible causes are:

1. Insufficient knowledge about seizures on the part of the patient.
2. Cognitive impairment due to treatment with ACDs especially phenytoin and barbiturates.
3. Rejection and ostracization by family/employer/friends.
4. Overprotection by family/friends.
5. Social isolation.
6. Depression.
7. Unemployment – especially in difficult economic times.

Psychological and social problems are common in patients with seizures

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In this type of situation the doctor can offer ongoing support in the form of a healthy doctor-patient relationship. He can also offer information and should strive to facilitate the clearing up of any misunderstandings. As a Family Practitioner, he may know the other members of the patients' family and be able to help with their education about epilepsy. By being patient-oriented rather than disease-oriented it should be possible to offer real and meaningful support to the patient in this setting.

On a far more concrete level, the patient should be warned of the hazards of open fires, deep baths etc. A home visit may help to clear up any problems in this regard. The patient should be advised to wear a Medic Alert bracelet. The patient can also be put in touch with the South African National Epilepsy League (SANEL) which is a national support group for patients with seizures.

The GP should educate family members about epilepsy

The question of what to do about a patient who wishes to drive a motor vehicle is a problematic one. In many cases the patient's livelihood may depend on being able to drive. In terms of the Road Traffic Ordinance a person is disqualified from obtaining or holding a driver's licence if he is suffering from (inter alia) *uncontrolled* epilepsy.[22] The act does not elaborate and the decision as to what constitutes control is open to debate. Practically speaking I feel that if a patient has been seizure free for two years, adequate control has been achieved.

Conclusion

Family Practitioners are ideally situated to offer comprehensive care to patients who suffer seizures. To do this optimally, they should obviously

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be equipped with adequate bioscientific knowledge, but must be able to individualise treatment in the light of their intimate knowledge of the patient as a person.

A treatment "protocol" in this context becomes a safety net, below which level of care the therapy must not sink. The Family Practitioner, more than any other, has the potential to far exceed the possibilities offered by any protocol by tailoring care for the individual patient as a person.

It is hoped that this article, along with the patient described earlier, will help to empower Family Practitioners to manage people who have seizurees with confidence.

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