Diagnosis and Management of Epileptic Patients

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Abstract:

Epilepsy is the second most common neurological disorder in developed countries. Recent advances in the understanding of pathogenetic mechanisms and in the diagnosis and management of epilepsy over the past decade have had a significant impact on every aspect of epilepsy management. A simple diagnosis is inadequate for both patients and physicians. A full diagnostic investigation to classify the type of epilepsy is now mandatory for appropriate care.

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Introduction:

Epilepsy is defined according to International League Against Epilepsy (ILAE) by any of the following conditions (at least two unprovoked seizures occurring greater than 24 hours apart, one unprovoked seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years, and also involved the diagnosis of an epilepsy syndrome **(1).**

Seizures are the manifestation of abnormal hypersynchronous or hyperexcitable discharges of cortical neurons. The clinical signs or symptoms of seizures depend on the location of the epileptic discharges in the cerebral cortex and the extent and pattern of the propagation of the epileptic discharge in the brain. Thus, seizure symptoms are highly variable, but for most patients with 1 focus, the symptoms are usually very stereotypic **(2).**

Epilepsy is a disease of the brain characterized by an enduring predisposition to generate epileptic seizures. It is one of the most common neurological illnesses, affecting individuals of any age and ethnicity **(3).**

Epilepsy affects 65 million people worldwide and entails a major burden in seizure-related disability, mortality, comorbidities, stigma, and costs. In the past decade, important advances have been made in the understanding of the pathophysiological mechanisms of the disease and factors affecting its prognosis (**4).**

Most of those with the disease (80%) are in the developing world with the incidence and prevalence rates were reported to be higher than in the developed world, where it may reach up to 57 per 1000 population with higher rates usually found in rural as opposed to urban

communities. These prevalence rates of epilepsy in the developing countries have traditionally been linked to a variety of conditions, including poverty, lack of prenatal, obstetric, and postpartum medical care, as well as malnutrition, infection and parasitic disorders, and street violence **(5).**

In Egypt many studies have been done on the prevalence of epilepsy in different population. While **El-Afify (6)** reported that the prevalence of epilepsy in Cairo is 9.8 per 1000, and was found in a population based study, in Sharkia Governorate, prevalence of epilepsy was 3.06 per 1000 . The prevalence rate was 9.3/1000 in Assiut Governorate as reported by **Khedr et al. (7).**

The prevalence of epilepsy was found to be higher in males than females and suggested that females might find it easier to conceal their fits **(8).**

Diagnosis of Epilepsy:

The diagnosis of epilepsy is typically made based on the description of the seizure and surrounding events. An electroencephalogram and neuroimaging are also usually part of the workup. While figuring out a specific epileptic syndrome is often attempted, it is not always possible. Video and EEG monitoring may be useful in difficult cases **(9).**

- **EEG in epilepsy**

In neurology, EEG is used in the diagnosis of epilepsy. EEG continues to play a central role in diagnosis and management of patients with seizure disorders—in conjunction with the new remarkable variety of other diagnostic techniques developed over the last years—because it is a convenient and relatively inexpensive way to demonstrate the physiological manifestations of abnormal cortical excitability that underlie epilepsy **(10).**

Noachtar and Remi (11) stated that EEG can answer three main questions in the diagnostic workup of patients suspected to have epilepsy: first, does the patient have epilepsy; second, where is the epileptogenic zone and lastly, how good is therapy?

Video EEG monitoring:

Inpatient video-EEG monitoring combines both a video and an EEG recording of clinical events. This test is used for diagnosis of true seizures and non-epileptic attacks **(12).**

In some series, more than 25 percent of individuals referred for monitoring for refractory epilepsy are found to have nonepileptic events, usually psychogenic nonepileptic seizures. EEG monitoring can also aid in seizure classification and is used for presurgical evaluation of epilepsy patients **(13).**

Invasive EEG:

Intracranial EEG is considered to be an invaluable tool in complex epilepsy surgeries, allowing surgeons to map functional cortex by placing electrodes on the brain surface or brain tissue, and pinpointing the precise location of seizure activity for removal in surgery **(14).**

It has many complications such as, infection, cerebrospinal fluid (CSF) leakage, brain

swelling, and hemorrhage. No permanent neurological deficits were incurred as a result of any adverse event associated with invasive recording, and no deaths occurred (15).

- **Neuroimaging of epilepsy**

It is presently recognized that epilepsy is often associated with gross or subtle structural or metabolic lesions of the brain. Modern neuroimaging is important in the diagnosis and treatment of patients with epilepsy, especially for those patients who have medically intractable seizures (16).

These neuroimaging modalities include computed tomography, magnetic resonance imaging, positron emission tomography, single photon emission tomography, magnetic resonance spectroscopy and functional magnetic resonance imaging (16).

- **Computed tomography:** Although the use of CT for patients with epilepsy has been greatly diminished by MRI, CT is still the technique of choice for the investigation of patients with seizures and epilepsy under certain conditions ,for example it accurately detect hemorrhage, infarctions, gross malformations, ventricular system pathologies, and lesions with underlying calcification. CT has many advantages, lower cost, scan speed, ready accessibility, and easy use, which provide a relatively reliable imaging modality for most patients. (17).

- **Magnetic Resonance Imaging (MRI):**

Indications for MRI in patients with epilepsy:

1. Focal onset of seizures.
2. Onset of generalized or unclassified seizures in the first year of life, or in adulthood.
3. Focal deficit on neurological or neuropsychological examination.
4. Difficulty in obtaining seizure control with first line EDS.
5. Loss of seizure control or change in the seizure pattern.

(18).

Role of MRI in treatment of epilepsy:

One of the most common and illustrative examples in which pathologic findings affect management in a patient with epilepsy is mesial temporal sclerosis. The presence of mesial temporal sclerosis in the context of temporal lobe epilepsy is a strong prognostic indicator for seizure intractability (19).

Other symptomatic epilepsies may include those associated with tumors and malformations of cortical development. In cases of tumors, the decision-making process is expedited by the imaging features. (16).

- **Single photon emission CT (SPECT):**

SPECT is not indicated for the majority of patients with epilepsy but has an important role in the investigation of surgical candidates. The use of SPECT in epilepsy stems from the known association of seizures with increased ictal regional cerebral perfusion or interictal decreases in perfusion (20).

- **Positron Emission Tomography (PET):**

Ictal PET studies of patients with partial seizures showed increase in regional cerebral glucose metabolism and blood flow in the region of epileptic focus. When a single region of metabolic abnormality corresponding to the EEG abnormality is detected, surgical treatment is effective in controlling seizures and improving developmental outcome (21).

- **Magnetic resonance spectroscopy (MRS):**

In epilepsy, the abnormalities typically consist of reduced NAA signal and increased choline, creatine and myoinositol signals (22).

Management of epilepsy:

➢ **Medications**

The mainstay treatment of epilepsy is anticonvulsant medications, possibly for the person's entire life. The choice of anticonvulsant is based on seizure type, epilepsy syndrome, other medications used, other health problems, and the person's age and lifestyle (23).

A single medication is recommended initially; if this is not effective, switching to a single other medication is recommended. Two medications at once is only recommended if a single medication does not work. In about half, the first agent is effective; a second single agent helps in about 13% and a third or two agents at the same time may help an additional 4%. About 30% of people continue to have seizures despite anticonvulsant treatment (24).

There are a number of medications available. Phenytoin, carbamazepine and valproate appear to be equally effective in both partial and generalized seizures (25). In the United Kingdom, carbamazepine or lamotrigine are recommended as first-line treatment for focal seizures, with levetiracetam and valproate as second-line due to issues of cost and side effects. Valproate is recommended first-line for generalized seizures with lamotrigine being second-line (9).

In those with absence seizures, ethosuximide or valproate are recommended; valproate is particularly effective in myoclonic seizures and tonic or atonic seizures. If seizures are well- controlled on a particular treatment, it is not usually necessary to routinely check the medication levels in the blood (26).

Adverse effects from medications are reported in 10 to 90% of people, depending on how and from whom the data is collected. Most adverse effects are dose-related and mild. Some examples include mood changes, sleepiness, or an unsteadiness in gait. Some medications have side effects that are not related to dose such as rashes, liver toxicity, or suppression of the bone marrow. Up to a quarter of people stop treatment due to adverse effects. (27).

Circulating markers of oxidative stress are increased in patients with epilepsy who received prolonged AEDS therapy and may be associated with subclinical atherosclerosis (28).

Oxidative stress plays an important role in the pathogenesis of both atherosclerosis and epilepsy and is a contributing factor in their comorbidity (29).

- **Epilepsy surgery:**

Epilepsy surgery should be considered in appropriate patients with drug resistant epilepsy when seizures are sufficiently frequent or severe as to significantly disrupt the patient's quality of life despite (DRE) defined as the failure of adequate trials of two tolerated, appropriately chosen and administered antiseizure drugs (whether as monotherapy or in combination) to achieve seizure freedom.

These considerations are necessarily individualized, but in general include those seizures that impair consciousness, cause injury, and occur sufficiently frequently as to be disabling (30).

- Vagus nerve stimulation:

Vagus nerve stimulation (VNS) has been approved for adjunctive treatment of medically intractable partial onset seizures in adults and children over 12 years of age. Approximately 30 to 40 percent of patients achieve a greater than 50 percent reduction in seizure frequency, a benefit that is sustained over time, Serious adverse events are rare (31).

- **Cortical stimulation:**

Responsive cortical stimulation is a valid treatment option for patients with refractory focal epilepsy and a well delineated seizure focus. Although resective surgery is still preferred in such patients because it offers a substantially greater potential for complete seizure remission, cortical stimulation may be useful when surgery is not possible (32).

Similar to VNS, responsive cortical stimulation appears to have sustained, if not increasing anti seizure effects over time (33).

- **Ketogenic diet:**

The ketogenic diet (high-fat, low protein) diet has demonstrated efficacy in children with IE, with more than one-third experiencing a 50 percent or greater reduction in seizures (34).

Drug resistant epilepsy:

The International League Against Epilepsy (ILAE) proposed that drug-resistant epilepsy be defined as the failure of adequate trials of two tolerated, appropriately chosen and administered antiseizure drugs (whether as monotherapy or in combination) to achieve seizure freedom .They also recommended replacing the term "intractable" with "drug-resistant" epilepsy **(35).**

Efficacy of anti-inflammatory drugs in the treatment of drug resistant epilepsy:

The use of steroids and adrenocorticotropic hormone in the treatment of infantile spasms has been established since the mid-20th Century. Since that time, despite the fact that solid evidence on efficacy or safety is still lacking for epilepsy other than West syndrome **(36).**

These drugs have also been utilized in other epileptic syndromes including Lennox–Gastaut, Landau–Kleffner, continuous spike and waves during slow sleep (CSWSS) and Rasmussen's encephalopathy **(25).**

The mentioned pathologies are termed 'epileptic encephalopathies' and share some common features as high frequency of seizures and/or of epileptic EEG abnormalities, arrest or regression of psychomotor development or of acquired skills (e.g., aphasia in Landau–Kleffner patients) and, at least in some instances, evidence of inflammation **(37).**

More interestingly, some observational studies suggest that corticoids could also be effective in other forms of generalized and focal epilepsies **(36).**

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