Pitfalls in Convulsive Disorders in Children

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**Definition:**

Epilepsy is a disorder of the central nervous system whose symptoms are seizures.

**Epilepsy Syndrome:**

A clinical entity with relatively consistent clinical features, including seizure type(s), etiology, EEG features, neurologic status, prognosis, and in some cases response to specific antiepileptic drugs.
Epilepsy Incidence: 1935 – 1984

Incidence (per 100,000 Person-Years)

Age (y)

Male
Female
Total
Etiology

Most common secondary causes:

- Genetic and developmental causes.
- Metabolic causes.
- Trauma.
- Infections.
Etiology (Cont.)

- Infections: systemic (sepsis), CNS, encephalitis, meningitis, febrile convulsion
- Focal infection- abscess
- Head injury
- Structural lesions- space occupying lesion- tumour
- Cerebral infarction, haematoma, intra-ventricular haemorrhage (IVH)
- Hypoxia
- Acidosis
- Metabolic disorders
- Electrolyte imbalances: hypocalcaemia, hypoglycaemia, hyponatraemia, hypernatraemia, dehydration
- Toxic ingestion
- Hypoxic ischaemic encephalopathy (HIE)
Prevalence of Generalized and Partial Seizures

Children <15 Years
- Complex partial: 23%
- Tonic-clonic: 19%
- Absence: 13%
- Other generalized: 11%
- Simple partial: 11%
- Myoclonic: 7%
- Other partial: 7%
- Unknown/multiple: 9%

Adults 35-64 Years
- Complex partial: 39%
- Tonic-clonic: 25%
- Absence: 13%
- Other generalized: 11%
- Simple partial: 21%
- Myoclonic: 2%
- Other partial: 9%
- Other generalized: 4%
Classification

• Seizure type > 4 years.
• Epileptic syndrome < 4 years.
• Age of onset.
• EEG.
• Eitology.
### Classification

Epilepsy syndrome by usual age of onset in years.

<table>
<thead>
<tr>
<th>Epilepsy syndrome</th>
<th>Age (yrs) at seizure onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal seizure</td>
<td>(0-1mon)</td>
</tr>
<tr>
<td>EMEE / EIEE</td>
<td>(0-6 wks)</td>
</tr>
<tr>
<td>Infantile spasm</td>
<td>(6mon -1)</td>
</tr>
<tr>
<td>Benign myoclonic epilepsy</td>
<td>(1-2)</td>
</tr>
<tr>
<td>Simple febrile seizure</td>
<td>(6 mon-5)</td>
</tr>
<tr>
<td>Lennox – Gastaut syndrome</td>
<td>(1-8)</td>
</tr>
<tr>
<td>Rolandic epilepsy</td>
<td>(4-19)</td>
</tr>
<tr>
<td>Childhood absence</td>
<td>(3-7)</td>
</tr>
<tr>
<td>GTCS on awakening</td>
<td>(6-22)</td>
</tr>
<tr>
<td>Juvenile absence</td>
<td>(10-15)</td>
</tr>
<tr>
<td>JME</td>
<td>(13-19)</td>
</tr>
</tbody>
</table>
Childhood onset epilepsies encompass all seizure types:
- Focal seizures with or without loss of consciousness.
- Epileptic spasm.
- Typical and atypical absence.
- Myoclonic seizure.
- Tonic, clonic, tonic-clonic and atonic seizure.

Adolescence –onset epilepsies:
- Partial seizure.
- Myoclonic seizure.
- GTCs.
- Rarely absence.

Adult – onset seizure:
- Partial seizure.
- GTCS.
- Myoclonic seizure.
Diagnosis

• Age of onset.
• Family history.
• Frequency of seizure.
• Type of seizure (description or videotape).
• EEG.
• Neuroimaging.
Benign Myoclonic Epilepsy in Infancy
West syndrome
Absence Epilepsy
Rolandic Epilepsy
Lennox-Gastaut Syndrome Atypical absence
Juvenile Myoclonic Epilepsy
Diagnosis by age of onset

1- Absence, tonic and atonic seizures and infantile spasm are diseases of childhood and not present in adolescence or adulthood.

2- Epileptic spasms beyond infancy have quite different presentation. For example, in older children they have mild expression with no obvious effect on cognition.
Differences in Epilepsy and its management in children.

1- High incidence in children compared to adults.
2- Incidence of genetic and developmental causes.
3- Epilepsy and AEDs sometimes cause cognitive and behavioral disorders.
4- Susceptibility to systemic adverse effects
   - Skin → CBZ, Lamotrigin
   - Hepatic → Valproat.
5- Clearance of AEDs (50% in children & 100% in infants).
6- Susceptibility to remission e.g. absence, myoclonus, 1ry GTCS
Seizure management

• A - Management of Acute Seizures

• THOSE CHILDREN WITH FIRST TIME ONE, OR NEW SEIZURES.
Management and goals

Treatment of a child with seizures requires:

- Maintenance of vital functions
- Abolition of seizures
- Elimination of any precipitating factors
- Reversing correctable causes
- Following protocols for management is vital
- Administer prescribed rectal/buccal/intravenous medication according to clinical service guidelines if required, ensuring the correct dosages are administered, this is according to the hospital guidelines for management of Seizures
The initial treatment is directed towards:

- Maintaining an airway
- Supporting breathing and administration of oxygen
- Support and maintenance of vital functions
STATUS EPILEPTICUS is a MEDICAL EMERGENCY

Definition of status epilepticus

• “Any seizure lasting for a duration of at least 30 minutes or repeated seizures lasting for 30 minutes or longer from which the patient does not regain consciousness”.

• Rectal diazepam is a safe, simple and effective treatment for pre-hospital management. Paraldehyde can also be used rectally.

• Midazolam has recently been found to be more advantageous than diazepam in emergency use as it can be given buccally in a syringe.
STATUS EPILEPTICUS is a MEDICAL EMERGENCY ( Cont. )

- The initial treatment for status epilepticus is also directed towards:
- Maintaining an airway
- Administration of oxygen
- Administration of rectal/buccal/intravenous medication according to clinical service guidelines, eg. Valium, Phenobarbital, Hydantoin or Depakin
- Hydration e.g., intravenous fluids if required.
- The child must be closely monitored during administration of intravenous anti-convulsants.
STATUS EPILEPTICUS is a MEDICAL EMERGENCY (Cont.)

- Monitor level of consciousness, vital signs of respirations, heart rate, blood pressure and temperature.
- If first-line drugs are ineffective progress to second-line drugs.
- The child may need respiratory support of intubation and ventilation on a paediatric intensive care unit.
- Outcome is related to aetiology and duration of the status epilepticus.
- Always ensure that the drugs are prescribed by the medical staff and that hospital policy and procedures are followed.
B - Treatment of epilepsy in children

New cases

Pharmacotherapy
AED in monotherapy

Drug refractory cases

1- Pharmacotherapy (Combination of AEDS)
2- Non pharmacological ttt:
   a) Ketogenic diet.
   b) High dose vitamin (pyridoxin)
   c) Surgery.
   d) Vagus nerve stimulation.
EVERYDAY TREATMENT OF EPILEPSY Choices and Outcomes

Antiepileptic drugs

Calendar year

- Bromide
- Phenobarbital
- Phenytin
- Primidone
- Sodium Valproate
- Ethosuximide
- Carbamazepine
- Zonisamide
- Tiagabine
- Topiramate
- Felbamate
- Vigabatrin
- Levetiracetam
- Oxcarbazepine
- Gabapentin
- Lamotrigine
- Fosphenytoin
- More

Outcomes
Choice of AED

1- Seizure type or epileptic syndrome.
2- Etiology.
3- Side effects.
4- Co morbid condition.
5- Age and sex.
6- Cost.
<table>
<thead>
<tr>
<th>Epileptic syndrome</th>
<th>First choice</th>
<th>Second choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>BECTS</td>
<td>Valproic acid</td>
<td>Gabapentin</td>
</tr>
<tr>
<td>Absence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10 years</td>
<td>Ethosuximide</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td>&gt;10 years</td>
<td>Valproic acid</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td>or with GTCS</td>
<td>Valproic acid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Valproic acid</td>
<td>Topiramate or Clonazepam</td>
</tr>
<tr>
<td>Juvenile myoclonic</td>
<td>Valproic acid</td>
<td></td>
</tr>
<tr>
<td>Lennox-Gastaut and related syndromes</td>
<td>Valproic acid</td>
<td>Topiramate &amp; Lamotrigine</td>
</tr>
<tr>
<td>Infantile spasms</td>
<td>ACTH &amp; Vigabatrin</td>
<td>Valproic acid &amp; Topiramate</td>
</tr>
<tr>
<td>Seizure type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focal onset</td>
<td>Carbamazepine</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td></td>
<td>Oxcarbazepine</td>
<td>Topiramate</td>
</tr>
<tr>
<td></td>
<td>Valproic acid</td>
<td></td>
</tr>
<tr>
<td>Generalized tonic – clonic</td>
<td>Valproic acid</td>
<td>Topiramate &amp; Phenytoin</td>
</tr>
</tbody>
</table>
## AEDS that may aggravate some epileptic syndromes

<table>
<thead>
<tr>
<th>Drug</th>
<th>Syndrome</th>
<th>Drug</th>
<th>Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>• Absence epilepsy&lt;br&gt;• Juvenile myoclonic&lt;br&gt;• Progressive myoclonic&lt;br&gt;• Rolandic epilepsy</td>
<td>Vigabaterin</td>
<td>• Absence epilepsy&lt;br&gt;• Epilepsy with myoclonus</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>• Absence epilepsy&lt;br&gt;• Progressive myoclonic</td>
<td>Gabapentin</td>
<td>• Absence epilepsy&lt;br&gt;• Epilepsy with myoclonus</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>• Lennox-Gastaut syndrome</td>
<td>Lamotrigine</td>
<td>• Severe myoclonic epilepsy&lt;br&gt;• Juvenile myoclonic epilepsy</td>
</tr>
<tr>
<td>Phenobarbitone</td>
<td>• Absence epilepsy</td>
<td></td>
<td></td>
</tr>
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</table>
EVERYDAY TREATMENT OF EPILEPSY Antiepileptic drugs

Efficacy

Exacerbation
### ESTABLISHED DRUGS AND SEIZURE TYPES

<table>
<thead>
<tr>
<th>Seizure Type</th>
<th>PB</th>
<th>PHT</th>
<th>CBZ</th>
<th>VPA</th>
<th>ESM</th>
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<tbody>
<tr>
<td>Partial/generalised</td>
<td><img src="light-green.png" alt="Green Light" /></td>
<td><img src="light-green.png" alt="Green Light" /></td>
<td><img src="light-green.png" alt="Green Light" /></td>
<td><img src="light-green.png" alt="Green Light" /></td>
<td><img src="light-green.png" alt="Green Light" /></td>
</tr>
<tr>
<td>Tonic-clonic</td>
<td><img src="light-red.png" alt="Red Light" /></td>
<td><img src="light-green.png" alt="Green Light" /></td>
<td><img src="light-green.png" alt="Green Light" /></td>
<td><img src="light-green.png" alt="Green Light" /></td>
<td><img src="light-green.png" alt="Green Light" /></td>
</tr>
<tr>
<td>Absence</td>
<td><img src="light-red.png" alt="Red Light" /></td>
<td><img src="light-red.png" alt="Red Light" /></td>
<td><img src="light-red.png" alt="Red Light" /></td>
<td><img src="light-green.png" alt="Green Light" /></td>
<td><img src="light-green.png" alt="Green Light" /></td>
</tr>
<tr>
<td>Myoclonic</td>
<td>?</td>
<td><img src="light-red.png" alt="Red Light" /></td>
<td><img src="light-red.png" alt="Red Light" /></td>
<td><img src="light-red.png" alt="Red Light" /></td>
<td><img src="light-green.png" alt="Green Light" /></td>
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<tr>
<td>Atonic/tonic</td>
<td><img src="light-red.png" alt="Red Light" /></td>
<td><img src="light-red.png" alt="Red Light" /></td>
<td><img src="light-red.png" alt="Red Light" /></td>
<td><img src="light-green.png" alt="Green Light" /></td>
<td><img src="light-green.png" alt="Green Light" /></td>
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</tbody>
</table>
# Newer Drugs and Seizure Types

<table>
<thead>
<tr>
<th></th>
<th>GBP</th>
<th>LTG</th>
<th>OXC</th>
<th>TPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial/generalised</td>
<td><img src="image1" alt="Green Light" /></td>
<td><img src="image2" alt="Green Light" /></td>
<td><img src="image3" alt="Green Light" /></td>
<td><img src="image4" alt="Green Light" /></td>
</tr>
<tr>
<td>Tonic-clonic</td>
<td><img src="image1" alt="Green Light" /></td>
<td><img src="image2" alt="Green Light" /></td>
<td><img src="image3" alt="Green Light" /></td>
<td><img src="image4" alt="Green Light" /></td>
</tr>
<tr>
<td>Absence</td>
<td><img src="image1" alt="Red Light" /></td>
<td><img src="image2" alt="Green Light" /></td>
<td><img src="image3" alt="Red Light" /></td>
<td><img src="image4" alt="Question Mark" /></td>
</tr>
<tr>
<td>Myoclonic</td>
<td><img src="image1" alt="Red Light" /></td>
<td><img src="image2" alt="Question Mark" /></td>
<td><img src="image3" alt="Red Light" /></td>
<td><img src="image4" alt="Green Light" /></td>
</tr>
<tr>
<td>Atonic/tonic</td>
<td><img src="image1" alt="Green Light" /></td>
<td><img src="image2" alt="Green Light" /></td>
<td><img src="image3" alt="Red Light" /></td>
<td><img src="image4" alt="Green Light" /></td>
</tr>
</tbody>
</table>
Choice of AED by etiology

1- Infantile spasms secondary to **tuberous sclerosis** show best response to **vigabatrin**.

2- **Carbamazepine** is highly effective in **autosomal dominant nocturnal frontal lobe epilepsy**.
Epileptic syndromes associated with medically refractory seizures in children

- Early myoclonic encephalopathy.
- Early infantile epileptic encephalopathy.
- Infantile spasm.
- Severe myoclonic epilepsy in infancy.
- Myoclonic astatic epilepsy.
- Myoclonic absences.
- Lennox – Gastaut syndrome.
- Continuous spike waves during slow sleep.
- Rasmussen syndromes.
Choice of AED by side effect

- Children with history of skin rash → avoid Lamotrigine, CBZ.
- Poor weight gain → avoid topiramate, Zonisamide
- Hyperactivity + cognitive impairment → avoid CBZ, PHT, PhB, primidom and gabapentin.
- Language dysfunction or behavioral changes → avoid Topiramat.
- Family history of renal stones → avoid topiramat, zonisamide
Gabapentin has a minimal drug – drug interaction.

Most of conventional AEDs (PHT, CBZ, PhB) are hepatic enzyme inducers.

Valproic acid is hepatic enzyme inhibitor.

New AEDs has benign side effects and minimal pharmacokinetic interactions.
Choice of AEDs by age and sex

- Serious skin rash are more common in children than adults (10 times) children 1-2% & adults 0.1%
- Toxic hepatic disorder also may occur with valproic acid in children but not in adults.
- Phenytoin may cause hirshitism, gum hyperplasia and or dysmorphic feature of face, so can be avoided in girls.
- Valproate may cause subfertility in girls.
Choice of AEDs by comorbid conditions

1) Migraine better valproate and gabapentin
2) Mood disorder better mood stabilizers:
   - Valproate
   - Carbamazepine
   - Lamotrigine
   - Topiramate
• In general, children require AED doses about 30% higher than adults on a mg/kg basis because faster renal and hepatic clearance.
Treatment of Intractable Epilepsy

• 20% of patients diagnosed as epilepsy are non epileptic.
• 20% of epileptic patients are refractory to AEDs
  1- Drug polytherapy.
  2- Ketogenic diet.
  3- High dose vitamins.
  4- Surgery.
1- Polytherapy

- Using drugs with complementary mood of action (GABA ergic, Glutamate antagonist, Na blocker, Ca blockers).
- **Best combination:** 1) Valproate + Carbamazepine.
  2) Valproate + lamotrigine
  3) Lamotrigine + Topiramat
- Older agents *(Clobazam and acetazolamide)* are useful as adjuvant treatment for cases of refractory epilepsy.
- The triad of **sodium valproate + lamotrigine + topiramate** can be effective in patients with *multiple seizure types.*
The diet was once thought to work because of ketosis that is achieved. However, the mechanism of action is unclear.

It is effective in children with very frequent medically intractable seizures in children myoclonic, atonic, absence seizure and infantile spasms.

Needs:
1- Admission to hospital
2- Supervised fasting starvation & dehydration ketones in urine ketogenic diet (high fat, low protein and carbohydrates + supplement with vitamins and minerals).
3- High dose vitamin therapy (pyridoxine)

B6 is Cofactor of glutamic acid decarboxylase.

Glutamic acid \rightarrow \text{GABA}

Glutamic acid decarboxylase
4- Surgery

A) **Resective surgery**:  
1- Localization related epilepsy.  
2- Refractory seizure.  
3- Identified seizure focus

B) **Corpus collosotomy**.

C) **Vagus nerve stimulation** (VNS).
Patients who are treated and controlled sooner have lower chances of developing:

1- Resistant disorder (GTCS).
2- Epileptic encephalopathy.

Seizure and/or epileptiform EEG decrease neurological and cognitive development and functioning.
Treatment can be withheld without significant risk in children.

1- Single seizure.

2- Febrile convulsions.

3- Rolandic epilepsy.

4- Adolescents with isolated seizure.
Conclusion

- The aim of treating epilepsy is control of the seizure with full respect of quality of life issues, including maintenance of cognitive functions.
- Some epilepsy syndromes are benign and seizures are known to be rare. In these cases, treatment is often unnecessary.
- Treatment should be started with a broad spectrum agent.
- Early surgery is appropriate in carefully selected patients with focal epilepsy.
In polytherapy, use drugs with complementary mode of action.

There are specific indications for some syndrome e.g. vigabatrin for infantile spasms and valproate for typical absences or juvenile myoclonic epilepsy.

There are specific contraindications, including aggravation of some seizures e.g. carbamazepine or phenytoin in absence seizure, lamotrigin in GME.
General Information

Date: 13 April, 2015  
Venue: Helnan Palestine Hotel, Alexandria, Egypt  
Language: English  
Certificate of Attendance: Will be available upon request  
Exhibition: There will be an exhibition of the latest technical equipment and pharmaceutical products at congress hotel  
Abstracts & Presentations: To be sent as word document size A4 with font (Arial) size (12) on this e-mail: abstracts@cme-group.net maximum by 15/01/2015  
(Please write the complete personal contact details in the e-mail)

Registration Packages

<table>
<thead>
<tr>
<th>Package</th>
<th>Before 15 Feb</th>
<th>After 15 Feb</th>
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<tbody>
<tr>
<td>Congress</td>
<td>150 USD</td>
<td>200 USD</td>
</tr>
<tr>
<td>Workshop</td>
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<td>SGL</td>
<td>3000 EGP</td>
<td>3400 EGP</td>
</tr>
<tr>
<td>DBL</td>
<td>3800 EGP</td>
<td>4200 EGP</td>
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</tbody>
</table>

Packages includes

1 Registration for 1 doctor  
2 nights’ accommodation  
1 Accompanying Person in case of DBL  
The Above rate excludes Transportation

Organized by:

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11th Pan Arab  
Child Neurology (PACNA)

In Collaboration With

19th Egyptian Society of Child Neuropsychiatry (ESCNP) Conference  
3rd Pediatric Neurology Unit (PNU), Alexandria University  
International Child Neurology Association (ICNA)  
African Child Neurology Association (ACNA)  
Saudi Pediatric Neurology Association (SPNS)  
Saudi Epilepsy Society (SES)

"New Horizon in Pediatric Neuropsychiatry"

April 1st - 3rd, 2015  
Helnan Palestine Hotel, Alexandria, Egypt