March 2015

Epilepsy in pakistan: national guidelines for clinicians

Fowzia Siddiqui
Aga Khan University, fowzia.siddiqui@aku.edu

Tipu Sultan
Children Medical Center, Lahore

Shahid Mustafa
Aga Khan University

Sarwar Jamil Siddiqui
Aga Khan karachi

Shaukat Ali
Neurospinal Institute, Karachi

See next page for additional authors

Follow this and additional works at: http://ecommons.aku.edu/pakistan_fhs_mc_surg_surg

Part of the Neurology Commons

Recommended Citation
Available at: http://ecommons.aku.edu/pakistan_fhs_mc_surg_surg/276
12-2015

Epilepsy in Pakistan: National Guidelines for Clinicians

Fowzia Siddiqui
Aga Khan University, Karachi, drfowzia@hotmail.com

Tipu Sultan
Children Medical Center, Lahore

Shahid Mustafa
Aga Khan University, Karachi

Sarwar Siddiqui
Aga Khan University, Karachi

Shaukat Ali
Neuropinal Institute, Karachi

See next page for additional authors

Follow this and additional works at: http://ecommons.aku.edu/pjns
Part of the Neurology Commons

Recommended Citation
Siddiqui, Fowzia; Sultan, Tipu; Mustafa, Shahid; Siddiqui, Sarwar; Ali, Shaukat; Malik, Abdul; Sajjad, Zafar; Barech, Saleem; and Jooma, Rasheed (2015) "Epilepsy in Pakistan: National Guidelines for Clinicians," Pakistan Journal of Neurological Sciences (PJNS): Vol. 10 : Iss. 3 , Article 11.
Available at: http://ecommons.aku.edu/pjns/vol10/iss3/11
Epilepsy in pakistan: national guidelines for clinicians

Authors
Fowzia Siddiqui, Tipu Sultan, Shahid Mustafa, Sarwar Siddiqui, Shaukat Ali, Abdul Malik, Zafar Sajjad, Saleem Barech, and Rasheed Jooma

This guidelines is available in Pakistan Journal of Neurological Sciences (PJNS): http://ecommons.aku.edu/pjns/vol10/iss3/11
EPILEPSY IN PAKISTAN: NATIONAL GUIDELINES FOR CLINICIANS

Dr Fowzia Siddiqui1, Tipu Sultan2, Shahid Mustafa1, Sarwar Siddiqui1, Shaukat Ali3, Abdul Malik4, Zafar Sajjad1, Saleem Barech5, Rasheed Jooma2
1 Department of Neurology, Aga Khan University, Karachi
2 Children Medical Center, Lahore
3 Department of Radiology, Aga Khan University, Karachi
4 Neurospinal Institute, Karachi
5 Neurocare and Falji center, Karachi
6 Bolan Medical University, Quetta
7 Department of Neurosurgery, Aga Khan University, Karachi

ABSTRACT

Introduction
Epilepsy is one of the most common chronic neurological disorders requiring prolonged treatments and drugs. According to The World Health Organization (WHO), epilepsy is one of those serious brain disorders that affect not only the individual but has a deep impact on the family and society in general. Approximately 50 million people are affected with epilepsy around the world36, though proper epidemiological studies do not exist for Pakistan it is estimated that the prevalence of epilepsy is 9.99/1000. Highest prevalence is seen in people younger than 30 years of age, i.e. about 2 million people and 1/10th of the world burden of epilepsy is in Pakistan! The guidelines available in developed countries are gauged in a setting where epilepsy care is provided by epileptologists/neurologists. In Pakistan the scenario is different, there is only one neurologist for 1.4 million (14lac) population contrast to US where one neurologist for 26 thousand people 29. So there is a desperate need to adapt to alternate guidelines with strategies to provide epilepsy management at a primary care level and to standardize epilepsy care on a National level.

Methods
To form these guidelines we reviewed and adopted from many different available guidelines mainly
1. Local adaptations of the WHO recommendations4
2. Modification of the ILAE treatment guide lines: evidence based analysis of AEDs 200611
3. Updated ILAE evidence review of AEDs special report 201312
4. Existing guidelines in other low income countries13-15
5. NICE, AAN, AES recommendations.17-21

Results
These guidelines consist of
1. The universally ILAE accepted definition and classification of epilepsy and Epileptic syndromes with A step wise approach to a patient with seizures and epilepsy in Pakistan.
2. Tables Selecting the right drug with evidence based references keeping in mind the cost and availability in Pakistan.
3. AED selection in special populations e.g. women20, children17 and elderly
4. Status Epilepticus Protocol
5. Algorithms and tables for easy access

(Due to the limitation of space, points 3 and 4 will be published subsequently)

CONCLUSION

The primary scope of these guidelines is to provide a concise practical management plan which considers the role of AEDs especially their judicial use. These guidelines hope to provide the physicians treating epilepsy patients with a step wise cost effective approach to the patient with epilepsy. A separate guideline to classification and diagnosis is also available, and the guidelines in entirety are also available online at the Pakistan Society of Neurology website.

Guidelines Introduction

Epilepsy is one of the most common chronic neurological disorders requiring prolonged treatments and drugs. It is a disorder that is widely misunderstood and carries a vicious stigma. Epilepsy comprises a vast group of disorders and syndromes with one common symptom, “The Seizure”. For the purpose of these guidelines we have integrated the International League Against Epilepsy (ILAE) definitions of seizures and epilepsy. There is a vast array of literature and guidelines that exist in developed countries for over a decade. These have been reviewed and compiled and modified to suit the Pakistani population and socioeconomic status. These guidelines hope to help improve medical decision making in Pakistan while treating the patient with epilepsy (PWE)

THE NEED FOR NATIONAL GUIDELINES FOR EPILEPSY IN PAKISTAN:

Epilepsy has varied etiologies and affects all age groups, but the vast majority of cases are treatable with Anti Epileptic Drugs (AEDs) most of which are easily available. However knowledge about epilepsy and its care is extremely low. The majority of people with epilepsy (PWE) are treated inadequately or inappropriately. According to The World Health Organization (WHO), epilepsy is one of those serious brain disorders that affect not only the individual but has a deep impact on the family and society in general. Approximately 50 million people are affected with epilepsy around the world, and this number will increase with the new definition. Though proper epidemiological studies do not exist for Pakistan it is estimated that the prevalence of epilepsy is 9.99/1000. Highest prevalence is seen in people younger than 30 years of age. That is: about 2 million people and 1/10th of the world burden of epilepsy is in Pakistan. The recent estimates of population of Pakistan exceed 180 million, whereas the total number of trained neurologists in Pakistan is estimated to be 135 (Pakistan Society of Neurology Directory 2013). Based on the available data, the estimated 2 million people suffering from epilepsy in Pakistan, makes it one neurologist available for every 15200 sufferers of epilepsy with only few trained in epilepsy. Despite efforts to create awareness there remains a wide treatment gap and misconception. The guidelines available in developed countries are gauged in a setting where epilepsy care is provided by epileptologists/ neurologists. In Pakistan it is a different scenario, there is only one neurologist for 1.4 million population contrast to US where one neurologist for 26 thousand people. So there is a desperate need to adapt to alternate guidelines with strategies to provide epilepsy management at a primary care level and to standardize epilepsy care on a National level. The primary care physicians in civil hospitals and dispensaries, and general practitioners (GPs), form the crux of health care in Pakistan and therefore see most of the PWE. Unfortunately neurology rotation is not a mandatory in undergraduate training thus most lack the information and skill needed for proper epilepsy diagnosis and management. In 2011, WHO mental health Gap Action Programme (mhGAP) released evidence based epilepsy care guidelines for use in low and middle income countries. These guidelines provide a crudePerforma that requires local adaptation for use within individual countries. The guidelines state “For effective implementation and sustainability, the sense of ownership and empowerment must be transferred from the global health authorities to the local people. Socio-cultural and financial barriers that impede the implementation of the guidelines should be identified and ameliorated.
Table 1: Factors to consider while developing National guidelines.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Developed country</th>
<th>Developing country like Pakistan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross National income</td>
<td>&gt; USD 3036</td>
<td>&lt; USD 565</td>
</tr>
<tr>
<td>Access to Health care</td>
<td>Primary care for all with established referral systems</td>
<td>Limited to very basic primary care</td>
</tr>
<tr>
<td>Health care funding</td>
<td>National programs and private insurance systems</td>
<td>Often ill funded rely on donors or volunteers. No set system of insurance</td>
</tr>
<tr>
<td>Cultural perception of seizures</td>
<td>Biomedical model</td>
<td>Traditional medicine, spiritual approach, contagion belief common</td>
</tr>
<tr>
<td>Common Epilepsy etiologies</td>
<td>Ideopathic, neoplastic cerebrovascular</td>
<td>Post infectious, antenatal, post traumatic</td>
</tr>
<tr>
<td>Socio-cultural attitudes towards epilepsy</td>
<td>At least social presentation of neutrality</td>
<td>Overt negative public perception, stigmatization, and discrimination common</td>
</tr>
<tr>
<td>Treatment gap</td>
<td>&lt;20%</td>
<td>70-94%</td>
</tr>
</tbody>
</table>

ARIAABLES AFFECTING SELECTION OF AEDS IN PAKISTAN

Epidemiological studies of prevalence and incidence reviewed are problematic in Pakistan due to lack of proper data collection teams and resources. Data concerning seizure type, etiology, and severity of seizures are contrasted with those from developed countries. Sociocultural aspects of epilepsy have been poorly studied, and yet are fundamental to effective medical management. Thus the principles and success of treatment in Pakistan may differ considerably from developed countries. The principles of drug therapy may not be understood by patients, and the supply of drugs is often erratic; and these are major reasons for poor compliance with treatment. Therapy need to be prioritized to cost effectiveness, requiring a cheaper drug eg. phenobarbital to be tried as first line contrary to international guidelines. Computations of treatment gap figures in three developing countries suggest that between 80-94% of patients with active epilepsy are not receiving anticonvulsant therapy, cost and cultural belief are two of the main factors.
in 2011 supported the use of LOLA for neuro-psychiatric detoxification of ammonia.20 Another meta analysis done randomized clinical trials including 646 patients that, studies. Bai et al concluded after meta-analysis of 8 detoxification of ammonia. L Ornithine L aspartate (LOLA) most of the treatments are targeted against the Hepatic Encephalopathy is a common neuro-psychiatric hepatic encephalopathy between two groups was grade III and 10(20%)  were in grade IV hepatic grade I, 12 (24%) were in grade II, 18(36%)  were in grade III, % were in grade II, 19(38%) were in grade III, (Table:III) In placebo group on day I encephalopathy, while on day III 4(8%)  were in grade encephalopathy. It can be recommended that LOLA efficacy L ornithine therapy with others drugs used for

Table 2: Factors affecting AED selection

<table>
<thead>
<tr>
<th>AED-specific variables</th>
<th>Patient-specific variables</th>
<th>Nation-specific variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure type or epilepsy syndrome</td>
<td>Genetic background</td>
<td>AED availability</td>
</tr>
<tr>
<td>specific efficacy or effectiveness</td>
<td>Age</td>
<td>AED cost</td>
</tr>
<tr>
<td>Dose-dependent adverse effects</td>
<td>Gender</td>
<td>Insurance coverage</td>
</tr>
<tr>
<td>Idiosyncratic reactions</td>
<td>Comedications</td>
<td>Socio-cultural issues</td>
</tr>
<tr>
<td>Chronic toxicities</td>
<td>Insufficiency</td>
<td>Compliance</td>
</tr>
<tr>
<td>Teratogenicity</td>
<td>Ability to swallow pills/tablets</td>
<td></td>
</tr>
<tr>
<td>Carcinogenicity</td>
<td>Pharmacokinetics</td>
<td></td>
</tr>
<tr>
<td>Pharmacokinetics</td>
<td>Interaction potential</td>
<td></td>
</tr>
<tr>
<td>Formulations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

To form these guidelines we reviewed and adopted from many different available guidelines mainly.

1) Local adaptations of the WHO recommendations (4)
2) Modification of the ILAE treatment guidelines: based analysis of AEDs 2006 (11)
3) Updated ILAE evidence review of AEDs special report 2013(12)
4) Existing guidelines in other low income countries (13141516)
5) NICE guidelines (17)
6) AAN practice parameters, (18)
7) AES recommendations.(19)
8) A multitude of literature to support our selection and recommendations (20-43)

Management Guidelines:

QUESTIONS ADDRESSED

Q1-Q3: AEDs Initiation of therapy/Mono therapy; Adjuvant therapy; Cessation of therapy
Q4-Q7: Women (fertility, contraception, conception, pregnancy, lactation, teratogenicity), Children, elderly differences
Q8-Q9: Status Epilepticus in Adults and children (protocols)
Q10-Q13: Access to medications, direct and indirect costs, co-morbid conditions, preventable causes
Q14-Q15: Alternate Therapies, diet.
Q16: Epilepsy surgery.
Q17-Q19: Lifestyle, Career choices, Driving.
Q20-23: Epilepsy Diaries, lockets, keychain or bracelets, Help line.

Monotherapy Guideline questions:

Q1-Q3: Patients (adults/elderly/children) with partial-onset seizures
Q4-Q5: Patients (adults/children) with generalized-onset tonic-clonic seizures
Q6: Children with idiopathic localization-related epilepsies and syndromes (BECS).
Q7-Q8: Children with idiopathic-generalized epilepsies (CAE, JME).
Q9: Special Issues related to Women.
Q10: Considerations in Elderly and Multiple handicapped

Questions 6-10 are discussed in the special population subset of these guidelines not published in this edition.

A person is considered to have epilepsy if they meet any of the following conditions:

At least two unprovoked (or reflex) seizures occurring greater than 24 hours apart.
One unprovoked (or reflex) 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.
Diagnosis of an epilepsy syndrome.
For Classification and Diagnosis guidelines see Appendix A

**MANAGEMENT OF EPILEPSY**

**Non-pharmacological Management:**

Once diagnosis is made patient and family members need to be counselled empathically. Since the disease still carries a strong stigma, confidentiality needs to be maintained at all steps, and the condition should be discussed with any family member with consent of the PWE.

- Establish the diagnosis
- Education/counselling
- Address psychosocial issues
- Lifestyle modifications

**Patients need counselling regarding the**

- Disease
- Drognosis
- Need for medication
- Compliance
- Life style

**Life style modification includes**

- Adequate sleep - early to bed early to rise
- Change in job e.g. occupation, driving, swimmers, boxers, airplane pilots etc.
- Avoidance of alcohol, stimulants, energy drinks, gutka, JM, etc.
- Stress reduction — specific techniques, Yoga, meditation, early morning walks
- Adequate diet – high protein. Low carbohydrate, Vit. D, B rich diet
- Joining support groups
- Avoid social isolation

**Pharmacological treatment of epilepsy**

The mainstay of treatment for epilepsy is antiepileptic drugs (AEDs) taken daily to prevent the recurrence of epileptic seizures. It is important that the treatment strategy and suitability of the AED is determined by the prescriber keeping the individual with epilepsy and the carer informed before drug therapy is started.

**When to Start AEDs after first seizures**

Whether to treat first seizure is controversial studies show 16-62% recur within 5 years, Relapse rate is reduced by antiepileptic drug treatment, and it is now recommended that since Neurological abnormalities, abnormal imaging, abnormal EEG or family history increase relapse risk these patients should be treated after first seizure.

<table>
<thead>
<tr>
<th>Definitely:</th>
<th>Possibly:</th>
</tr>
</thead>
<tbody>
<tr>
<td>With structural lesion like Brain tumor, AVM,</td>
<td>Unprovoked seizure</td>
</tr>
<tr>
<td>Infection,</td>
<td></td>
</tr>
<tr>
<td>Without structural lesion:</td>
<td>Alcohol withdrawal</td>
</tr>
<tr>
<td>h/o Epilepsy in sibling</td>
<td>Drug abuse</td>
</tr>
<tr>
<td>EEG with definite pattern.</td>
<td>Szw with acute illness</td>
</tr>
<tr>
<td>Prior but remote sz prior</td>
<td>Post impact seizure</td>
</tr>
<tr>
<td>neurological hist.</td>
<td>A benign epilepsy syndrome</td>
</tr>
<tr>
<td>Todds post ictal paresis status epilepticus at</td>
<td>Excessive sleep deprivation.</td>
</tr>
</tbody>
</table>

AED should be selected according to suitability of the patient, type of epilepsy etc.

Table 3 shows factors determining suitability.

<table>
<thead>
<tr>
<th>Factors determining AED suitability include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>seizure type and/or epilepsy syndrome;</td>
</tr>
<tr>
<td>childbearing potential;</td>
</tr>
<tr>
<td>the presence of comorbidity;</td>
</tr>
<tr>
<td>individual and/or carer preferences;</td>
</tr>
<tr>
<td>the presence of contraindications to the drug;</td>
</tr>
<tr>
<td>potential interactions with other drugs;</td>
</tr>
<tr>
<td>potential adverse effects</td>
</tr>
<tr>
<td>the licensed indication of the drug.</td>
</tr>
<tr>
<td>Cost of AED</td>
</tr>
<tr>
<td>Patients socio-economic status</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Compliance</td>
</tr>
<tr>
<td>AED availability</td>
</tr>
<tr>
<td>Adult lifestyle</td>
</tr>
</tbody>
</table>

The diagnosis of epilepsy needs to be critically evaluated if events continue despite an optimal dose of a first line AED. Before combination therapy is considered, PWE should be given a trial of at least 2-3 appropriate monotherapy regimens, with caution during the transition.

**General Recommendations:**

1) It is recommended that PWE should be treated with a single AED (monotherapy). If the initial treatment is unsuccessful, then monotherapy using another drug can be tried.
Lola was beneficial in both overt and minimal hepatic studies. Bai et al concluded after meta-analysis of 8 complications in CLD. High levels of ammonia in the body are important treatment in reducing seizures and tolerance of side effects.

**DISCUSSION**

Statistically non-significant (p-values > 0.05) while on day I, clinical difference in grading of grade III and 10(20%) were in grade IV hepatic encephalopathy, while on day III 4(8%) were in grade II, 19(38%) were in grade III, and 22(44%) were in grade IV hepatic encephalopathy. To assess clinical improvement with Lola, it was non-significant in placebo group (p value 0.124).

Serum ammonia levels before (day 1) and after (day 3) were 74.16 micromol/L in the trial group. In placebo group mean range: 6-47 micromol/l. In placebo group mean was 105.2 micromol/l.

**CONCLUSION**

Other national and international studies and meta analysis show similar results. Lola dose and duration may vary in bioavailability or pharmacokinetic profiles and care needs to be taken to avoid reduced effect or excessive side effects. Where partial seizures are suspected prefer sodium channel blockers as first line AEDs (see fig 1).

When generalized seizure syndromes are suspected consider broader spectrum AEDs (see fig 1). Phenobarbitone is a broad spectrum efficacious AED that is easily available in Pakistan at minimal price, therefore should still be considered as first line therapy where affordability is an issue as risk of seizures outweigh the long term side effects.

Phenobarbitone should be offered where compliance due to cost is suspected.

If using carbamazepine, check LFTs.

When prescribing sodium valproate to women of present and future childbearing potential, discuss the possible risk of malformation and neurodevelopmental impairments in an unborn child, particularly with high doses of this AED or when using as part of polytherapy. Vit B, folate and calcium supplements should be added.

Lamotrigine should be administered with caution and slow titration when given as monotherapy and with even slower titration when combined with inducers like valproate to avoid the risk of idiosyncratic reactions like Steven Johnson’s syndrome and toxic epidermolysis. All patients should be counseled and warned to stop medication and contact the physician immediately if any rash appears.

Levetiracetam should be given with neuropsychiatric issues in mind and pyridoxine supplement.

Maintain a high level of vigilance for treatment emergent adverse effects (for example, bone health issues, blood dyscrasias, and neuropsychiatric issues).
23) If management is complicated, PWE should be referred to specialist.
24) The prescriber must ensure that the PWE and/or carers as appropriate are fully informed about treatment including action to be taken after a missed dose or after a gastrointestinal upset.
25) Regular blood test monitoring in PWE is not recommended as routine, and should be done only if clinically indicated or non-compliance is suspected as below.

**Examples of blood tests include:**

Before surgery – clotting studies in those on sodium valproate. For Patients on enzyme inducing AEDs: CBC, Electrolytes, LFTs, Vit D levels, every 1-2 years. Test for serum amino acids, TSH and urine for organic acids in all children with neonatal non-infectious seizures and refractory seizures.

26) Asymptomatic minor abnormalities in test results are not necessarily an indication for changes in medication.
27) Every patient when stable should still have a 6 monthly follow-up to ensure compliance, and review treatment plan and side effects.
28) For uncontrolled patients treatment should be reviewed at regular intervals so PWE are not maintained for long periods on treatment that is ineffective or poorly tolerated, when in doubt early referral is more cost effective.
29) **Compliance can be optimized with the following:**

- Educating PWE and their families and/or carers in the understanding of their condition and the rationale of treatment
- Reducing the stigma associated with the condition
- Using simple medication regimens
- Positive relationships between healthcare professionals PWE, and their family.
- SMS bulk reminder module

30) The risks and benefits of continuing or withdrawing AED therapy should be discussed with PWE and/or carers as appropriate, who have been seizure free for at least 2 years. At the end of the discussion, they should understand their risk of seizure recurrence off treatment. This discussion should take into account details of the PWE’s epilepsy syndrome, prognosis and life style.
31) When AED treatment is being discontinued in PWE who has been seizure free, it should be carried out slowly (at least 2-3 months) and one drug should be withdrawn at a time.
32) Particular care should be taken when withdrawing benzodiazepines and barbiturates (may take up to 6 months or longer) because of the possibility of drug- related withdrawal symptoms and/or seizure recurrence.
33) PWE and carer should be counseled whereby if seizures recur the last dose reduction is reversed and medical advice is sought.

**Table 6:** List of available AED’s worldwide vs those available in Pakistan with abbreviations, dosage, indication and common side effects.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Usual Starting Dose</th>
<th>Titrated Up or Down By</th>
<th>Usual Maximum Daily Dose</th>
<th>Common Side Effects</th>
<th>Summary Of Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetazolamie (AZM)</td>
<td>250 mgs bd</td>
<td>250 mgs every 1/52</td>
<td>1000 mgs daily In divided doses</td>
<td>GIT Dist. U&amp;E Dist † urine output</td>
<td>Adjunctive for all sz types especially drop attacks</td>
</tr>
<tr>
<td>Carbamazepine (CBZ)</td>
<td>100-200 mgs 1-2 times daily 2-3mg/kg/day</td>
<td>100 mgs every 1/52</td>
<td>2000 mgs daily In divided doses 10-20mg/kg/day</td>
<td>GIT Dist. Rash Hyponatremia agranulocytosis</td>
<td>Mono/adjunctive therapy. Worsens myoclonic and absence seizures</td>
</tr>
<tr>
<td>Clobazam (CBZ)</td>
<td>5-10 mgs daily</td>
<td>5-10 mgs every 1/52</td>
<td>Up to 60 mgs daily</td>
<td>Drowsiness</td>
<td>Adjunctive for all sz type</td>
</tr>
<tr>
<td>Clonazepam (CLB)</td>
<td>0.5 mgs bd</td>
<td>0.5 mgs</td>
<td>8 mgs daily</td>
<td>Drowsiness</td>
<td>Mono/adjunctive for all sz types</td>
</tr>
</tbody>
</table>
### TABLE I: Medications Included in the Trial

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diazepam</strong> (DZP)</td>
<td>5-10mgs daily</td>
<td>Drowsiness, Prolonged/cluster seizures</td>
</tr>
<tr>
<td>Ethosuximide* (ESM)</td>
<td>250 mgs bd</td>
<td>Mono/adjunctive for absence szs</td>
</tr>
<tr>
<td><strong>Felbamate</strong></td>
<td>300 mgs tds</td>
<td>Adjunctive for all Szs types which have failed all other AEDs. Used under strict specialist supervision</td>
</tr>
<tr>
<td>Gabapentin (GBT)</td>
<td>200-300 mgs tds</td>
<td>Mono/adjunctive for partial onset szs +/- sec gen</td>
</tr>
<tr>
<td>Lacosamide (LCM)</td>
<td>Initially 50mgs bd 1-2mg/kg/day Increase weekly by 50mg bid 200mgs bd or 6-9mg/kg/day</td>
<td>Nausea, dizziness, somnolence, headache Adjunctive for partial onset szs +/- sec gen</td>
</tr>
<tr>
<td>Lamotrigine (LTG)</td>
<td>25 mgs od 25 mgs alternate days When on VPA To a target dose of 100mgs BD Children 0.5mg/kg/day 500 mgs daily Children 10mg/kg/day</td>
<td>#Rash Insomnia GIT Dist. Headache Tremor with VPA Mono/adjunctive for all sz types</td>
</tr>
<tr>
<td>Levetiracetam (LEV)</td>
<td>250 mgs bd 250mgs od if Adjunctive therapy 10mg/kg/day 250-500 mgs every week 3000 mgs daily (1.5g bd) 20-60mg/kg/day</td>
<td>Psychosis Low Mood GIT Mono/adjunctive for all sz types</td>
</tr>
<tr>
<td>Lorazepam (LZP)</td>
<td>1-2 mgs daily</td>
<td>Drowsiness Dependence Adjunctive for all sz types Rescue use.</td>
</tr>
<tr>
<td>Midazolam</td>
<td>10 mgs daily</td>
<td>Drowsiness For prolonged or clusters of all szs, Rescue use Status Epilepticus</td>
</tr>
<tr>
<td>Oxcarbazepine (OXC)</td>
<td>Initially 300mgs twice daily Increased according to 2400 daily In divided doses</td>
<td>Encephalopathy Neutropenia Mono/adjunctive for partial onset Szs +/- sec gen</td>
</tr>
</tbody>
</table>

---

**Hepatic Encephalopathy**

Among these, raised level of ammonia level was 110.52 micromol/L. On comparison of the over encephalopathy. In the review of local data, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LOLA as addition to other national and international studies and meta analysis, we can recommend use of LO...
Encephalopathy, causes both clinical and biochemical.

Randomized clinical trials including 646 patients that, studies. Bai et al concluded after meta-analysis of 8

In our study, it was observed that the LOLA has beneficial

is a major cause of hepatic encephalopathy, that's why

In developing countries like Pakistan cirrhosis liver is more

statistically non significant. (p-values > 0.05) while on

On Day I 10(20%) were in grade II, 17(34%) were

On Day II 8(16%) were in grade II, 10(20%) were in grade III,

On Day III 4(8%) were in grade II, 19(38%) were in grade III,

was associated with rapid clinical recovery and decrease

ammonia level was 112.28 micromol/l on Day

was 74.16 micromol/L. In placebo group mean

range: 6-47 micromol/l). In placebo group mean

value < 0.05.(Table: III)

Future other standard therapies of hepatic encephalopathy since

may be used in the patients with hepatic

characteristics

as causes clinical improvement in patients with hepatic

response by 250 mg s every 3 days

it was non significant in placebo group.(p value 0.124)

Cluster of all szs. clusters of all szs.

response by 250

for absence szs

Prolonged/cluster

VOL. 10 (3) JUL  -  SEPT 2015PAKISTAN JOURNAL OF NEUROLOGICAL SCIENCES

5-8mg/kg/day response in steps of up to 600mgs daily at weekly

5-15mg/kg/day

Hyponatremia

*Rash

Phenytoin

(PHT)

150-300mgs daily 5mg/kg/day Increased gradually as necessary (with plasma phenytoin concentration monitoring

Usual dose is 200-500mgs daily10-15mg/kg/day

GIT Dist.

Gingival Hypertrophy

Hirsutism

*Rash

Mono/adjunctive for all sz types Status Epilepticus

Phenobarbitone

(PB)

30 mgs daily 15 mgs every month

180 mgs daily

Drowsiness

Mono/adjunctive for all sz types Status Epilepticus

Pregabilin

Initially 25mgs bd

50mgs every 1/52

600 mgs daily

Weight gain

Adjunctive for partial onset szs +/- sec gen

Pramidone*

(PMD)

Initially 125mgs at bed time

Increased by 125mgs every 3 days to 500mgs daily in 2 divided doses (250mgs bd), then increased according to response by 250 mg s every 3 days

1500 mgs daily

In 2 divided doses

Drowsiness

Mono/adjunctive for all sz types

Rufinamide*

200 mgs BD daily

200 mgs every 1/52

1600 mgs BD daily

GIT Dist.

Dizziness, fatigue

Adjunctive for Lennox – Gastaut

Tiagabine*

(TGB)

5mgs bd

5-10mgs every 1/52

30-45mgs daily (doses above 30 mgs given in 3 divided doses)

Diarrhoea

Dizziness

Nervousness

Adjunctive for partial onset szs +/- sec gen

Topiramate

(TPM)

25 mgs daily 1mg/kg/day

25 mgs every 1/52

400mgs daily (mono) In 2 divided doses 800mgs (adjunctive) In 2 divided doses (6-9 mg/kg/day)

Weight Loss ↑ Renal Calculi Word Finding Difficulties Pins and needles

Mono/adjunctive for all sz types

Valproate

(VPA)

300 mgs bd 5mg/kg/day

100-250 mgs every week

3000 mgs daily 15mg/kg/day

Weight Gain Tremor, hair loss Liver Toxicity

Mono/adjunctive for all sz types

* Rash

** Constipation, protein overload, internal bleeding or conditions associated with excess ammonia

*** Decrease plasma phenytoin concentration

**** Status Epilepticus
Encephalopathy is a complex neuropsychiatric syndrome affecting 50-70% of all patients with cirrhosis. Hepatic encephalopathy is associated with elevated ammonia levels in the brain, which can be induced or hepatic enzyme inhibition. Various studies have been conducted over the past 25 years to compare standard treatments with LOLA (L-Ornithine L-Aspartate) and assess clinical improvement.

Sharma et al. conducted a study in 2014, concluding that LOLA, probiotics, and rifaxamine were all superior to standard treatments in decreasing hyperammonemia and the severity of hepatic encephalopathy.

Over the past 25 years, various studies have been performed to compare standard treatments with LOLA and assess clinical improvement.

**Material and Method**

A total of 50 patients were included in the study, with 25 patients in each group (LOLA and Placebo). Clinical improvement was assessed using clinical grading of hepatic encephalopathy.

**Results**

On Day I, clinical difference in grading of hepatic encephalopathy was observed, with 10(20%) patients in grade II, 17(34%) in grade III, 15(30%) in grade IV, and 3(6%) in grade V. On Day III, 4(8%) patients were in grade III, while 23(46%) were in grade IV.

**AED Interactions**

Some common interactions between antiepileptic drugs and non-antiepileptic drugs are listed below in Table 7. For a full list consult the PDR Summary of Product Characteristics for each drug.

**Note**

- Enzyme inducing AED’s increase the rate of metabolism of Warfarin and The INR should be monitored carefully when an enzyme AED is added or discontinued.
- Aspirin enhances valproate and phenytoin effects.
- Antibiotics, macrolides (clarithromycin/erythromycin) increase the plasma concentration of carbamazepine and inhibit the metabolism of phenytoin. Erythromycin possibly inhibits the metabolism of valproate.
- Meropenam, reduces plasma concentrations of valproate.
- Rifamycins accelerate phenytoin metabolism.
- Analgesics, NSAIDs enhance the effects of phenytoin.
- Estrogens, enzyme inducing drugs accelerate metabolism of Estrogens reducing contraceptive effects. Estrogens reduce lamotrigine levels.
- Plasma concentration of lamotrigine increased by valproate.
Lola was beneficial in both overt and minimal hepatic randomized clinical trials including 646 patients that, studies. Bai et al concluded after meta-analysis of 8 infusion of Lola. These results were comparable to other stimulates the urea cycle and ammonia utilization that's most of the treatments are targeted against the complication in CLD. High levels of ammonia in the body Hepatic Encephalopathy is a common neuro-psychiatric prevalent compared to developed countries. In fact both encephalopathy. On Day I clinical difference in grading of grade III and 10(20%) were in grade IV hepatic grade I, 12 (24%) were in grade II, 18(36%) were in 19(38%) were in grade IV hepatic encephalopathy, while in placebo group on day I 8(16%) in grade III and zero were in grade IV hepatic In to assess clinical improvement with Lola, we serum ammonia levels before(day 1) and after (day 3) I.(Table:II) On Day III mean ammonia level in the trial ammonia level was 112.28 micromole /dl on Day range: 6-47 micromol/l). In placebo group mean was associated with rapid clinical recovery and decrease associated with acute or chronic hepato-cellular failure 50-70% of all patients with cirrhosis.(1) Hepatic Cirrhosis or end stage liver disease is destruction of

### Table 7. Examples of important Drug interactions

<table>
<thead>
<tr>
<th>Agents</th>
<th>General interactions</th>
<th>Agents that may increase plasma levels</th>
<th>Agents that may decrease plasma levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>The simultaneous administration of other liqu- id medicines with CBZ suspension can cause rubbery precipitate in stool. Co-administration with lithium can↑ neurotoxic SE. Other AEDs may alter thyroid functions. ↓ es efficacy of hormonal contraceptives.</td>
<td>CYP 3A4 inhibitors Propoxiphene, Vigabatrin, VPA, protriptyline, loxopine, sertraline, ritonavir, nafmidone, isoniazid, verapamil, ketoconazole, cimetidine, flunerazine, vloxazine, macrolides, diltiazem</td>
<td>CYP 3A4 inducers, felbamat, PHT, mefloquin</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>CNS depressants, MAOls, TCAs and some anti convulsants may increase depressant effects of CNZ. With VPA in Absence seizures can induce absence status!</td>
<td>CYP 3A inhibitors Azole antifungals, cimetidine</td>
<td>CBZ</td>
</tr>
<tr>
<td>Divalproate Sodium, Valproacid</td>
<td>Drugs that elevate expression of hepatic enzymes increase the clearance of valproate. It increases free levels of warfarin</td>
<td>Asprin, felbamate, macrolides especially clarithromycin</td>
<td>Cholestyramine, meropenum, CBZ, PHT, PB, rifampin. Primidone, TPM</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Needs caution with other albumin binding drugs, PB, VPA, have un-predictable effect on levels. Antacids with calcium inhibit absorption. TCAs ↑ risk for Sz.</td>
<td>CYP inhibitors, Azoles,, trimethoprin, chloramphenicol, isoniazid, disulfiram, phenylbutazone, cimetidine, SSRI, felbamate, TPM, CBZ, ranitidine, ibuprofen, amiodrone, diltiazem.</td>
<td>CYP inducers, Rifampin, doxorubicin, VPA, vigabatrin.</td>
</tr>
</tbody>
</table>

Fig 1: Mechanisms of action of antiepileptic drugs modified from j. physiology 2006
Initiation of AEDs Drug choice with seizure type:

Treatment (Monotherapy) of patients with newly diagnosed focal (partial, complex partial and secondarily generalized) seizures:

A) Adults with focal(partial) onset seizures (ILAE 2013)

RECOMMENDATIONS

1) Offer CBZ/ OXC or PB (where cost is an issue) as first line treatmentas firstline treatment to patients with newlydiagnosed focal seizures.

2) Offer LTG, PHT, OXC or VPA if CBZ and PB are unsuitable or not tolerated. If the first AED tried is ineffective, offer an alternative from these 5 AEDs. (Be aware of the teratogenic risks of sodium valproate and idiosyncratic rash of lamotrigine )

3) Consider adjunctive treatment if a second well tolerated AED is ineffective

4) If adjunctive treatment is ineffective or not tolerated, discuss with, or refer to, an epilepsy specialist or neurologist. Other AEDs that may be considered by the epilepsy specialist are eslicarbazepine acetate (ECA), clobazam, lacosamide, phenytoin, pregabalin, tiagabine, vigabatrin and zonisamide. Carefully consider the risk benefit ratio when using vigabatrin because of the risk of an irreversible effect on visual fields.

Table 8. Medication Selection In Patients with Focal onset seizures or symptomatic lesion related Epilepsies.

<table>
<thead>
<tr>
<th>1st line AEDs</th>
<th>2nd Line AEDs</th>
<th>3rd Line AEDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine CBZ</td>
<td>Levitiracetam LEV</td>
<td>Clonazepam CNZ</td>
</tr>
<tr>
<td>Phenytoin PHT</td>
<td>Valproate VPA</td>
<td>TiagabinTGN*</td>
</tr>
<tr>
<td>Oxcarbazepine OXC</td>
<td>Topiramate TPM</td>
<td>EstilCarbazepine Acetate ECA*</td>
</tr>
<tr>
<td>Lamotrigine LTG</td>
<td>Gabapentine GBP</td>
<td>ZonisamideZNS*</td>
</tr>
<tr>
<td>Phenobarbitone PB</td>
<td>Lacosamide LCM</td>
<td>Perampanel*</td>
</tr>
</tbody>
</table>

*Not available in Pakistan*

Table 9. Focal Seizures AED Selection guide by seizure type

<table>
<thead>
<tr>
<th>Clinical Situation</th>
<th>Simple Partial Sz</th>
<th>Complex Partial Sz</th>
<th>Secondary generalized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Monotherapy</td>
<td>CBZ</td>
<td>CBZ</td>
<td>CBZ</td>
</tr>
<tr>
<td>OXC</td>
<td></td>
<td>OXC</td>
<td>PHT</td>
</tr>
<tr>
<td>PHT</td>
<td></td>
<td>PHT</td>
<td>OXC</td>
</tr>
<tr>
<td>LTG</td>
<td></td>
<td>LTG</td>
<td>LTG</td>
</tr>
<tr>
<td>LEV</td>
<td></td>
<td>VPA</td>
<td>VPA</td>
</tr>
<tr>
<td>ZNS</td>
<td></td>
<td>LEV</td>
<td>ZNS</td>
</tr>
</tbody>
</table>

Pharmacological management (monotherapy) of Adults with newly diagnosed Generalized Epilepsy Syndromes (IGE).

The absence of class I and II RCTs (randomized controlled trials) for adults with GTC seizures implies a marked deficiency in published studies. No AED has reached the highest level of evidence (level A and B) for efficacy. VPA, LTG, TPM, OXC, PB, PHT, TPM, and CBZ are possibly level C, and GBP, LEV, and VGB are
potentially level D efficacious/effective as initial monotherapy for adults with newly diagnosed or untreated generalized onset tonic-clonic seizures. Class IV evidence suggests that CBZ and PHT and other sodium channel blockers may precipitate or aggravate generalized onset seizures. (ILAE updates 2013).

RECOMMENDATIONS

1) Offer sodium valproate as first line treatment to adults with newly diagnosed GTCs. (Be aware of teratogenic risks of sodium valproate in women of child bearing age)

2) Offer lamotrigine if sodium valproate is unsuitable. If the person has myoclonic seizures or is suspected of having juvenile myoclonic epilepsy (JME), be aware that lamotrigine may exacerbate myoclonic seizures. Be aware of idiosyncratic reaction of lamotrigine by slow escalation

3) Consider levitiracetamand Phenobarbital in patients where VPA and LTG are not suitable.

4) Offer clobazam, CBZ, OXC and TPM as adjunctive treatment to adults with GTC seizures if first line treatments as above are ineffective or not tolerated. (Be aware of the risk of exacerbating myoclonic or absence seizures with CBZ and OXC)

5) If there are absence or myoclonic seizures, or if JME is suspected, do not offer carbamazepine, gabapentin, oxcarbazepine, phenytoin, pregabalin, tiagabine or vigabatrin.

Table 10: Generalized Tonic Clonic Epilepsy – AEDs of choice

<table>
<thead>
<tr>
<th>1st line</th>
<th>2nd line</th>
<th>3rd line</th>
</tr>
</thead>
<tbody>
<tr>
<td>VPA</td>
<td>TPM</td>
<td>CNZ</td>
</tr>
<tr>
<td>LTG#</td>
<td>ZNS*</td>
<td>CBM</td>
</tr>
<tr>
<td>TPM</td>
<td>LEV</td>
<td>GBP</td>
</tr>
<tr>
<td>LEV</td>
<td>PB</td>
<td>CBZ#</td>
</tr>
<tr>
<td>PHT#</td>
<td>OXC#</td>
<td>VIGABATRIN ETHOSUXIMIDE</td>
</tr>
</tbody>
</table>

#Avoid in myoclonus  *not available in Pakistan

Table 11. Idiopathic Generalized Epilepsy: Medication Selection

<table>
<thead>
<tr>
<th>AED selection</th>
<th>Clinical situation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GTC</td>
</tr>
<tr>
<td>Initial monotherapy</td>
<td>LPA</td>
</tr>
<tr>
<td>LTG</td>
<td>ESM</td>
</tr>
<tr>
<td>2nd Monotherapy if VPA failed</td>
<td>LTG</td>
</tr>
<tr>
<td>LEV</td>
<td>LTG</td>
</tr>
<tr>
<td>2nd Monotherapy if LTG/LEV failed</td>
<td>TPM</td>
</tr>
<tr>
<td>LEV</td>
<td>VPA</td>
</tr>
<tr>
<td>LTG</td>
<td>ESM</td>
</tr>
<tr>
<td>ZNS</td>
<td>ZNS</td>
</tr>
</tbody>
</table>

KETOCENIC DIET

INTRODUCTION

The ketogenic diet (KD) is a high fat, low carbohydrate and protein diet designed to mimic the biochemical response of the body to starvation when ketone bodies become the main fuel for the brain’s energy demands (Hartman 2008). It has long been used in the treatment of refractory epilepsy in children, although the exact mechanism of action is unclear. The KD diet was initially reported for use in epilepsy in 1921 (Wilder 1921). The initial diet used was the classical ketogenic diet, based on the ratio of fat to carbo-hydrate (with protein), of 3 or 4:1. Later an alternative was suggested using triglyceride oil as a supplement, the Medium chain Triglyceride (MCT) Diet (Huttenlocher et al 1971). These diets have to be carefully administered with the aid of a dietician.

- There is no evidence of efficacy of ketogenic diet in adults.
- 50% efficacy range is achieved in children.
- Recommended in refractory epilepsies in children where multiple regimens of AEDs proven ineffective.
- Local ketogenic receipes are available and cost effective.

Epilepsy Surgery

**FDA approved surgical procedures:**

- Vagus nerve stimulation
- Surgical treatment

**Investigational:**

- Deep brain stimulation
- Gene therapy
The absence of class I and II RCTs (randomized Pharmacological management (monotherapy) of marked deficiency in published studies. No AED has
tiagabine or vigabatrin.
JME is suspected, do not offer carbamazepine,
tolerated. (Be aware of the risk of exacerbating
treatments as above are ineffective or not
patients where VPA and LTG are not suitable.
reaction of lamotrigine by slow escalation)
suspected of having juvenile myoclonic epilepsy

• Gene therapy
  Investigational:
  • Vagus nerve stimulation
  • There is no evidence of efficacy of ketogenic

The ketogenic diet (KD) is a high fat, low carbohydrate

VOL. 10 (3) JUL - SEPT 2015


Surgical Treatment

• Upto 85% seizure-free rates
• Resections:
  - lesionectomy, lobectomy, hemispherectomy
• Disconnections:
  - Callosotomy, subpial transection, steriotactic ablations
• Augmentations:
  - Vagal, cerebellar, thalamic, deep brain stimulation

All patients with focal onset seizures that are refractory
to an adequate trial of two or more AEDs of choice and are refractory to treatment should be referred for phase 1 surgical evaluation to an epilepsy specialist. All lesion-related Epilepsy syndromes should be considered for surgical management

SUMMARY:

These guidelines hope to highlight the problems that exist in the care and management of epilepsy patients like Patient and physician awareness, social and cultural beliefs, easy access to treatment, misdiagnosis, inappropriate or inadequate treatment, sudden unexpected death that might have been prevented, preventable etiologies, Women with epilepsy, epilepsy in children, epilepsy in the elderly, advice about pregnancy and contraception and management of status epilepticus in children and adults. These guideline will be revisited and modified on applicability every four years and it is vital that a spotlight is kept on the need to further develop variable services for people with epilepsy. The place of newly licensed drugs, stigmas, and cost for epilepsy also needs careful consideration. The primary scope of these guidelines of course is to provide a concise practical management plan which considers the role of AEDs especially their judicial use. The role of established and newly licensed drugs is considered with comparison of cost effectiveness. People with epilepsy remain at the centre of this guideline, and the need for services to consider the needs of each individual and their care givers have been focused. Attention has been paid to ensure that the recommendations are written in clear language and be accessible, and, I hope, useful to all. We remain committed to the care of people with epilepsy and commend these guidelines to you in that light.

REFERENCES


  Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). Epilepsia 2005;46:470-472
13. Malaysian Epilepsy practice consensus 2010
15. Singapore Epilepsy guidelines 2012
16. AAN current guidelines, reaffirmed July 2013
The absence of class I and II RCTs (randomized adults with newly diagnosed Generalized Epilepsy, Pharmacological management (monotherapy) of efficacy. VPA, LTG, TPM, OXC, PB, PHT, TPM, and CBZ

3) Consider levitiracetam and Phenobarbital in
1) Offer sodium valproate as first line treatment to sodium channel blockers may precipitate or aggravate
IV evidence suggests that CBZ and PHT and other monotherapy for adults with newly diagnosed or potentially level D efficacious/effective as initial monotherapy for adults with newly diagnosed or potenstial JME is suspected, do not offer carbamazepine, (JME), (be aware that lamotrigine may exacerbate in women of child bearing age)
Be aware of teratogenic risks of sodium valproate

• Gene therapy
• Deep brain stimulation
Investigational:

KETOGENIC DIET

REFERENCES


38. Engel J. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of the ILAE task force on diagnosis of epilepsy


Adults with newly diagnosed Generalized Epilepsy
Pharmacological management (monotherapy) of marked deficiency in published studies. No AED has controlled trials for adults with GTC seizures implies a IV evidence suggests that CBZ and PHT and other untreated generalized onset tonic-clonic seizures. Class monotherapy for adults with newly diagnosed or potentially level D efficacious/effective as initial treatment to adults with GTC seizures if first line. If the person has myoclonic seizures or is (Be aware of teratogenic risks of sodium valproate adults with newly diagnosed GTCs.

Deep brain stimulation proven ineffective. Recommended in refractory epilepsies in the age is achieved in children. There is no evidence of efficacy of ketogenic triglyceride oil as a supplement, the Medium chain mechanism of action is unclear. The KD diet was initially accessible, and, I hope, useful to all. We remain needs of each individual and their care givers have been consideration. The primary scope of these guidelines stigmas, and cost for epilepsy also needs careful the need to further develop variable services for people

REFERENCES

1. Callosotomy, subpial transection, steriotactic
Augmentations:
Resections:

15. Singapore Epilepsy guidelines 2012
13. Malaysian Epilepsy practice consensus 2010
12. Bharucha NE. Epidemiology of epilepsy in India.
10. Aziz H, Akhtar SW, Hasan KZ. Epilepsy in Pakistan:
9. JuriKatchanov, Berbeck GL, Epilepsy Care
8. MacDonald BK, Johnson AL, Goodridge DM et al.
7. Bell GS, Sander JW. The epidemiology of
5. Engel J, Jr. A proposed diagnostic scheme for
4. Duncan JS, Shorvon SD, Fish DR. Clinical epilepsy.
1. Data collection, data analysis.

Dr. Saleem Barech:
Dr. Tipu Sultan:
Dr. Shaukat Ali:
Dr. Shahid Mustafa:
Dr. Saleem Barech:
Dr. Sarwar Siddiqi:
Dr. Abdul Malik:
Dr. Zafar Sajjad:
Dr. Rasheed jooma:

Conflict of Interest: Author declares no conflict of interest.
Funding Disclosure: Nil
Author’s contribution:

Dr. Fowzia Siddiqi: Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review
Dr. Shaukat Ali: Data analysis, manuscript review
Dr. Tipu Sultan: Collection, data analysis, manuscript writing Child Epilepsy.
Dr. Shahid Mustafa: Data analysis, manuscript review.
Dr. Saleem Barech: Data collection, data analysis.
Dr. Sarwar Siddiqi: Manuscript writing, manuscript review
Dr. Abdul Malik: Data collection, manuscript writing
Dr. Zafar Sajjad: Manuscript writing, Seizure protocol neuroimaging, manuscript review
Dr. Rasheed jooma: Data analysis, manuscript writing Epilepsy Surgery, manuscript review