Different modalities of treatment for epilepsy: review article

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Abstract— Background: Epilepsy is one of the most common neurological disorders influencing not less than 50 million patients worldwide. It is a chronic disorder of the brain characterized by epileptic seizures due to the abnormal electrical discharges in the brain. Epilepsy is classified according to the etiology into four categories: idiopathic, symptomatic, provoked and cryptogenic. Seizures are classified according to the etiology and site of origin into focal seizures and generalized seizures.

Objectives: Several studies have been conducted to figure out how to manage and treat the disease . The aim of this review article is to evaluate the effectiveness of different modalities of treatment and find another approaches other than typical antiepileptic drugs.

Review of literature: *Different approaches are present for the treatment of epilepsy. Pharmacological treatment includes a variety of anticonvulsant drugs. Carbamazepine was found to be effective in generalized tonic clonic, neonates with familial epilepsy and children with partial onset of drug resistant epilepsy. Levetiracetam is used in drug resistant temporal lobe epilepsy, frontal lobe epilepsy, pregnant women with myoclonic epilepsy and idiopathic generalized epilepsy syndrome. Valproate is effective in myoclonic epilepsy, adults with partial epilepsy and children with idiopathic generalized epilepsy. Lamotrigine is effective in myoclonic epilepsy, partial onset of drug resistant epilepsy and generalized epilepsy. Ethosuximide is effectively used in absence seizures. Another approach is the dietary approach which includes ketogenic diet, modified atkins diet and low glycemic index treatment. Ketogenic diet was found to be effective in tonic clonic seizures, children with resistant astatic myoclonic epilepsy, adults and pregnant women. Modified atkins diet is used in patients with north see progressive myoclonus epilepsy, young children and adults. Low glycemic index treatment is effective in angelman syndrome with epilepsy. The third approach is the surgical treatment which includes lobe resection such as temporal lobectomy, corpus callosotomy, multiple subpial transection and vagus nerve stimulation. Temporal lobectomy is used in mesial temporal lobe epilepsy. Corpus callosotomy is effective in atonic seizures and startle epilepsy. Multiple subpial transection was found to be effective in patients with epileptogenic foci. Vagus nerve stimulation is used in children with genetic intractable epilepsy.*

Conclusion: Researchers found that there are different modalities of treatment such as pharmacological treatment, surgical treatment and dietary therapy. Pharmacological treatment includes first and second generation antiepileptic drugs. Surgical treatment includes lobe resection, Corpus callosotomy, Multiple subpial transection and vagus nerve stimulation. Finally, Dietary therapy which includes ketogenic diet modified atkins diet and low glycemic index treatment.

Index Terms—epilepsy, seizures, Antiepileptic drugs, anticonvulsant drugs, Corpus callosotomy, Lobe resection, Vagus nerve stimulation, ketogenic diet, atkins diet.

INTRODUCTION

Epilepsy is one of the most common neurological disorders influencing large population of people not less than 50 million patients worldwide. It is a heterogeneous disorder including both usual and uncommon forms, which makes its epidemiological examination difficult (1).

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures. It has neurological, psychological, social and cognitive consequences. A transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous electrical activity in the brain is known as seizure (2).

Epilepsy is classified according to the etiology into four categories (3):

- Idiopathic epilepsy: characterized by an epilepsy of mostly hereditary or assumed hereditary origin and in which there is no gross neuroanatomical or neuropathological anomaly.
- Symptomatic epilepsy: characterized by an epilepsy of an acquired or hereditary cause, related with gross anatomical or pathological anomalies, as well as clinical manifestations, that indicate underlying disorder or condition.
- Provoked epilepsy: characterized by an epilepsy in which a particular systemic or environmental variable is the major reason for the seizure and in which there are no gross neuroanatomical or neuropathological changes.
- Cryptogenic epilepsy: characterized by an epilepsy of assumed symptomatic nature in which the cause has not been identified.

Seizures are also classified according to the site of origin and clinical presentation into (4):

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1- Focal (partial) seizures :

In this type of seizures, only a portion of one lobe of the hemisphere is affected with abnormal electrical discharges. It is classified into the following subtypes:

- Simple partial seizures:

These seizures are caused by a group of neurons that are hyperactive and cause abnormal electrical activity. There is no spread of the electrical discharge and there is no loss of consciousness. There is involvement of a specific group of muscles or a single limb that is controlled by the disturbed region of the brain. Simple partial seizure activity may progress to become complex partial seizure.

- Complex partial seizures:

These seizures show complex sensory hallucinations and mental distortion. There is also motor dysfunction such as chewing movements, diarrhea and/or urination. There is alteration in the consciousness level.

2- Generalized seizures:

Generalized seizures may start locally and then spread to include abnormal electrical discharges throughout both hemispheres of the brain. It is associated with loss of consciousness. It is classified into the following subtypes:

- Tonic-clonic seizures:

These seizures cause loss of consciousness, followed by tonic (continuous contraction) phase and clonic (rapid contraction and relaxation) phase.

- Absence seizures:

These seizures are characterized by short limited loss of consciousness and it is manifested by staring and rapid eye blinking for 3 – 5 seconds.

- Myoclonic seizures:

These seizures are characterized by short episodes of muscle contractions that may last for several minutes and associated with brief jerks of the limbs.

- Clonic seizures:

These seizures are similar to myoclonic seizures (short episodes of muscle contractions), but consciousness is more impaired in clonic seizures.

- Tonic seizures:

These seizures are characterized by increased tone in the extensor muscles and they usually last less than 60 seconds.

- Atonic seizures:

These seizures are characterized by a sudden loss of muscle tone.

The diagnostic criteria for epilepsy include any one of the following criteria (5):

(1) Not less than two unprovoked (or reflex) seizures separated by more 24 hours. (2) one unprovoked (or reflex) seizure and a likelihood of further seizures (not less than 60%) after two unprovoked seizures, happening throughout the following 10 years. (3) diagnosis of an epilepsy syndrome.

This review article aims to:

- Show different modalities of treatment that are available to manage the disease.
- Find another approaches other than typical antiepileptic drugs (pharmacological approaches), because some of them are well known for their serious adverse effects.
- Show the effectiveness of antiepileptic drugs in treating the disease and reducing the frequency of seizures**.**

LITERATURE REVIEW:

In this literature review, I will discuss different modalities of treatment that include pharmacological treatment, surgical treatment and dietary therapy.

A. Pharmacological treatment:

Antiepileptic drugs are classified into two categories (6):

- First generation: such as Phenytoin, Phenobarbital, Ethosuximide, Carbamazepine and Valproate.

- Second generation: such as Felbamate , Gabapentin , Lamotrigine , Topiramate , Tiagabine , Zonisamide , Levetiracetam , Oxcarbazepine , Pregabalin.

IN THIS REVIEW ARTICLE, I WILL DISCUSS THE MOST COMMON USED ANTIEPILEPTIC DRUGS THAT INCLUDE CARBAMAZEPINE, VALPROATE, LEVETIRACETAM, LAMOTRIGINE AND ETHOSUXIMIDE.

1. CARBAMAZEPINE:

CARBAMAZEPINE IS ONE OF THE ANTIEPILEPTIC DRUGS THAT FOUND TO BE EFFECTIVE IN THE TREATMENT OF GENERALIZED TONIC-CLONIC SEIZURES (7). SEVERAL STUDIES HAVE BEEN CONDUCTED TO SHOW THE EFFICACY OF CARBAMAZEPINE IN TREATING EPILEPSY. ONE OF THE STUDIES SHOWED THAT NEONATES WITH FAMILIAL EPILEPSY

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had recovery from seizures after hours of using carbamazepine. It has a quick and safe effect (8). Another study showed that carbamazepine has a positive impact on children with partial onset and drug resistant epilepsy. They found that 83.5% had a remission for 2 years, 72.7% responded well to the drug, and only 10.6% had a recurrence of seizures after remission for 2 years (9).

2. Levetiracetam:

Levetiracetam is one of the second generation antiepileptic drugs. Levetiracetam is effective in drug resistant temporal lobe epilepsy (10). Another study was conducted to estimate the efficacy of Levetiracetam on children with refractory epilepsy and symptomatic cause such as lesions showed in MRI. The result of the study showed that 37% of the patients experienced a reduced number of seizures, and 78% of them did not experience major side effects (11). Levetiravetam helps in achieving control of seizures and it is a better option for treating women with myoclonic epilepsy than valproate due the adverse effects of valproate on pregnant women (12). Another study showed that it is effective in controlling seizure in people with idiopathic generalized epilepsy syndrome (absence epilepsy, myoclonic epilepsy, generalized tonic clonic epilepsy) particularly in patients with adolescence onset of the disease (13).

3. Valproate:

Valproate is one of the first generation antiepileptic drugs and used in the treatment of myoclonic epilepsy (14). A comparative study was done to compare between the efficacy of valproate and topiramate (a second-generation antiepileptic drug) for patients with myoclonic epilepsy. They suggested that topiramate can be used instead of valproate because it has less sever and more tolerable side effects than valproate (15). A study was conducted to evaluate the efficacy of valproate in children with idiopathic generalized epilepsy. They found that 57% of them achieved seizure free (16). Another study reported that valproate is also effective in adult patients with partial or generalized epilepsy (17). Long term use of valproate increases the expression of neuropeptide Y which is a neurotransmitter that has a role in controlling epileptic seizures in a rat model with absence epilepsy (18).

4. Lamotrigine:

Lamotrigine is an antiepileptic drug that is effective in myoclonic adult epileptic patients (19). A comparative study found that lamotrigine was more effective than carbamazepine, gabapentin and topiramate for treating patients with refractory epilepsy and with partial onset of the disease (20). In another study they found that Valproate was more effective than lamotrigine and has less severe side effects than topiramate in patients with generalized epilepsy (21). Lamotrigine was found to suppress hippocampal paroxysmal discharges in a dose dependent manner for temporal lobe epilepsy in a mouse model (22).

5. Ethosuximide:

It is an old antiepileptic drug that is considered as the first line of treatment for people with absence seizure. It showed a reduction effect on epileptogenesis in genetic generalized epilepsy (GGE) with absence seizures in a rat model (23). In a comparative study that compares between the efficacy of Ethosuximide, valproic acid and lamotrigine in children with absence epilepsy, they found that the drug of choice is exthosumimide; because it has better control for seizures than lamotragine, and more tolerable side effects than valproic acid (24). Another study found that they have the same effectiveness. However, they found that exthosumimide has a rapid onset of efficacy rather than valproic acid and lamotragine (25).

B. Surgical treatment:

Surgery is an option for the treatment of epilepsy. The criteria which determine the effectiveness of surgery in treating epilepsy are (26):

1- The patient has enough unsuccessful trials of controlling

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epilepsy with antiepileptic drugs.

2- Patient with uncontrolled seizures experiences social, physical and psychological consequences.
3- There is an epileptogenic focus in an area of the brain that can be removed without causing neurological problems.

There are different types of surgery for patients with epilepsy that include the following:

1. LOBE RESECTION:

In this procedure, brain tissue is removed from the lobe of the cerebrum (temporal – frontal – parietal – occipital lobes) that is responsible for experiencing seizures (27).

In this review article, I will discuss the most common types of lobe resection that include temporal lobectomy and frontal lobectomy.

Temporal lobectomy has a positive impact on patients with mesial temporal lobe epilepsy that is refractory to medications. A study was conducted in Iran to evaluate the outcome of temporal lobectomy. They found that 81.8% of the patients had good outcomes after surgery (28). Patients with mesial temporal lobe epilepsy (it is a form of partial epilepsy which is caused mainly by temporal lobe sclerosis) (29) may have a good prognosis and better surgical outcomes if the following features present as they thought to be indicators for a good prognosis: duration of the seizure before the surgery is less than ten years, history of positive febrile seizures, simple complex partial seizure, positive MRI results and the local video-EEG spikes is unilateral (30). In a study that compares the effectiveness of anterior temporal lobectomy and selective amygdalohippocampectomy in patients with mesial temporal lobe epilepsy, they found that there was no significant difference in the outcomes but Anterior temporal lobectomy was found to be associated with more considerable complications and more effect on verbal memory than selective amygdalohippocampectomy (31). A study was conducted to assess the neuropsychological outcomes that include motor and cognitive functions after frontal lobectomy for patients with drug resistant epilepsy. The study showed that most of the patients had normal functions and they did not experience alterations in the motor and cognitive functions (32).

2. CORPUS CALLOSOTOMY:

Corpus callosum is a band of nerve fibers that connect the two hemispheres of the brain together. In this procedure, the surgeon disturbs the communication between the two hemispheres by cutting corpus callosum which stop spreading the seizures from one hemisphere to another (27). Atonic seizures are sever forms of epilepsy, which are usually resistant to antiepileptic drugs. There are two available modalities of treatment for atonic seizure: corpus callosotomy (CC) and vagus nerve stimulation (VNS). It has been found that corpus calloostomy has better outcome in controlling epilepsy in patients with atonic seizures than vagus nerve stimulation. It has been found that 58% of the patients who underwent corpus callosotomy were seizure free while only 21.1% of the patients who underwent vagus nerve stimulation were seizure free, and 88.6 % of the patients had a reduction in the frequency of seizures after corpus callosotomy, while only 52% of patients underwent vagus nerve stimulation had a reduction in the frequency of seizures (33). Another study was conducted to evaluate the efficacy of corpus callosotomy for childhood onset of drug resistant epilepsy. The study included 7 patients who failed to respond to antiepileptic drugs and vagus nerve stimulation. They found that one patient has a complete recovery from seizures, and five patients have a reduction in the frequency of seizures for not less than 50% (34). Startle epilepsy is a form of reflex epilepsy in which seizures are stimulated by auditory stimuli. A study was conducted on a patient with startle epilepsy and tonic-clonic seizures that are refractory to antiepileptic drugs to evaluate the efficacy of corpus callosotomy. They found that after corpus callosotomy and follow up for one year the patient had no attacks of seizures (35).

3. Multiple subpial transection (MST):

This procedure can help control seizures that start in parts of the brain that cannot be removed without causing damage. The surgeon makes superficial cuts (transections) in the tissues of brain. These cuts interfere with the stream of seizure impulses but they do not interfere with normal activity of the brain (27). A study was conducted to evaluate the anatomical and neuroradiological alterations and changes in the memory after multiple hippocampal transection combined with multiple subpial transection for patients with temporal lope epilepsy compared to anterior temporal lobectomy. They found that multiple hippocampal transection combined with multiple subpial transection has a better outcome for preserving memory when compared to lobe resection surgery (36). Another study showed that multiple subpial transection is an effective procedure for patients with epileptogenic foci situated in cortical areas and refractory to antiepileptic drugs (37).

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4. Vagus nerve stimulation (VNS):

Vagus nerve stimulation is effective in children with genetic intractable epilepsy associated with mutation in the SCN1A Gene (a mutation in the gene that is responsible for functioning of voltage-gated sodium channel). It has been found that it could reduce frequency of seizures for not less than 50 %. It also showed improvement in the cognitive and speech abilities (38). A case report study of an eight year old girl with genetic intractable epilepsy with a mutation in the cyclin-dependent kinase-like 5 gene evaluated the efficacy of vagus nerve stimulation. They found that there was a reduction in the frequency of seizures and abnormal brain activities after vagus nerve stimulation from multiple seizures per day to weekly seizures. Also, they found that there was an improvement in the quality of her life depending on quality of life assessment (39). Another study was conducted in china to estimate the effectiveness of vagus nerve stimulation for adult and pediatric patients with drug resistant epilepsy. They found that 63.8% has a reduction in the frequency of seizures for not less than 50 % while 8.5% of them were completely recovered from seizures (40).

C. Dietary therapy:

1. Ketogenic Diet:

Ketogenic diet is a special diet that contains high amount of fat and low amount of carbohydrate. It is named ketogenic diet because it produces large amount of ketones (acetone) in the body (ketones are synthesized when fat becomes the main source of energy) (41). In a rat model with different types of seizures (tonic-clonic seizures -typical absence seizures - complex partial seizures – atypical absence seizures), it has been found that acetone has an anticonvulsant activity, as it decreases the frequency of seizures (42). Ketogenic diet is also effective in children with resistant astatic myoclonic epilepsy. It has been found that 54% of the patients recovered from seizures after 6 months of treatment with ketogenic diet, and 86% had a reduction of 70% in the frequency of seizures after two months of the treatment (43). Another study was conducted to estimate whether ketogenic diet is effective in adults or only in children with epilepsy. The study found that ketogenic diet is also effective in adolescents and adults with epilepsy (44). Two cases of pregnant women with epilepsy have been included in a study to evaluate the effectiveness of ketogenic diet therapy for pregnant women. They found that ketogenic diet reduced seizure frequency and increased number of days of seizure remission, and it did not result in any neurodevelopmental problems for their babies (45).

2. Modified Atkins Diet:

Modified atkins diet is a modified ketogenic diet which is less restrictive than traditional ketogenic diet. One of the major differences between ketogenic diet and modified atkins diet that there is no fluid, proteins or calorie restriction in the modified atkins diet. The percentage of fat in the diet are not measured, but carbohydrates weight in the diet is monitored (41). Modified Atkins Diet might be beneficial for some patients with North Sea Progressive Myoclonus Epilepsy which is a rare form of epilepsy resulted from mutation in the GOSR2 gene (46). A prospective study in India was done to estimate whether modified atkins diet is effective in young children with refractory epilepsy or not. They found that it produced a reduction in the frequency of seizures more than 50% in 54.8 % of them after 3 months of treatment and 29% of them after 6 months of treatment and it has minimal side effects (47). Another prospective study was conducted to estimate the efficacy of modified atkins diet in adults with idiopathic generalized epilepsy. The study results showed that modified atkins diet reduced frequency of seizures about 50% (48).

3. Low Glycemic Index Treatment:

The main principle of Low glycemic index treatment is consuming carbohydrate that has Low glycemic index. Glycemic index means how much the food can elevate the blood sugar when compared to a reference food like sugar. Low glycemic index treatment is somehow different from the ketogenic diet. The Acceptable amount of carbohydrates per day is higher in low glycemic index treatment than ketogenic diet (41). A retrospective study

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THAT WAS DONE TO ESTIMATE THE EFFECTIVENESS OF LOW GLYCEMIC INDEX TREATMENT IN COMBINATION WITH ANTIEPILEPTIC DRUGS FOR PEOPLE WITH ANGELMAN SYNDROME WHO ARE SUFFERING FROM EPILEPSY AND MANY OF THEM ARE REFRACTORY TO MEDICATIONS. THE STUDY FOUND THAT LOW GLYCEMIC INDEX TREATMENT REDUCED FREQUENCY OF SEIZURES AND SOME OF THE PATIENTS HAD FULL RECOVERY FROM SEIZURES (49). ANOTHER STUDY WAS CONDUCTED TO EVALUATE THE EFFICACY OF LOW GLYCEMIC INDEX TREATMENT AS AN ADJUVANT TREATMENT IN CHILDREN WITH REFRACTORY EPILEPSY. THE STUDY FOUND THAT 77.8% OF THE PATIENTS HAD A REDUCTION IN THE FREQUENCY OF SEIZURE MORE THAN 50% AFTER TWO MONTHS OF THE TREATMENT (50). LOW GLYCEMIC INDEX TREATMENT IS EFFECTIVE FOR EPILEPSY IN PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX (IT IS A GENETIC DISEASE THAT AFFECTS MANY ORGANS IN THE BODY INCLUDING THE BRAIN AND CAUSES SEIZURES) (51).

CONCLUSION

The aim of this review article is to evaluate the effectiveness of different modalities of treatment. In this review article, I mentioned the most common used. One of them is pharmacological approach which includes first and second generation antiepileptic drugs. antiepileptic drugs were found to be effective in treating epilepsy with different types of seizures such as generalized tonic clonic, myoclonic and absence seizures. Another modality of treatment is dietary therapy. The most common types of dietary therapy for treating patients with epilepsy include: ketogenic diet, modified atkins diet and low glycemic index treatment. The last mentioned modality of treatment is the surgical treatment .There are different types of surgery done for treating epilepsy such as lobe resection, Corpus callosotomy, Multiple subpial transection and vagus nerve stimulation. Each modality of treatment has a better and stronger effect on specific types of seizures rather than other types. because of that, the effectiveness of each modality of treatment is mentioned in this review article.

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REFERENCES

1. *Behr C, Goltzene M, Kosmalski G, Hirsch E, Ryvlin P. Epidemiology of epilepsy. Revue Neurologique. 2016; 172(1):27-36.*
2. *Blume W, Lüders H, Mizrahi E, Tassinari C, Van Emde Boas W, Engel J. Glossary of Descriptive Terminology for Ictal Semiology: Report of the ILAE Task Force on Classification and Terminology. Epilepsia. 2001; 42(9):1212-1218.*
3. *Shorvon, S.D . The etiologic classification of epilepsy. Epilepsia. 2011;52(6):1052-1057.*
4. *Jaman P.Neurological Diseases. In: Kumar P, Clark M (eds) Clinical Medicine. 8th edn. Saunders Elsevier, Spain; 2012. p 1067-1154*
5. *Fisher R, Acevedo C, Arzimanoglou A, Bogacz A, Cross J, Elger C et al . ILAE Official Report: A practical clinical definition of epilepsy. Epilepsia. 201 4;55(4):475-482.*
6. *Perucca E. An Introduction to Antiepileptic Drugs. Epilepsia. 2005;46:31-37.*
7. *Kenyon K, Mintzer S, Nei M. Carbamazepine treatment of generalized tonic–clonic seizures in idiopathic generalized epilepsy. Seizure. 2014;23(3):234-236.*
8. *Sands T, Balestri M, Bellini G, Mulkey S, Danhaive O, Bakken E et al. Rapid and safe response to low-dose carbamazepine in neonatal epilepsy. Epilepsia. 2016;57(12):2019-2030.*
9. *Aungaroon, G. Holland, K. D. Horn, P. S. Standridge, S. M. Imming, C. M. Drug-resistant epilepsy in children with partial onset epilepsy treated with carbamazepine. The International journal of neuroscience. 2016;:1-5.*
10. *Wandschneider B, Stretton J, Sidhu M, Centeno M, Kozak L, Symms M et al. Levetiracetam reduces abnormal network activations in temporal lobe epilepsy. Neurology. 2014;83(17):1508-1512.*
11. *Muramatsu, K. Sawaura, N. Ogata, T. Makioka, N. Tomita, K. Motojima, T et al. Efficacy and tolerability of levetiracetam for pediatric refractory epilepsy. Brain and development . 2017;39(3):231-235.*
12. *Sala-Padro, J. Toledo, M. Santamarina, E. Gonzalez-Cuevas, M. Raspall-Chaure, M. Sueiras-Gil, M et al. Levetiracetam and Valproate Retention Rate in Juvenile Myoclonic Epilepsy. Clinical neuropharmacology. 2016;39(6):299-301.*
13. *Rosenfeld WE , Benbadis S, Edrich P, Tassinari CA, Hirsch E. Levetiracetam as add-on therapy for idiopathic generalized epilepsy syndromes with onset during adolescence: analysis of two randomized, double-blind, placebo-controlled studies. Epilepsy Research. 2009;85(1):72-80.*
14. *Hernandez-Vanegas, L. E. Jara-Prado, A. Ochoa, A . Rodriguez, Y. Rodriguez N . Duron, R. M et al. High-dose versus low-dose valproate for the treatment of juvenile myoclonic epilepsy: Going from low to high. Epilepsy & behavior. 2016;61:34-40.*

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ISSN 2229-5518

15. *Park K . Kim S . Nho S . Shin K . Park J. Ha S et al. A randomized open-label observational study to compare the efficacy and tolerability between topiramate and valproate in juvenile myoclonic epilepsy. Clinical Neuroscience. 2013;20(8):1079–1082.*
16. *Holland, K. D . Monahan, S . Morita, D. Vartzelis, G. Glauser, T. A. Valproate in children with newly diagnosed idiopathic generalized epilepsy. Acta neurologica Scandinavica. 2010;121(3):53-149.*
17. *Richens A, Davidson D, Cartlidge N, Easter D. A multicenter comparative trial of sodium valproate and carbamazepine in adult onset epilepsy. Adult EPITEG Collaborative Group. Journal of Neurology, Neurosurgery & Psychiatry. 1994;57(6):682-7.*
18. *Elms J, Powell K, van Raay L, Dedeurwaerdere S, O'Brien T, Morris M. Long-Term Valproate Treatment Increases Brain Neuropeptide Y Expression and Decreases Seizure Expression in a Genetic Rat Model of Absence Epilepsy. PLoS ONE. 2013;8(9)*
19. *Machado R, García V, Astencio A, Cuartas V. Efficacy and tolerability of lamotrigine in Juvenile Myoclonic Epilepsy in adults: A prospective, unblinded randomized controlled trial. Seizure. 2013;22(10):846-55.*
20. *Marson A, Al-Kharusi A, Alwaidh M, Appleton R, Baker G, Chadwick D et al . The SANAD study of effectiveness of carbamazepine, gabapentin, lamotrigine, oxcarbazepine, or topiramate for treatment of partial epilepsy: an unblinded randomised controlled trial. The Lancet. 2007;369(9566):1000-1015.*
21. *Marson A, Al-Kharusi A, Alwaidh M, Appleton R, Baker G, Chadwick D et al. The SANAD study of effectiveness of valproate, lamotrigine, or topiramate for generalised and unclassifiable epilepsy: an unblinded randomised controlled trial. The Lancet. 2007;369(9566):1016-1026.*
22. *Duveau V, Pouyatos B, Bressand K, Bouyssières C, Chabrol T, Roche Y et al. Differential Effects of Antiepileptic Drugs on Focal Seizures in the Intrahippocampal Kainate Mouse Model of Mesial Temporal Lobe Epilepsy. CNS Neuroscience & Therapeutics. 2016;22(6):497-506.*
23. *Dezsi G, Ozturk E, Stanic D, Powell K, Blumenfeld H, O'Brien T et al. Ethosuximide reduces epileptogenesis and behavioral comorbidity in the GAERS model of genetic generalized epilepsy. Epilepsia. 2013;54(4):635-643.*
24. *Glauser T, Cnaan A, Shinnar S, Hirtz D, Dlugos D, Masur D et al. Ethosuximide, valproic acid, and lamotrigine in childhood absence epilepsy: Initial monotherapy outcomes at 12 months. Epilepsia. 2012;54(1):141-155.*
25. *Millichap J. Long-Term Effectiveness of Ethosuximide, Valproic Acid and Lamotrigine in Absence Epilepsy. Pediatric Neurology Briefs. 2012;26(6):42.*
26. *Kilpatrick C . Epilepsy and its neurosurgical aspects. In: Kaye AH (ed) . Essential Neurosurgery. 3rd edn. Blackwell Publishing, Massachusetts, USA, (pp 269-280);2005.*
27. *Neil L . Surgical Options for Epilepsy [Internet]. WebMD. 2017 [cited 13 March 2017]. Available from: http://www.webmd.com/epilepsy/surgical-options-epilepsy*
28. *Asadi-Pooya, A. A. Rakei, S. M. Kamgarpour, A. Taghipour, M. Ashjazadeh, N. Razmkon, A et al .Outcome after temporal lobectomy in patients with medically-refractory mesial temporal epilepsy in Iran. Journal of neurosurgical sciences. 2017;61(3):277-282.*
29. *Engel J. Mesial Temporal Lobe Epilepsy: What Have We Learned? The Neuroscientist. 2001;7(4):340-352.*
30. *Sun Z, Zuo H, Yuan D, Sun Y, Zhang K, Cui Z et al. Predictors of prognosis in patients with temporal lobe epilepsy after anterior temporal lobectomy. Experimental and Therapeutic Medicine. 2015;10(5):1896-1902.*
31. *Nascimento F, Gatto L, Silvado C, Mäder-Joaquim M, Moro M, Araujo J. Anterior temporal lobectomy versus selective amygdalohippocampectomy in patients with mesial temporal lobe epilepsy. Arquivos de Neuro-Psiquiatria. 2016;74(1):35-43.*
32. *Busch R, Floden D, Ferguson L, Mahmoud S, Mullane A, Jones S et al. Neuropsychological outcome following frontal lobectomy for pharmacoresistant epilepsy in adults. Neurology. 2017;88(7):692-700.*
33. *Rolston J, Englot D, Wang D, Garcia P, Chang E. Corpus callosotomy versus vagus nerve stimulation for atonic seizures and drop attacks: A systematic review. Epilepsy & Behavior. 2015;51:13-7.*
34. *Arya R, Greiner H, Horn P, Turner M, Holland K, Mangano F. Corpus Callosotomy for Childhood-Onset Drug-Resistant Epilepsy Unresponsive to Vagus Nerve Stimulation. Pediatric Neurology. 2014;51(6):800-5.*
35. *Gomez, N. Hamad, A. Marinho, M. Tavares, I. Carrete, H. Caboclo, L et al..Corpus callosotomy in a patient with startle epilepsy. Epileptic disorders : international epilepsy journal. 2013;15(1):76-9.*
36. *Usami K, Kubota M, Kawai K, Kunii N, Matsuo T, Ibayashi K et al. Long-term outcome and neuroradiologic changes after multiple hippocampal transection combined with multiple subpial transection or lesionectomy for temporal lobe epilepsy. Epilepsia. 2016;57(6):931-940.*
37. *Ntsambi-Eba G, Vaz G, Docquier M, van Rijckevorsel K, Raftopoulos C. Patients With Refractory Epilepsy Treated Using a Modified Multiple Subpial Transection Technique. Neurosurgery. 2013;72(6):890-7.*
38. *Fulton, S. Van Poppel, K . McGregor, A. Mudigoudar, B . Wheless, J Vagus Nerve Stimulation in Intractable Epilepsy Associated With SCN1A Gene Abnormalities. Journal of child neurology. 2017;32(5):494-498.*
39. *Baba, S. Sugawara, Y. Moriyama, K. Inaji, M. Maehara, T. Yamamoto, T et al . Amelioration of intractable epilepsy by adjunct vagus nerve stimulation therapy in a girl with a CDKL5 mutation. Brain & development. 2017;39(4):341-344.*
40. *Meng, F. Jia, F. Ren, X. Ge, Y. Wang, K. Ma, Y et al . Vagus Nerve Stimulation for Pediatric and Adult Patients with Pharmaco-resistant Epilepsy. Chinese medical journal. 2015;128(19):2599-604.*
41. *Kossoff E. Dietary Therapies [Internet]. Epilepsy Foundation. 2017 [cited 15 March 2017]. Available from: http://www.epilepsy.com/learn/treating-seizures-and-epilepsy/dietary-therapies.*

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42. *Likhodii S, Serbanescu I, Cortez M, Murphy P, Snead O, Burnham W. Anticonvulsant properties of acetone, a brain ketone elevated by the ketogenic diet. Annals of Neurology. 2003;54(2):219-226.*
43. *Stenger E, Schaeffer M, Cances C, Motte J, Auvin S, Ville, D et al. Efficacy of a ketogenic diet in resistant myoclono-astatic epilepsy: A French multicenter retrospective study. Epilepsy Research. 2017;131:64-69.*
44. *Nei M, Ngo L, Sirven J, Sperling M. Ketogenic diet in adolescents and adults with epilepsy. Seizure. 2014;23(6):439-442.*
45. *van der Louw, E. J. Williams, T. J. Henry-Barron, B. J. Olieman, J. F. Duvekot, J. J. Vermeulen, M. J et al . Ketogenic diet therapy for epilepsy during pregnancy: A case series. Seizure. 2017;45:198-201.*
46. *Van Egmond M, Weijenberg A, van Rijn M, Elting J, Gelauff J, Zutt R et al. The efficacy of the modified Atkins diet in North Sea Progressive Myoclonus Epilepsy: an observational prospective open-label study. Orphanet Journal of Rare Diseases. 2017;12(1).*
47. *Sharma S, Mehta R, Goel S, Jain P, Mukherjee S, Aneja S. Efficacy and tolerability of the modified Atkins diet in young children with refractory epilepsy: Indian experience. Annals of Indian Academy of Neurology. 2016;19(4):523.*
48. *Kverneland M, Selmer K, Nakken K, Iversen P, Taubøll E. A prospective study of the modified Atkins diet for adults with idiopathic generalized epilepsy. Epilepsy & Behavior. 2015;53:197-201.*
49. *Grocott O, Herrington K, Pfeifer H, Thiele E, Thibert R. Low glycemic index treatment for seizure control in Angelman syndrome: A case series from the Center for Dietary Therapy of Epilepsy at the Massachusetts General Hospital. Epilepsy & Behavior. 2017;68:45-50.*
50. *Karimzadeh P, Sedighi M, Beheshti M, Azargashb E, Ghofrani M, Abdollahe-Gorgi F. Low Glycemic Index Treatment in pediatric refractory epilepsy: The first Middle East report. Seizure. 2014;23(7):570-572.*
51. *Larson A, Pfeifer H, Thiele E. Low glycemic index treatment for epilepsy in tuberous sclerosis complex. Epilepsy Research. 2012;99(1-2):180-182.*