GSC Biological and Pharmaceutical Sciences

eISSN: 2581-3250 CODEN (USA): GBPSC2

Cross Ref DOI: 10.30574/gscbps

Journal homepage: https://gsconlinepress.com/journals/gscbps/

(RESEARCH ARTICLE)

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Effects of antiepileptic drugs on serum lipids profile among young adult Sudanese patient with epilepsy at Aljazeera State

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GSC Biological and Pharmaceutical Sciences, 2021, 14(01), 175–182

Publication history: Received on 14 January 2021; revised on 23 January 2021; accepted on 25 January 2021

Article DOI: https://doi.org/10.30574/gscbps.2021.14.1.0027

Abstract

consequences that lead to an increase in risk of atherosclerosis in patients with epilepsy, several studies have reported that the patients commonly used antiepileptic drugs like phenytoin, and carbamazepine increase serum total Cholesterol, High Density Lipoproteins Cholesterol (HDL-C) Low Density lipoprotein Cholesterol (LDL-C) levels and Triglyceride (TG) .The aim of this study to assess and compare serum lipid profile of young adult patients treated by anti-epileptic drugs (phenytoin, oxcarbazepine and valproic acid) . Materials and Methods a cross-sectional study was conducted in Aljazeera state. Epileptic patients were of recruited. and taking antiepileptic drugs for more than six months and on regular follow up; approximately 120 patients on commonly used antiepileptic drugs (40 on phenytoin, 40 on oxcarbazepine, 40 on valproic Acid). Age and sex matching 40 controls were taken. our results show significant difference in the of mean TC, TG, HDL, and LDL-C levels in the group receiving phenytoin for more than six months when compared with control group P value (0.00) for all lipid profile. Also significant difference between the mean of TC, TG, HDL-C and LDL-C levels in the group receiving oxcarbazepine for more than six months when compared with control P value (0.00) for all lipid profile.

From the present study we concluded that CYP enzyme inducer anti-epileptic medicines like phenytoin and oxcarbazepine is strongly associated with increased levels of TC, LDL-C, HDL-C and TG, where asvalproate showed no significant change. Therefore, the serum cholesterol level should be regularly monitored in patients undergoing. Therapy with inducer anti-epileptic medicines.

Keywords: Anti-epileptic; Lipid profile; Sudan

1. Introduction

Epilepsy refers to a disorder of brain characterized by the periodic and unpredictable occurrence of seizure [1]. The term 'Seizure' refers to a transient alteration of behaviour due to the disordered , synchronous, And rhythmic firing of populations of brain neuron [2]. The episodes of seizures are unpredictable and their frequency is highly variable. WHO, epilepsy is one of the most common serious brain disorder that affects not only the individual , but also disturbs the family and the society in general [3].

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Epilepsy can be considered a spectrum disorder because of its different causes , different seizure types , its ability to vary in severity and impact from person to person and its range of co-existing conditions [4] . Some people may have convulsions (sudden onset of repetitive general contraction of muscles) and lose consciousness. Others may simply stop what they are doing , have a brief lapse of awareness, and stare into space for a short period [5] . Some people have seizures very infrequently, while Terms in italics appear in a Glossary found at the end of this document [6].

Other people may experience hundreds of seizures each day. There also are many different types of epilepsy, resulting from a variety of causes. Recent adoption of the term " the epilepsies " underscores the diversity of types and causes . In general, a person is not considered to have epilepsy until he or she has had two or more unprovoked seizures separated by at least 24 hours [7].

In contrast, a provoked seizure is one caused by a known precipitating factor such as a high fever, nervous system infections , acute traumatic brain injury , or fluctuations in blood sugar or electrolyte levels . Anyone can develop epilepsy [8]. About 2.3 million adults and more than 450,000 children and adolescents in the United States currently live with epilepsy. Each year, an estimated 150,000 people are diagnosed with epilepsy [9]. Epilepsy affects both males and females of all races, ethnic backgrounds, and ages [10]. In the United States alone, the annual costs associated with the epilepsies are estimated to be $15.5 billion in direct medical expenses and lost or reduced earnings and productivity. The majority of those diagnosed with epilepsy have seizures that can be controlled with drug therapies and surgery. However , as much as 30 to 40 percent of people with epilepsy continue to have seizures because available treatments do not completely control their seizures (called intractable or medication resistant epilepsy) [11] .

While many forms of epilepsy require lifelong treatment to control the seizures , for some people the seizures eventually go away . The odds of becoming seizure -free are not as good for adults or for children with severe epilepsy syndromes, but it is possible that seizures may decrease or even stopover time.

The anticonvulsants also commonly known as antiepileptic drugs are a diverse group of pharmaceuticals used in the treatment of epileptic seizures. The goal of an anticonvulsant is to suppress the rapid and excessive firing of neurons that start a seizure [12]. Treatment of epilepsy is often a lifelong affair.

Several studies have reported that commonly used antiepileptic drugs like phenytoin, and carbamazepine, increase serum HDL-C levels, while some others documented no such effect. Further, some researchers also observed that valproic acid has no influence on serum lipid profile [13] [14] [3].

Serum concentration of certain lipids and lipoproteins in young adults are important risk factors for the development of coronary heart disease in later life. Considerable data has suggested that besides total cholesterol (TC) , elevated triglyceride (TG) concentrations , increased LDL-C and decreased HDL-C contribute to cardiovascular diseases. Thus, assessing changes in serum lipid levels following antiepileptic drugs may be useful to choose the safest drug and prevention of cardiovascular complications in later life [15]. So , the present study was planned to find and compare the effect of conventional and newer antiepileptic drugs on lipid profile of epileptic patients.

1.1. Objectives

To evaluate the effects of antiepileptic drugs on serum lipid profile among young adults Sudanese patient with epilepsy in Wad Madeni.

2. Material and methods

- Study Design: Cross sectional study.
- Study area: The study was conducted at Aljazeera state during September to December 2016.
- Study population: This study includes 160 participants, 120 patients of epilepsy (case) and 40 healthy participants (control). 81 of them were male and the rest 79 were female. The age of them was ranged from 14 to 34 years old.
- Collection of Samples: Blood sample will be collected both from study subjects and controls. 5ml of venous blood will be collected by trained lab technician under sterile conditions using a disposable syringe between 8.00 to 10.00 a.m. after overnight fasting and the sample will be tested for TC, HDL-C, LDL-C and TG.

- Exclusion criteria: Patients with secondary epilepsy, Patients with other neurological or psychiatric disorder, Patients with other genetic or medical disorder, Pregnant females on antiepileptic drugs, Patients with serious illness, malignancy or other complications, Patients taking hypolipidemic drugs and , Patients on more than one antiepileptic drug.
- Inclusion criteria: Young adult patients between 18 to 40 years of age (both sex), Taking antiepileptic drugs for last 6 months or more and
- Data collection: All data will collect by questionnaire from each patient
- Data analysis: All data will analyze by using the statistical package for Social Sciences (SPSS)
- Ethical Considerations: After explaining the details and utility of the study, informed and written consent will be taken from both cases and controls; ethical clearance will be taken from the ethical committee of federal ministry of health –Sudan.

3. Methods

Under sterile conditions using a disposable syringe between 8.00 to10.00 a.m. after overnight fasting and the sample was tested for TC, HDL-C, LDL-C and TG. The blood was allowed to clot in a plain bulb at room temperature, and the serum was separated by centrifugation at 3000rpm for 10min. It was then kept frozen at -20°C to be analysed later on.TC was calculated by enzymatic method and expressed in mg/dl. HDL-C was calculated using polyanion precipitation and expressed as mg/dl. LDL-C was calculated using Fried Ewald's equation and expressed in mg/dl. Triacylglycerol (TAG) in serum was converted to glycerol and then estimated using glycerol kinase enzyme based kinetic method and expressed in mg/dl.

4. Results

160 participants, 120 patients have epilepsy (case) and 40 healthy participants select as (control). 81 (50.6%) of them were male and the rest 79 (49.4%) were female. The age of them was ranged from 14 to 34 years old with mean of 24.9 years. Out of the 120 case participants, 40 using Phenytoin, 40 using oxcarbazepine and 40 using Valproic acid for treatment. We observed statistically significant difference in the mean of TC, TG, HDL-C, and LDL-C levels in the case group receiving anti-epileptic drug for more than six months when compared with control group The mean TC, TG, HDL-C, LDL-C and levels were (168.9 ± 11.16 / 156.6 ± 8.5) mg/dl, (135.5 ± 11.65 /126.55 ± 20.5) mg/dl , (74.4167±9.71059 / 65.5 ± 5.3) mg/dl ,(76.9 ± 8.3 / 69.1 ± 6.7) mg/dl, respectively p value (0.00) shown in Table (1).

Table 1 Comparison of biochemical measured among the study group.

Lipid profile Parameters	Case (Mean±SD)	Control (Mean±SD)	P value
T.C	168.9 ± 11.16(150.0 -190.0)	156.6 ± 8.5(139.0 -174.0)	0.000
T.G	135.5 ± 11.65(119.00-181.00)	126.55 ± 20.5(15.00-150.00)	0.001
HDL	74.4167±9.71059(56.0 -95.0)	65.5 ± 5.3(56.0 -74.0)	0.000
LDL	76.9 ± 8.3(57.00-97.00)	69.1 ± 6.7 (59.0 - 86.0)	0.000

The t-test was used to calculate P value; P value less than 0.05 considered significant; Mean± Std. Deviation; Minimum- Maximum between the brackets

We find statistically significant difference in the mean of TC, TG, HDL-C LDL-C levels in the group receiving phenytoin , for more than six month when compared with control group The mean TC, TG, HDL-C, LDL-C and levels were (172.5 ± 8.9 / 156.6 ±8.5) mg/dl ,(140.7 ± 9.7 / 126.6 ± 20.5) mg/dl,(76.3 ±10.23 / 65.5 ± 5.27) mg/dl,(80.0 ±8.8 / 69.1 ± 6.7)mg/dl, , respectively p value (0.00) shown in Table (2).

Statistically significant difference in the mean of TC, TG, HDL-C LDL-C, levels in the group receiving oxcarbazepine , for more than six month when compared with control group .The mean TC, TG, HDL-C, LDL-C and levels were (177.85 ± 6.0 /156.6 ±8.5) mg/dl,(140.9 ± 11.7 /126.6 ± 20.5) mg/dl ,(81.2 ± 6.7/65.45 ±5.3) mg/dl,(81.1± 6.3 /69.1 ± 6.7) mg/dl respectively p value (0.00) shown in Table (3).

No statistically difference among the mean of TC, HDL-C, LDL-C and TG levels in the group receiving Valproic acid for more than six months when compared with control group p value > 0.05. Table (4).We observed positive correlation between drug duration with TC in phenytoin group p value (0.00) R= 0.811, Figure (1). Also We

observed positive correlation between the dose of phenytoin , oxcarbazepine, valproic acid with TC respectively (P value 0.000 R= 0.657 Figure (2)) TC (P value 0.000 R= 0.570 Figure (3) p value (0.009) R= - 0.409 Figure (4). Positive correlation between the dose of oxcarbazepine with TG P value (0.026) R= 0.352 Figure (5). Positive correlation between the dose of Tegretol with HDL-c and LDL-C (P value 0.013 R= 0.388 Figure (5), P value (0.045) R = 0.319 Figure (6)

Table 2 Comparison of biochemical measured among the case group using Phenytoin and control group.

Lipid profile Parameters	Case (Mean±SD)	Control (Mean±SD)	P value
T.C	172.5 ± 8.9 (156.0 -190.0)	156.6 ±8.5 (139.0 -174.0)	0.000
T.G	140.7 ± 9.7 (123.0 -160.0)	126.6 ± 20.5(15.0 -150.0)	0.000
HDL	76.3 ±10.23 (56.00-92.00)	65.5 ± 5.27(56.00-74.00)	0.000
LDL	80.0 ±8.8 (57.00-97.00)	69.1 ± 6.7(59.0 -86.0)	0.000

The t-test was used to calculate P value; P value less than 0.05 considered significant; Mean± Std. Deviation; Minimum- Maximum between the brackets

Table 3 Comparison of biochemical measured among the case group using Oxcarbazepine and control group.

Lipid profile Parameters	Case (Mean±SD)	Control (Mean±SD)	P value
T.C	177.85 ± 6.0 (167.0 -190.0)	156.6 ±8.5(139.0 -174.0)	0.000
T.G	140.9 ± 11.7(125.00-181.00)	126.6 ± 20.5(15.0 -150.0)	0.000
HDL	81.2 ± 6.7 (65.0 - 95.0)	65.45 ±5.3(56.0 -74.0)	0.000
LDL	81.1± 6.3(68.0 -91.0)	69.1 ± 6.7(59.0 -86.0)	0.000

The t-test was used to calculate P value; P value less than 0.05 considered significant; Mean± Std. Deviation; Minimum- Maximum between the brackets

Table 4 Comparison of biochemical measured among the case group using Valproic acid and control group.

Lipidprofile Parameters	Case (Mean±SD)	Control (Mean±SD)	P value
T.C	156.4000±2.86267(150.00-162.00)	156.6000±8.48468(139.00-174.00)	0.888
T.G	125.0250±3.59834(119.00-132.00	126.5500±20.50510(15.00-150.00)	0.644
HDL	65.8000±3.32974(60.00-73.00)	65.4500±5.27184(56.00-74.00)	0.724
LDL	69.8250±3.83565(62.00-78.00)	69.0750±6.71160(59.00-86.00)	0.541

The t-test was used to calculate P value; P value less than 0.05 considered significant; Mean± Std. Deviation; Minimum- Maximum between the brackets

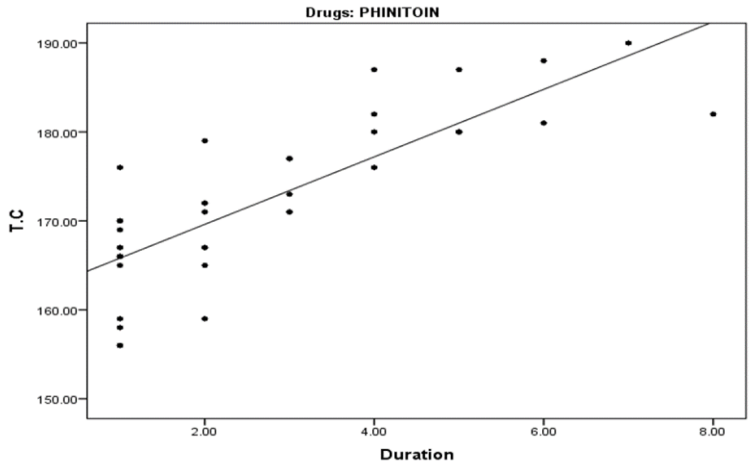

Figure 1 Correlation between TC concentration and duration of phenytoin use.
P value (0.000) R= 0.811

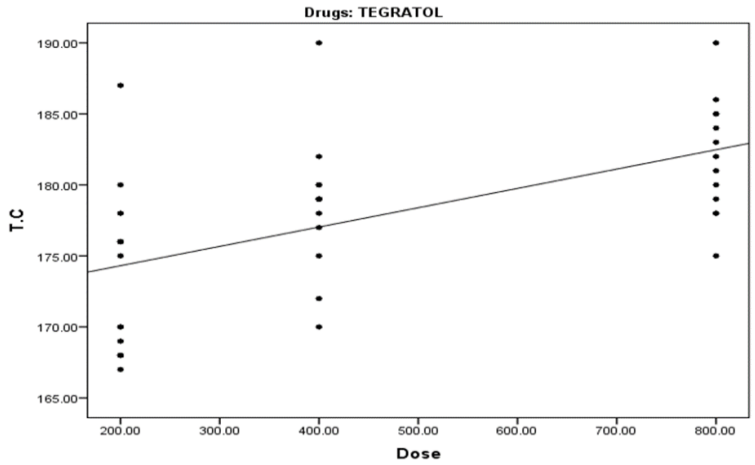

Figure 2 Correlation between TC concentration and duration of Tegretol use.
P value 0.000 R= 0.570

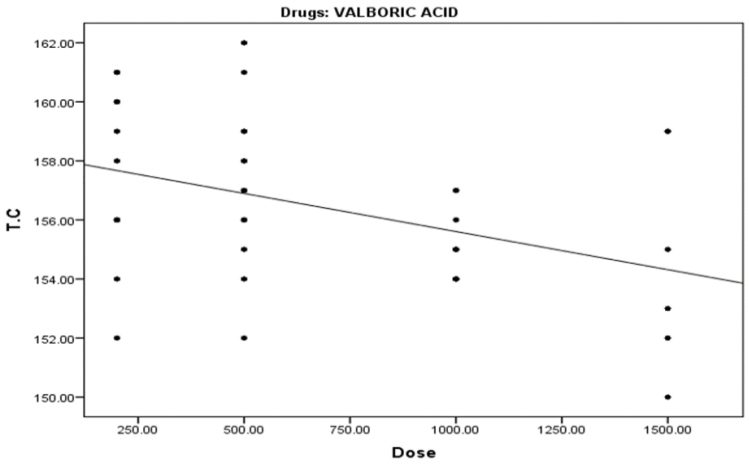

Figure 3 Correlation between TC concentration and duration of valproic acid use.
P value (0.009) R= - 0.409

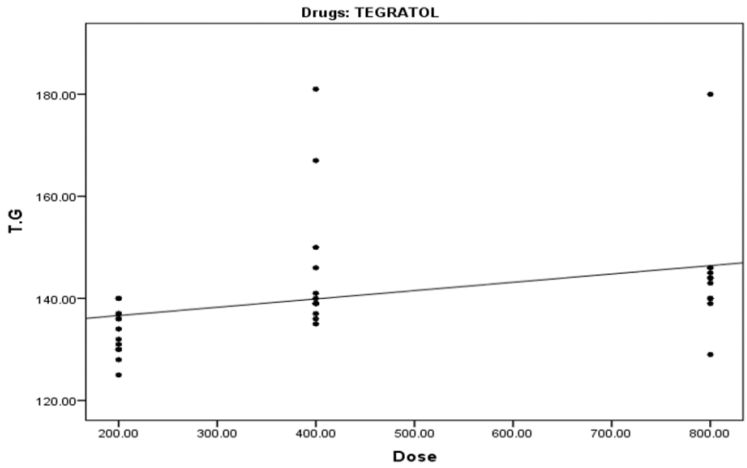

Figure 4 Correlation of dose of Tegretol with TG
P value 0.026 R= 0.352

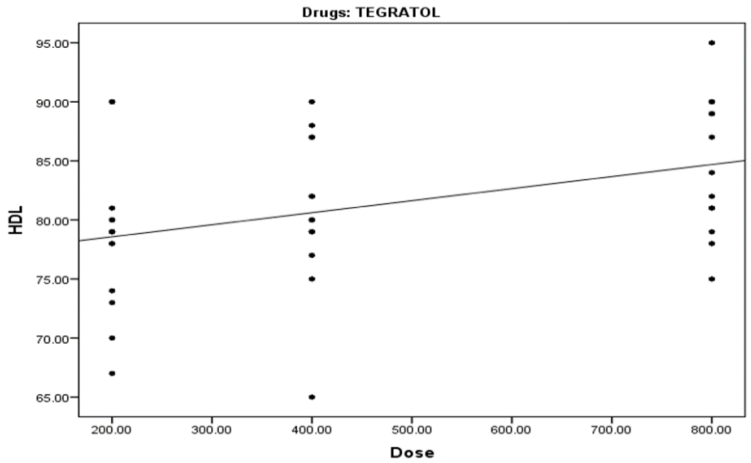

Figure 5 Correlation of dose of Tegretol with HDL
P value 0.013 R= 0.388

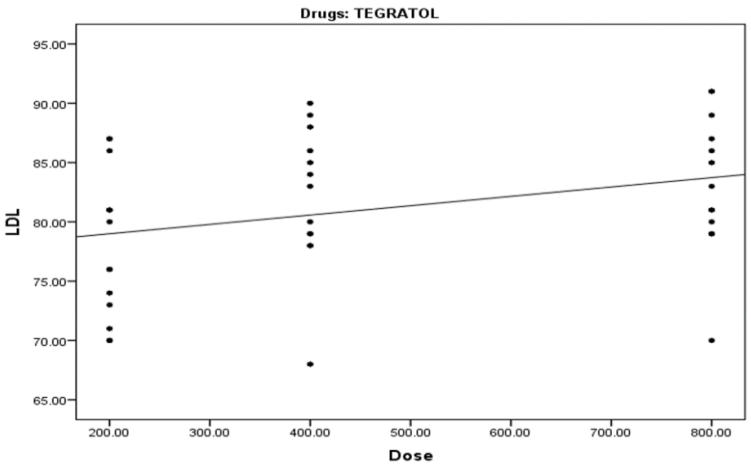

Figure 6 Correlation between LDL concentration and duration of tTegretol use.
P value (0.045) R= 0.319

5. Discussion

The present study was designed to investigate the effect of common antiepileptic drugs on lipid profile parameters such as TC, HDL-L, LDL-C and TAG. this study revealed significant increase in mean TC, HDL-C, LDL-C and TG levels when compared with the control in patients receiving phenytoin for or more than six months , The results in our study shows similar finding to those other investigations done by P Kumar et al., Pelkonen et al., Nikkila et al., and Luoma et al.,. Also reported same findings i.e. an increase in TG, LDL-C and HDL-C levels in epileptic patients on long-term treatment with Phenytoin [5.6,8] .

In this study a significant increase in mean TC, HDL-C, LDL-C and TG levels when compared with the control in patients receiving oxcarbazepine for or more than six months , The results in our study findings are similar to those other investigations done by K. Manimekalai et al , K. Phabphal et al [5,6] also reported same findings like an increase in TG, LDL-C and HDL-C levels in epileptic patients on long-term treatment with Phenytoin [5-8]. Study results conducted by Calandre et al., and Dewan P et al., observed higher HDL-C and TC levels but no effect on LDL-C levels in epileptic patients on long-term treatment with phenytoin [9,10].

The effect of phenytoin and carbamazepine may be due to the induction of CYP enzyme. They are the inducers of CYP51 enzyme. CYP51 is a housekeeping gene of the cytochrome P450 super family which is involved in cholesterol biosynthesis in humans. The CYP450 enzyme system is involved in the synthesis and metabolism of cholesterol[16]. In particular; CYP51A1 plays a key role in cholesterol synthesis[17]. Also, carbamazepine stimulates the hepatic synthesis of cholesterols and increase the formation and pool size of bile acids, which in turn raise the level of intestinal absorption of cholesterol by facilitating micelle formation [17].

The patients who were on valproate and levetiracetam showed no significant change in TC, HDL-C, LDL-C and TG levels when compared with control. Study done by Mohamed Kantoush et al., showed decreased levels of LDL and TG on valproic acid which are contrasting our study results [18].Based on cardiovascular epidemiological literature, an increase in serum cholesterol particularly high levels of LDL-C may be regarded as an adverse effect on long-term anticonvulsant treatment as it increases the risk of coronary heart disease. This may be due to complex action i.e. increase in HDL-C (positive cardiovascular effect), TC and LDL-C (negative cardiovascular effect) levels associated with phenytoin and carbamazepine [19].

6. Conclusion

From the present study we can conclude that CYP enzyme inducer anti-epileptic medicines like phenytoin and oxcarbazepine is strongly associated with increased levels of TC, LDL-C, HDL-C and TG, where valproate and levetiracetam showed no significant changes. Therefore, the serum cholesterol level should be regularly monitored in patients undergoing therapy with inducer anti-epileptic medicines.

Compliance with ethical standards

Acknowledgments

Grateful thank to the patients and healthy who agreed to participate in this study.

Disclosure of conflict of interest

There was no conflict of interest in this study. Statement of informed consent Informed consent was obtained from all individual participants included in the study.

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References

[1] A Rahman, AJ Akhtar, SA Mateen. I NTERNATIONAL J OURNAL OF P HARMACY & L IFE S CIENCES Current therapeutic approaches to epilepsy. 2014; 4(1): 2282–2287.

[2] AR Ziyaurrahman, J Patel. Anticonvulsant effect of Boswellia serrata by modulation of endogenous biomarkers. 2012; 4(4): 1308–1325.

[3] O Article, K Manimekalai, B Visakan, KJ Salwe, S Murugesan. "Evaluation of Effct of Antiepileptic Drugs on Serum Lipid Profile among Young Adults with Epilepsy in a Tertiary Care Hospital in Pondicherry. 2014.

[4] N. isorders. Seizures and the Epilepsies: Hope Through Research.

[5] B Learning. Chapter 12 Neurologic Emergencies. 227–246.

[6] NLC Talbot. The glossaries package v4 . 15 : a guide for beginners. 2015; 1–22.

[7] Nikkila EA, Kaste M, Ehnbolm C, Viikari J. Increase in serum high-density lipoprotein in Phenytoin users. Br Med J. 1978; 2: 99-103.

[8] MZ Rahman. Predicting Epileptic Seizure from Electroencephalography(EEG)using Hilbert Huang Transformation and Neural Network By Md . Naushad Karim. 2015.

[9] N Coast, CF Campaign. s Continuing Co ontinu ing a Legacy y. 2016.

[10] PN Banerjee, WA Hauser. Chapter 5, Incidence and Prevalence. 2007.

[11] Bramswig S, Sudhop T, Luers C, et al. Lipoprotein(a) concen-tration increases during treatment with carbamazepine. Epilepsia. 2003; 44: 457-60.

[12] D Nirmala. Studies on anticonvulsant activity of annacyclus pyrethrum in albino mice. 8(4): 2015.

[13] K Phabphal, K Limapichat, P Sathirapanya, S Setthawatcharawanich, A Geater. Characterization of glucose homeostasis and lipid profile in adult , seizure-free , epileptic patients in Asian population. 2012; 1–7.

[14] S Svalheim, G Luef, M Rauchenzauner, L Mørkrid, L Gjerstad. Cardiovascular risk factors in epilepsy patients taking levetiracetam , carbamazepine or lamotrigine. 2010; 122(13): 30–33.

[15] X Pintó, A Muñoz, M Zúñiga, J Rubiés-prat, LF Pallardo, L Masana. Lipoprotein ratios : Physiological significance and clinical usefulness in cardiovascular prevention. 2009; 757–765.