

Poor treatment outcomes and associated factors among epileptic patients at Ambo Hospital, Ethiopia

Etiyopya Ambo Hastanesi'nde epilepsi hastalarında kötü tedavi sonuçları ve ilişkili faktörler

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Abstract

Approximately one third of patients with epilepsy continue to experience seizure despite the prescription of appropriate doses of anti-epileptic drugs. The objective of this study was to assess treatment outcomes and associated factors for poor treatment outcomes among patients taking anti-epileptic drugs at Ambo Hospital, West Shewa, Ethiopia. A hospital based cross-sectional study was conducted. Verbal consent from participants was taken before interview. Fifty-nine patients (44.7%) had poor seizure control. The most common seizure triggering factors were emotional stress (97.4%), sleep deprivation (78.1%), missing meal (29.8%) and missing medication (21.9%). Seventy one patients (53.8%) were non-adherent to medication. Therefore there is significant association between level of adherence ($P=0.001$), number of seizure attacks before anti-epileptic drugs initiation ($p=0.028$), electroencephalogram (neurologic abnormality) ($p=0.04$) and age at onset of seizure (diagnosis) ($p=0.026$). Poor treatment outcomes among epileptic patients is associated with level of adherence, number of seizure attacks before anti-epileptic drugs initiations, electroencephalogram (neurologic abnormality) and age at onset of seizure (diagnosis). The most common seizure triggering factors were emotional distress, sleep deprivation, missing meal, missing medication and noise. Strict medication adherence evaluation and enhancement through continues health education, close follow up with multidisciplinary approach are fundamental to the successful management of epileptic patients.

Keywords: Epilepsy, seizure, treatment outcome, Ambo Hospital

Özet

Epilepsi hastalarının yaklaşık üçte biri, anti-epileptik ilaçlar uygun dozda reçetelenmesine rağmen nöbet geçirmeye devam ederler. Bu çalışmanın amacı Ambo Hastanesi, WestShewa, Etiyopya'da anti-epileptik ilaç alan hastalarda tedavi sonuçlarını ve kötü tedavi sonuçları ile ilgili faktörleri değerlendirmek içindi. Hastane temelli kesitsel bir çalışma yürütüldü. Katılımcılardan görüşmeden önce sözlü onam alındı. Elli dokuz hastada (% 44.7) kötü nöbet kontrolü vardı. En yaygın tetikleyici faktörler duygusal stres (% 97.4), uyku yoksunluğu (%78.1), yetersiz beslenme (%29.8) ve eksik ilaçtır (%21.9). Yetmiş bir hasta (% 53.8) ilaç bağımlı değildi. Kötü tedavi sonuçları ile bağıllık düzeyi ($p=0.001$), anti-epileptik ilaç başlamadan önce nöbet atağı sayısı ($p=0.028$), elektroensefalografi (nörolojik bozukluk) ($p = 0.04$) ve nöbetin ilk başladığı yaş ($p = 0.026$) arasında anlamlı ilişki vardır. Epileptik hastalarda kötü tedavi sonuçları ile bağıllık düzeyi, anti-epileptik ilaçlar başlamadan önce nöbet atak sayısı, elektroensefalogram (nörolojik bozukluk) ve nöbetin (hastalık tanısı konduğu) ortaya çıktığı yaş arasında ilişki vardır. En yaygın nöbeti tetikleyici faktörler duygusal sıkıntı, uyku yoksunluğu, beslenme yetersizliği, eksik ilaç ve gürültüydü. Medikasyona sıkı bağıllığı değerlendirme, sağlık eğitimini devamlı geliştirme, multidisipliner yaklaşımla yakından takip epileptik hastalarda başarılı bir yönetim için esastır.

Anahtar kelimeler: Epilepsi, nöbet, tedavi sonucu, Ambo Hastanesi

Introduction

Epilepsy with its spectrum of manifestations is a common neurological disease affecting almost 50 million people worldwide (1, 2). Approximately 85% of people afflicted with epilepsy live in developing countries and Ethiopia is not an exception. The treatment of epilepsy in developing countries remains far from satisfactory, mainly because of the general lack of medical personnel; non-availability of medications; and lack of information and/or

education on epilepsy for both patients and medical staff (1, 3-5). Poor control of epilepsy is still a major problem with a prevalence of 40%.

Even though the current available therapies against epilepsy could successfully treat a great proportion of newly diagnosed patients, inappropriate drug therapy in combination with non-adherence is leading to significant poor epilepsy control (1, 6). Proper patient education, avoidance of triggering factors such as sleep deprivation and adherence has been implicated for better treatment outcomes by various studies (7-12).

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Thus the aim of this study was to determine seizure prevalence, treatment profiles, adherence, and outcome with its common associated factors, and to give recommendation for health professional and concerned bodies, those giving care for patients in Ethiopia, specifically in Ambo Hospital. Finally, yet importantly, since there are no investigations on this topic in the country especially in Ambo Hospital, it can be used as initial point or reference for those interested in this topic.

Method and Participants

Study setting and participants

The study was carried out from February 24 to January 9, 2014 at Ambo Hospital. Ambo located 126 km west of Addis Ababa. A hospital based cross sectional study was conducted to assess the poor treatment outcome and associated factors among 132 on follow up epileptic patients' at Ambo Hospital.

Study design and data collection

Patient chart review and Self-report was used to determine the various variables. Patients were picked conveniently. Patients who fulfill the following criteria were included as study unit. Patients presented with a history of Epilepsy at Ambo Hospital for at least six months duration and on medication during the study period. Patients with chronic disease as co morbid and epileptic patients were a part of the study proved that they are on anti-epileptic drugs (AEDs) during the study period. Epileptic patients, whose age were equal and greater than 15 years, Patients who had no active mental problems and who can communicate (conscious). Epileptic patients on admission (in ward) were excluded. Data collectors who were 4th year pharmacy students were trained for two days. Pre-testing of the questionnaire was done on 10 patients. Data was checked for completeness.

Data Analysis

The data was coded, and checked for its completeness and consistency and then compiled manually. All the statistics were calculated using scientific calculator. Chi-squared test was analyzed to draw association between different factors. A p-value of 0.05 or less was considered statistical significant.

Ethical Statement

Permission letter numbered JUDP234/2006 was obtained from School of Pharmacy College of Public Health and Medical Science Jimma University and Ambo Hospital. Verbal consent from participants was taken before the interview. Respondents were assured about confidentiality of the information. The right of the respondents for being interviewed was respected.

Operational definitions

Adherence to AEDs- has been defined according to Morisky's 8 items medication adherence questionnaires. High adherence is considered if the

patient score 0/8, medium adherence if score is 1-2 out of 8 and low adherence if score is >2 out of 8, according to the. Poor treatment outcome is defined as increase in number of seizure episode or uncontrolled seizure in patients taking AEDs due to different reasons. If the patient is not seizure free for at least one year it is considered as uncontrolled seizure per this study paper. Seizure triggering factors- factors which increase the number of seizure attacks in individual person. Standard Definitions: Epilepsy-Epilepsy is characterized by a tendency to recurrent seizures and it is defined by two or more unprovoked seizures (generally within 2 years) (1).

Results

Socio-Demographic Characteristics of the Study Subjects (Table 1)

One hundred thirty two epileptic patients were interviewed and their medical record data was revised. There were 69 (52.3%) female. The majority of patient's age falls between 15 and 30 years.

Table 1. Socio Demographic Characters of Epilepsy Patients on AEDs (n=132)

Socio demographic characteristic	n (%)	
Age	15- 30	75 (56.8)
	31-45	36 (27.3)
	46-60	21 (15.9)
Sex	Female	69 (52.3)
	Male	63 (47.7)
Ethnicity	Oromo	109 (82.6)
	Amhara	12 (9.1)
	Gurage	7 (5.3)
	Tigre	4 (3)
Religion	Orthodox	68 (51.5)
	Protestant	45 (34.1)
	Muslim	12 (9.1)
	Others (wakefata, Hawariat)	7 (5.3)
Marital status	Single	76 (57.6)
	Married	47 (35.6)
	Divorced	6 (4.6)
Occupation	Widow	3 (2.3)
	Student	56 (42.4)
	Farmer	30 (22.7)
	Government employee	20 (15.2)
	Merchant (business man/woman)	12 (9.1)
	Unemployed	9 (6.8)
	Other (NGOs, daily labour, house wife)	5 (3.79)
Residence	Rural	82 (62.1)
	Urban	50 (37.9)
Education	Illiterate(not educated)	24 (18.2)
	Primary	55 (41.7)
	Secondary	30 (22.7)
	University/college	23 (17.4)
Monthly income	< 500	68 (51.5)
	500-1000	18 (13.6)
	1001-2000	21 (16.7)
	>2000	24 (18.2)

Clinical characteristics of study subjects (Table 2 and Figure 1)

The duration of patients on AEDs were greater than 1 year for 81.8% and follow up in the clinic was greater than a year for 75.7% of the patients. Nearly 23.5% had other chronic disease in addition to epilepsy. One

hundred forty patients 86.4% were reported one or more triggering factors that can increase their seizure attacks. Only 73 of the patients had controlled seizure. Among patients with co morbid conditions (31), psychiatric is the leading co morbid condition which accounts for 18 (58.1%). As indicated on figure 2, the most common triggering factors were: emotional stress (97.4%), sleep deprivation (78.1%), missing meal (29.8%), missing medication (21.9%) and noise (15.5%) as reported by the patients. There were no patients diagnosed with more than one type of seizure. All 132 patients have only one seizure type.

Among those patients 3(2.3%) have Absence seizure and 129(97.7%) have generalized tonic clonic seizure (GTC).

Table 2. Clinical characteristics of the participants

Clinical information and determinants of prognostic factors	n(%)	
Time on AEDs(in Years)	<1/2	24 (18.2)
	1 to 5	62 (47)
	>5	46 (34.8)
Follow up in the clinic(in Years)	<1/2	3 (2.3)
	1/2 to 1	29 (22)
	>1	100 (75.7)
Time since seizure free* n=73	1 to 2	23 (31.5)
	2 to 5	44 (60.3)
	>5	6 (8.2)
Time to enter remission phase* (n=73)	<1/2	7 (9.6)
	1/2 to 1	11 (15.1)
	1 to 5	33 (45.2)
	>5	22 (30.1)
Comorbid condition	Psychiatric	58.1
	Hypertension	19.4
	Diabetes Mellitus	16.1
	HIV	1.5
	No	101 (76.5)
Triggering factors	Yes	114 (86.4)
	No	18 (13.6)
Status of seizure treatment outcome	Controlled	73 (55.3)
	Not controlled	59 (44.7)
Dose titration for phenobarbitone	Yes	61 (55)
	No	50 (45)
Dose titration for carbamazepine	Yes	2 (8.3)
	No	22 (91.7)

Medication experience of participants (Table 3 and Figure 2)

Since the major type of epilepsy diagnosed was GTC seizure, the initial AED prescribed was phenobarbitone 123 (93.2%); the remaining percentage accounts for phenytoin and Na valproate. As indicated on table 3 and 4, among patients who used carbamazepine as 2nd drug with phenobarbitone (33), nine of them controlled with initial dose of 200mg/day as 2nd drug and 2 patients titrated to 400mg/day, while 22 (66.7%) still continued to have seizure.

Table 3. Medication experience of participants

Characteristics	Values	n(%)
AEDs prescribed as initial	Phenobarbitone	123 (93.2)
	Phenytoin	6 (4.5)
	Valproic acid	3 (2.3)
AEDs prescribed as add on	Carbamazepine	33 (75)
	Phenytoin	9 (20.5)
Poly-pharmacy with AEDs	Valproic acid	2 (4.5)
	No	88 (66.7)
Poly-pharmacy irrespective of AEDs	Yes	44 (33.3)
	No	57 (43.2)
Phenobarbitone(N=52)	Yes	75 (56.8)
	Sedation	52 (42.3)
	Confusion/in concentration	46 (37.4)
	Behavioural change/irritability	31 (25.2)
	Weakness/lethargy	23 (18.7)
Carbamazepine (N=23)	Others(headache, dizziness,rash, ataxia)	8 (6.5)
	Sedation	20 (60.6)
	GI irritation	18 (54.6)
	Confusion/in concentration	7 (21.2)
	Dizziness	6 (18.2)
Phenytoin (N=4)	Others(headache, blurred vision)	3 (9.1)
	Facial coarsening	2 (20)
	Sedation	3 (20)
	Gingival hyper-plasia	1 (6.7)
Valproicacid (N=2)	GI irritation	2 (40)
	Sedation	1 (20)

Of all patients on poly-pharmacy or 2 AEDs (44 patients), 16 patients (36.4%) of them were seizure free, while 28 (63.6%) of patients on 2 drugs continue to have seizure. The maximum AEDs prescribed for the patients were 2 drugs. Among patients only on phenobarbitone (n=123), 54 (43.9%) patients were seizure free.

Time length for dose titration for phenobarbitone after no response to initial dose, among patients for whom dose titration was done (61 patients) as indicated on table 2, for majority of the patient (40 (65%)) titration was done after 6 months (Refer Figure3.)

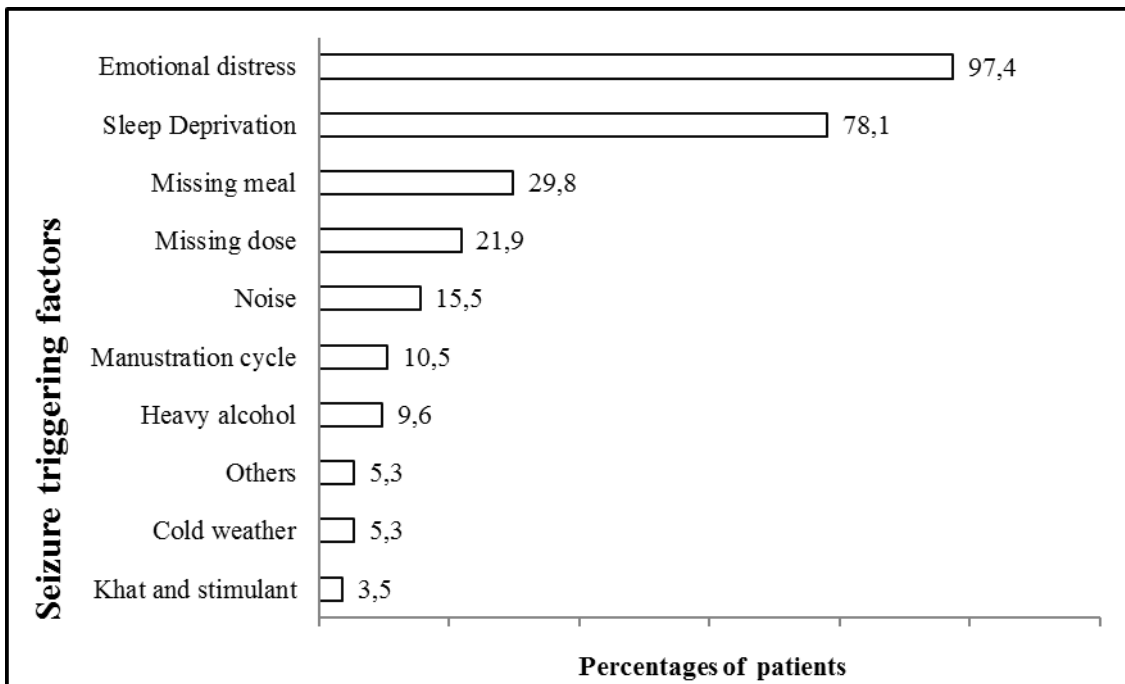


Figure 1. Seizure triggering factors (n=114)

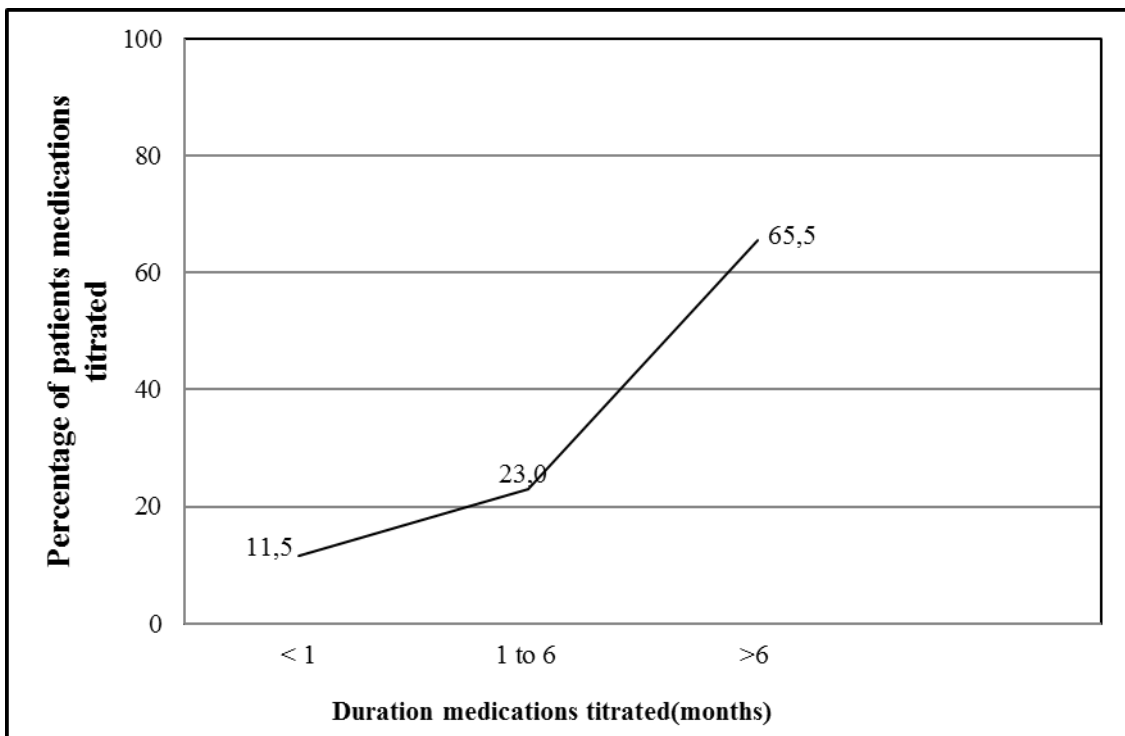


Figure 2. Phenobarbitone dose titration after no response to initial dose (n=61)

Among 132 patients on AEDs, 55 (41.7) complain one or more adverse effects from AEDs. Among 123 patients on phenobarbital, 33 patients on carbamazepine, 15 patients on phenytoin, and 5 patients on valproate, respectively 52 (42.3%), 23(69.7%), 4(26.7%) and 2(40%) reported one or more adverse effects to the respective drugs.

However, data were collected by patient self-report, which may lead to over or under report of the side effect and or bias of side effects of other medication they used during on AEDs.

Adherence profile (Table 4)

Seventy one patients (53.8%) were classified as non-

adherent to medication. The most common reason for non-adherence was forgetfulness (73.2%) followed by feeling sick, side effects (60.6%).

Table 4. Reason for non-adherence

Reasons for non-adherence- general		n(%)
Patient related factors	Forgetfulness	52 (73.2)
	Inconvenient work schedule	19 (26.8)
	Unaffordability	7 (9.9)
System Factors	Don't believe in the medication	2 (2.8)
	Poor relationship between patient and physician	7 (9.9)
Medication Factors	Irregular or poor drug supply	6 (8.5)
	Feeling sick, side effects	43 (60.6)
	Poly-pharmacy (Drugs are too many)	16 (22.5)
Socioeconomic factors	local beliefs or beliefs about the origin of illness	9 (12.7)
	Long distance from treatment setting	4 (5.6)
Condition related factors	Duration, and previous treatment failures	13 (18.3)

Treatment Outcome and Associated Factors (Table 5)
Among patients with high adherence to AEDs 75% were significantly seizure free ($p=0.001$) while among non-adherent (medium adherent plus poor adherent to AEDs) 71 patients, only 38% were seizure free($p=0.001$). Patients whose seizure was diagnosed at early age has poor treatment prognosis. Among patients diagnosed at age of ≤ 15 years has poor treatment outcome (63.4% of them were not controlled). Among patients, seizure diagnosed at age of greater than 15 years has good treatment outcome (34.8% of them were not controlled).

Among 132 epileptic patients 30(22.7%) reported that they have brain injury due to different insults. From those 30 patients, 21(70%) reported that the brain injury was before the occurrence of seizure, while the remaining 9(30%) reported that their brain injury is after the occurrence of seizure. There is no significant association between brain injury and epilepsy treatment outcome ($p=0.61$). In addition there is no significant association between seizure treatment out come and weather brain injury is before seizure occurrence or after seizure occurrence ($p=0.2$).

Table 5. Treatment outcome and associated factors (n=30)

Factors affecting treatment outcome		Seizure treatment outcome		P value
		Controlled	Not controlled	
Adherence status	High	46(75)	15(24.6)	0.001
	Medium	16(59.3)	11(40.7)	
	Low	11(25)	33(75)	
Age at diagnosis(Years)	≤ 5	1(20)	4(80)	0.026
	6 to15	15(42.1)	23(57.9)	
	16 to45	50(63.3)	29(36.7)	
	>45	7(60)	3(40)	
Brain injury present	Yes	15(50)	15(50)	0.610
	No	58(56.9)	44(43.1)	
Brain injury	Before seizure occurrence	9(42.9)	12(57.1)	0.200
	After seizure occurrence	6(66.7)	3(33.3)	
EEG abnormality	Yes	3(27.3)	8(72.7)	0.040
	No	12(75)	4(25)	
	Not known	58(55.3)	47(44.7)	
Seizure frequency per week)	≤ 3 attacks	40(63.9)	21(36.1)	0.028
	≥ 4 attacks	33(47.9)	38(52.1)	
Monotherapy with	Phenobarbitone	54 (43.9)	69 (56.1)	0.449
	Phenytoin	2 (33.3)	4 (66.7)	
	Valproic acid	1 (33.3)	3 (66.7)	
	Phenobarbitone + Carbamazepine	11 (33.3)	22 (66.7)	
Polytherapy with	Phenobarbitone + Phenytoin	3 (33.3)	6 (66.7)	-
	Phenobarbitone + Valproic acid	2 (100)		

Among study participants, 105 (79.5%) had no neurologic examination electroencephalogram (EEG) compared with those who had EEG examination, 11 (8.3%) had confirmed EEG abnormality. Even though the majority of the patients had no EEG examination 79.6%, those who had EEG abnormality among examined one have poor seizure treatment prognosis (72.3% have poor seizure control, $p=0.04$) while among patients who had no EEG abnormality (75% were seizure free, $p=0.04$) which indicate significant association between EEG abnormality and treatment outcome.

The numbers of patients who reported seizure greater than 3 attacks per week before AEDs initiation accounts for, 71 (53.8%) while the remaining reported less than or equal to 3 attacks. Among patients with seizure attack of ≤ 3 per week before AEDs initiation had 63.9% seizure free while those who had more than 3 attacks per week had 47.9% seizure free ($p=0.028$).

There is strong (significant) association between frequency of seizure attacks and treatment outcome, those patients who had few seizure attacks before initiation of AED has good seizure treatment outcome than with high attacks (greater than or equal to 4 attacks per week).

Discussion

There was no published study to investigate the level of adherence to treatment, level of treatment outcome and related factors in epilepsy patients in Ethiopia. It was found that psychiatric diseases are prevalent among epileptic patients as it has been demonstrated in a study done in England and Taiwan (4, 13). The nature and frequency of seizure triggering factors obtained in our study has also been demonstrated in reasonably similar studies (8, 13-16).

The entire epileptic patients who were diagnosed with either Absence or generalized tonic-clonic seizure is not in agreement with any retrieved studies. The fact that the set up doesn't have any neurologist and good diagnostics tools that might explain this, and affirms the seizure is not controlled in the majority of the patients.

The finding that the majority of our participants were prescribed with phenobarbitone is in line with WHO recommendation (1), and another review (17) conclusion that suggested phenobarbitone as the first line anti-epileptic drug as it is claimed to be available, affordable, effective and tolerated in patients in developing countries if appropriately titrated with strict adherence. Majority of the patients were on mono-therapy for AEDs, which accounts 66.7% and on poly-therapy 56.8% which is in agreement with a study done in United Kingdom (18).

Even though evidences suggested that up to 70% of children and Adults newly diagnosed with epilepsy can be successfully treated with antiepileptic drug (1), poor seizure control regardless of the drug prescribed and the titration done was observed in this study. The poor drug adherence seen in this study which is consistent with other studies (7, 19-21) might confirm this finding. Negligence to titrate to the maximum tolerable dose that can stop seizure can be an additional factor. For example, in majority of the cases, the drug used as add on (second AED) is carbamazepine 200mg/day, which is not the maximum dose. As much as the patient tolerate we can titrate up to 1800mg/day, however, this was not performed in this study.

Although maximum doses were not used, a considerable proportion of patients were the victim of untoward effects of the drugs. The observed side effect spectrums were in line with the prescribed medications. A study done in UK demonstrated that the same nature and frequency of side effects profiles (18), but the fact that our study was based on self-report that might limit head to head comparisons. The side effects were implicated for the poor adherence to the medication in this study as it was in other study (22).

Almost one-third of the patients have faced seizure attack despite appropriate antiepileptic drug treatment, placing them at considerable risk of cognitive and psychosocial dysfunction and death (13). As it was suggested by our finding, among patients with high adherence to AEDs, 75% were seizure free while among non-adherent, only 38% were seizure free. Therefore, there is significant association between level of adherence and seizure treatment outcome. Patient whose seizure was diagnosed at early age has poor treatment prognosis which indicate that there is a significant association b/n age at diagnosis of epilepsy and treatment outcome. The reported triggering factors in this study were in line with other studies (16, 23).

As indicated in this study's result, there was no significant association between brain injury and epilepsy treatment outcome. When this result is compared with other research, however, it is in opposite direction (24). This may be because of the reason that this study did not differentiate superficial brain injury from penetrating brain injury at its data collection period, as superficial brain injury is not that has much effect on seizure treatment outcome. For example, the patient may report superficial/minimum injury as traumatized or penetrating brain injury, which has no effect on their seizure treatment outcome. The majority of the patients had no EEG examination. In the current study, patients who had EEG abnormality had poor seizure treatment outcome compared to those patients who had no EEG abnormality.

In conclusion, poor adherence to prescribed medication was the major cause of unsuccessful drug treatment for epilepsy. Forgetfulness, Feeling sick/side effects, work interference, being away from home and taking too many drugs have contributed to this poor adherence. Moreover, delay in dose titration and refusal to titrate AEDs dose have caused delay in time to remission phase, which later contributed to non-adherence to AEDs to our epileptic patients. Besides, age at diagnosis, seizure frequency and abnormal EEG have contributed to poor treatment outcomes in epileptic patients. The most common seizure triggering factors in this particular study were emotional distress, sleep deprivation, missing meal, missing medication and noise as reported by our patients. Strict medication adherence evaluation and enhancement through proper health education, close follow up with multidisciplinary approach are fundamental to the successful management of epileptic patients. We can say the moment patient education and adherence cease the patients seizure.

Acknowledgement

We would like to forward our gratitude to Jimma University for financial support and Ambo Hospital staffs and patients for their pleasurable cooperation.

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How to cite:

Tefera GM, Woldehaimanot TE, Angamo MT. Poor Treatment Outcomes and Associated Factors among Epileptic Patients at Ambo Hospital, Ethiopia. Gaziantep Med J 2015 21 (1): 9-16.