DETERMINATION OF THE FACTORS LEADING TO NONCOMPLIANCE WITH ANTIEPILEPTIC DRUG

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ABSTRACT

Background: Epilepsy is a chronic disorder or group of chronic disorder in which the indispensable feature is recurrence of seizures that are typically unprovoked and usually unpredictable. It is well established that non-adherence to antiepileptic drugs may lead to a loss of seizure control. Negative outcomes that may be associated with a loss of seizure control include: injury, increase hospitalizations, and decrease in productivity. All of these contribute to increased direct and indirect healthcare costs related to epilepsy. **Objective:** To determine factors leading to non-compliance with antiepileptic drugs in patients attending a tertiary care hospital. **Methods & Results:** In the cross-sectional study design, total 203 patients, attending neurology outpatient clinic at Department of Neurology Civil Hospital Karachi, Pakistan, from August, 2010 to February, 2011, with epilepsy were included in the study. Non probability, purposive sampling technique was applied. Detailed history was taken from each patient. A structured proforma was filled for each patient at the time of visit and note was made of the factors that were responsible for non-compliance. Overall mean (±SD) age was 29.1 ±16.9 years (ranging from 6 to 60 years) with Male: Female = 1.9: 1. Most common reason for non compliance was high cost of antiepileptic drugs 126 (62.1%) followed by unemployment in 58 (28.6%) patients, more than one antiepileptic drug in 35 (17.2%) patients, side effects of antiepileptic drugs 19 (9.4%), freedom free periods from fits 18 (8.9%), deviation from prescription 13 (6.4%) and Non Availability of drugs 12 (5.9%). **Conclusion:** In this study, high cost of antiepileptic drugs was the most common reason for non compliance and non-availability of drugs was the least common reason. While unemployment was the second common reason for non-compliance

Key Words: Epilepsy, AED, non-compliance, epileptic seizure

INTRODUCTION

In medicine, by the word compliance we mean how much a patient behaves in accordance with medical advice regarding medication usage, modification of lifestyle and follow up visits to the attending physician. With respect to drug therapy, compliance is defined as the degree of correspondence of the actual dosing history with the prescribed drug regimen.[1] Epilepsy is one those chronic conditions where failure to comply with treatment regimen leads to two major consequences: an unfavorable and unwanted health outcome for the patient and an increase in health care costs. Negative health outcomes include loss of seizure control with resultant injury, increased morbidity and even death. An increase in health care cost is attributed to an increase in physician office visits, emergency room care and/or hospitalizations, and a decrease in productivity (e.g., missing school and work).[2] Studies regarding adherence have found four primary factors associated with medication non-adherence: patient-related factors (e.g., socio-economic characteristics, and perceptions and beliefs), illness-related factors (e.g., severity of illness and frequency of symptoms), medication-related factors (e.g., number of daily doses, efficacy, and side effects), and physician-related factors (e.g., patient-physician relationship).[3] Research regarding patient adherence to AEDs has focused largely on the impact of the patient physician relationship on adherence and potential education programs intended to improve adherence. Findings suggest that patients tend to be more adherent when physicians have open dialogue regarding epilepsy and its treatments and when patients are comfortable speaking with their physician.[4] Due to the paucity of published studies on non adherence among patients with epilepsy, this study investigates the factors associated with non-adherence to AEDs and help in taking possible measures to improve antiepileptic drug compliance and prevent consequences of uncontrolled seizures. The prevalence of epilepsy in Pakistan is about 9.99/1000. Highest prevalence is seen in people younger than 30 years of age. Higher prevalence is observed in rural population. Only 27.5% epileptic persons in urban areas and 1.9%

in the rural areas were treated with antiepileptic drugs.[3] When treating epilepsy, the ideal is to achieve complete seizure control if compliant; up to 70 per cent of people with epilepsy can expect to become seizure free with optimal AED therapy.[5]

Methods

This was a cross-sectional study carried out at the Department of Neurology, Dow University of Health Sciences and Civil Hospital Karachi. All the patients with epilepsy attending Neurology outpatient Clinic between a period of six months extending from February 2010 to August 2010 were analyzed and study group was selected according to the predetermined inclusion and exclusion criteria. In addition to demographic data, factors responsible for non compliance were assessed with the help of a structured proforma designed specifically for this purpose. In this cross-sectional study, a total of 203 patients with epilepsy, attending Neurology Outpatient Clinic at Civil Hospital Karachi during a period of six months extending from August 2010 to February 2011 were included. Non probability, purposive sampling technique was applied. Detailed history was taken from each patient. A structured proformas was filled for each patient at the time of visit to note the factors that were responsible for non-compliance. Following is Patient Inclusion Criteria

- Diagnosis of idiopathic epilepsy irrespective of the duration of disease and have been prescribed antiepileptic drug by a physician with a proper prescription
- Patients skipping at least one dose of antiepileptic drug in a week.
- Or missing the dose infrequently but missing resulting in seizure.
- Age: 06 to 60 years either male or female.

Patients with following criteria were excluded

- Patients with symptomatic epilepsy
- Diagnosed case of chronic renal or hepatic failure or any other metabolic disorder that would have impaired the concentration of AED.
- Patients who were given inadequate dosage or inadequate instructions by their physicians.

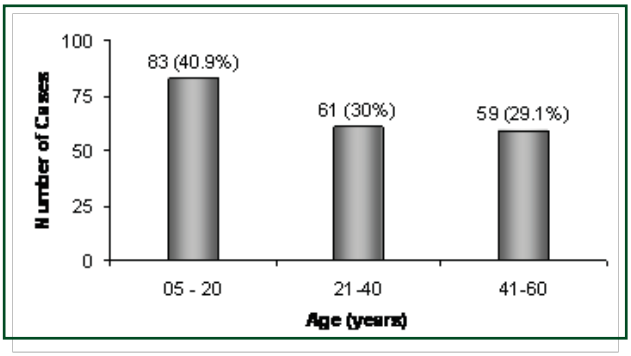
Data was analyzed on SPSS version 14.0. Frequencies and percentages were computed for qualitative variables, gender, age group, educational status and factors leading to non-compliance (e.g high cost, unemployment, kept on more than on drug, side effects, freedom from fits, deviation from prescription, non availability of drugs, personal belief-taboos and taking other medicines). Mean and standard deviation was computed for quantitative variables like age. Stratification was done on age, gender and education status to see the effects on outcome.

Results

A total of 203 diagnosed cases of epilepsy were included in this study. Of 203 cases of epilepsy, 133 (65.5%) patients were male and 70 (34.5%) female (Male: Female = 1.9: 1). (Table-1)

Gender	n	%
Male	133	65.5
Female	70	34.5

The mean age of patients attended Department of Neurology, Civil Hospital Karachi was 29.1 ±16.9 years and their age ranged from 6 years to 60 years. Majority 83 (40.9%) of cases had age between 5 – 20 years. (Figure-1)



Education level of participants was also noted .The majority of patients were illiterate 101(49.8%), 82 (40.4%) participants were educated up to matric, 18 (8.9%) were intermediate and only 2 (1%) patients were graduate. (Table-2)

Education Level	n	%
Illiterate	101	49.8%
Matric	82	40.4%
Intermediate	18	8.9%
Graduation	2	1.0%

Most common reason for non compliance was high cost of antiepileptic drugs 126 (62.1%). Fifty eight (28.6%) patients had poor drug compliance because they were not employed consequently do not have enough money to buy medicine, 35 (17.2%) patients skipped from timely dose because they were prescribed more than one antiepileptic drug followed by side effects of antiepileptic drugs 19 (9.4%), freedom from fits 18 (8.9%), deviation from prescription 13 (6.4%) and Non Availability of drugs 12 (5.9%) (Table-3)

Factors	Gender	
	Male n(%)	**Female n(%)**
High Cost	90 (71.4)	36 (28.6)
Non Availability of drugs	6 (50.0)	6 (50)
Personal belief-taboos	4 (36.4)	7 (63.6)
Freedom from fits	12 (66.7)	6 (33.3)
Unemployment	57 (98.3)	1 (1.7)
Side Effects	11 (57.9)	8 (42.1)
Taking other medicines	2 (40.0)	3 (60)
Kept on more than on drug	17 (48.6)	18 (51.4)
Deviation from Prescription	5 (38.5)	8 (61.5)

In male patients most dominant reason for poor drug compliance was unemployment 57 (98.3%), followed by high cost 90 (71.4%), freedom from fits 12(66.7%), side effects 11 (57.9%) and non availability of drugs 6 (50%). (Table-4)

Whereas in female patients the most prominent reason for poor drug compliance was personal belief –taboos 7 (63.6%), followed by taking other medicines for other illness 3 (60%), deviation from prescription 8 (61.5%) and kept on more than one antiepileptic drug 18 (51.4%). (Table-4)

Factors	Gender	
	Male n(%)	**Female n(%)**
High Cost	90 (71.4)	36 (28.6)
Non Availability of drugs	6 (50.0)	6 (50)
Personal belief-taboos	4 (36.4)	7 (63.6)
Freedom from fits	12 (66.7)	6 (33.3)
Unemployment	57 (98.3)	1 (1.7)
Side Effects	11 (57.9)	8 (42.1)
Taking other medicines	2 (40.0)	3 (60)
Kept on more than on drug	17 (48.6)	18 (51.4)
Deviation from Prescription	5 (38.5)	8 (61.5)

When reasons for noncompliance were cross tabulated against different age groups, Unemployment (44.8%) was found most prominent reason of poor drug compliance in age groups 21-40 and 41-60. Personal belief-taboos (45.4%) was associated with younger age group 5-20. (Table-5)

Factors	Age Group (Years)		
	05-20	**21-40**	**41-60**
High Cost	51 (40.47%)	36 (28.5%)	39 (30.9%)
Non Availability of drugs	4 (33.3%)	5 (41.6%)	3 (25%)
Personal belief-taboos	5 (45.4%)	2 (18.1%)	4 (36.3%)
Freedom from fits	5 (27.7%)	7 (38.8%)	6 (33.3%)
Unemployment	6 (10.3%)	26 (44.8%)	26 (44.8%)
Side Effects	15 (78.9%)	2 (10.5%)	2 (10.5%)
Taking other medicines	0.0%	0.0%	100.0%
Kept on more than on drug	20 (57.1%)	6 (17.1%)	9 (25.7%)
Deviation from Prescription	6 (46.1%)	5 (38.4%)	2 (15.3%)

Factors associated to noncompliance were also analyzed against education level of patients. Non availability of antiepileptic drug 9 (75%) was the major cause of poor compliance in illiterate patients. Unemployment 30 (51.7%) and high cost 61 (48.4%) were the main causes of non compliance in matriculate patients. (Table-6)

Factors	No Education	Matriculation	Intermediate	Graduate
High Cost	50 (39.7%)	61 (48.4%)	13 (1.6%)	2 (1.6%)
Non Availability of drugs	9 (75%)	3 (25%)	0 (0%)	0 (0%)
Personal belief-taboos	8 (72.7%)	3 (27.3%)	0 (0%)	0 (0%)
Freedom from fits	12 (66.7%)	4 (22.2%)	2 (11.1%)	0 (0%)
Unemployment	23 (39.7%)	30 (51.7%)	5 (8.6%)	0 (0%)
Side Effects	11 (57.9%)	6 (31.6%)	1 (5.3%)	1(5.3%)
Taking other medicines	2 (40%)	2 (40%)	1 (20%)	0 (0%)
Kept on more than on drug	19 (54.3)	13 (37.1%)	2 (5.7%)	1 (2.9%)
Deviation from Prescription	6 (46.2%)	5 (38.5%)	2 (15.4%)	0 (0%)

Discussion

Compliance with a prescribed medicine regimen is a ubiquitous problem not confined to the treatment of asymptomatic conditions. Despite this, the poor compliance in patients with epilepsy is somewhat surprising given that patients are aware of the serious consequences in terms of seizures and even death. In this context it is important that we look for ways to improve epilepsy patients' adherence to the prescribed medication as a way of improving outcome. There are many factors that influence compliance in people with epilepsy but the frequency, type and severity of seizures do not in themselves appear to influence compliance rates.[6] Irregular requests for repeat AED prescriptions, lack of response to appropriate therapy and an increase in seizure frequency may indicate non-compliance. It is, however, difficult to identify all patients who do not comply with their AED therapy. Health professionals should therefore be alert to the potential for non-compliance in all patients with epilepsy, enquiring non-judgementally about medicine taking at each consultation and being prepared to support patients in complying with their treatment. In addition to the diagnosis of epilepsy in a considerable number of patients depressive mood changes exist. In those patients rates of adherence is reduced and requires special strategies for continuous treatment.[7] The patients can have poor compliance if they do not understand the importance of taking their medication, if they experience side effects, feel stigmatized by their condition, have difficulty in swallowing their medication or have multiple doses.[8] These issues can be multiplied if the patient is on multiple medications for concomitant conditions. Age can also be a factor with compliance being particularly poor in teenagers.[9] Although non-compliance in epilepsy may be unintentional, most non-compliance with AEDs is intentional and results from conscious choices by patients.[10] These decisions are based on patients' beliefs about medicines in general that are affected by the experience of family and friends, culture, education, social circumstances, fears and anxieties and may be the result of an incomplete understanding of epilepsy and the proposed treatment. The result may be that patients are unsure that the benefits of AED treatment outweigh the perceived risks of taking medication. [11] In this study most common reason for non compliance was high cost of antiepileptic drugs (62.1%). (28.6%) patients had poor drug compliance because they were not employed consequently do not have enough money to buy medicine, 35 (17.2%) patients skipped from timely dose because they were prescribed more than one antiepileptic drug followed by side effects of antiepileptic drugs (9.4%), freedom from fits (8.9%), deviation from prescription (6.4%) and Non Availability of drugs (5.9%). A survey undertaken by Neurologists (n=661) in the USA10 revealed that 71% of patients with epilepsy forgot to take their AED (anti-epileptic drug) at least once per month and it was evident that the chance of a patient missing a dose increased with the number of tablets prescribed. Of patients that missed a dose 45% reported a seizure. Patients taking a larger number of tablets/capsules increased their odds of having a seizure after a missed dose by 43%. Similar results were reported in a recent UK study [12] which revealed that 59% of epilepsy patients had poor compliance and that this was related to an increased frequency of seizures. A study in Germany[13] measured post-ictal serum levels of anti-epileptic medications and confirmed that in at least 44% of cases the seizure was related to poor compliance. A review of 10,892 epilepsy patients in a USA managed care system [14] revealed that poor adherence was associated with a 11% increase in hospitalization and a 47% increase in emergency admissions and as a consequence there was significantly increased healthcare costs. It is evident that if patients' seizures are not controlled by one AED there may be no point changing to another if the reason for lack of efficacy is non-compliance. Studies have investigated a range of interventions, but improving compliance in chronic conditions such as epilepsy is a complex task.[15] Clinical guidelines provide detailed recommendations about the importance of ongoing counseling, education and support for people with epilepsy[16], and it is also essential to ask about practical problems that may reduce compliance, including any difficulties in taking the medicine, side-effects or inconvenient AED dosing. The number of daily doses is the most consistent predictor of noncompliance with AED treatment and an increased risk of seizure.[10] The aim should be to move towards an easy-to-take once daily medication whenever possible. Opportunities to simplify the dosage of an AED are limited since the majority of these drugs must be taken twice or three times daily and the licensed indications of some once-daily drugs are limited.

Conclusion

In this study, high cost of antiepileptic drugs was the most common reason for non compliance and non-availability of drugs was the least common reason. While unemployment was the second common reason for non-compliance. These findings underscore the factors associated with and the impact of non-adherence in adult patients with epilepsy. Targeted epilepsy management programs and communication strategies are necessary to improve adherence and to avoid the clinical consequences of poor adherence.

References

1. Urquhardt J. Role of patient compliance in clinical pharmacokinetics: review of recent research. Clin Pharmacokinet1994; 27: 202–215
2. Wirrell EC. Epilepsy-related injuries. Epilepsia 2006;47:79–86.
3. Greenhouse WJ, Meyer B, Johnson SL. Coping and medication adherence in bipolar disorder. J Affect Disord 2000;59:237–41
4. Schachter SC. Epilepsy: quality of life and cost of care. Epilepsy Behav 2000;1:120–7.
5. Harden CL, Goldstein MA. Mood disorders in patients with epilepsy: epidemiology and management. CNS Drugs 2002;16:291-302.
6. Buck D, Jacoby A, Baker GA, Chadwick DW. Factors influencing non-compliance with antiepileptic drug regimes. Seizure 1997;6:87-93.
7. Vergouwen AC, van Hout HP, Bakker A. Methods to improve patient compliance in the use of antidepressants. Ned Tijdschr Geneeskd, 2002;146:204-7
8. Carter S, Taylor D, Levenson R. A question of choice compliance in medicine taking. A preliminary review (2nd edition). London: Medicines Partnership 2003.
9. Kerr M. Epilepsy and learning disability. In: Sander JW, Walker MC. Smalls JE (Eds). Epilepsy 2007: From Cell to Community, a Practical Guide to Epilepsy. Eleventh edition. International League Against Epilepsy (UK Chapter) and the National Society for Epilepsy, London.
10. Cramer JA, Glassman M, Rienzi V. The relationship between poor medication compliance and seizures. Epilepsy & Behavior 2002;3:338-42.
11. WHO (World Health Organisation). Adherence to Long-Term Therapies: Evidence for Action. World Health Organisation, Geneva. 2003
12. Jones RM, Butler JA, Thomas VA. Adherence to treatment in patients with epilepsy: associations with seizure conrol and illness beliefs. Seizure 2006;15:504-8.
13. Specht U. Postictal serum levels of antiepileptic drugs for detection of non-compliance. Epilepsy & Behavior 2003;4:487-95.
14. Davis KL. Prevalence and cost of nonadherence with antiepileptic drugs in an adult managed care population Epilepsia. 2005;49:446-54.
15. Haynes RB, Ackloo E, Sahota N. Interventions for enhancing medication adherence. Cochrane Database of Systematic Reviews 2008;2: CD000011
16. Stokes T, Shaw EJ, Juarez-Garcia A. Clinical guidelines and evidence review for the epilepsies: diagnosis and management in adults and children in primary and secondary care. London: Royal College of Physicians, 2004.

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Author's contribution:

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