

A Study Of Factors Associated With Adherence To Treatment In Patients With Epilepsy.

¹Dr. Suman Bala , ²Dr. Rohitash Sharma, ³Dr. Shreshth Khanna, ⁴Dr. Yashpal Singh, ⁵Dr. Nikku Yadav, Dr. Yashbir Dewan

¹ Professor , Department of Pharmacology, Shri Guru Ram Rai Institute of medical & health sciences Shri Mahant Indires Hospital Dehradun.(Corresponding author)

² Assistant Professor Department of Neurology, Shri Guru Ram Rai Institute of medical & health sciences Shri Mahant Indires Hospital Dehradun.

³ Assistant Professor Department of Pharmacology, Hamdard institute of medical sciences and research, Jamia Hamdard, New Delhi.

⁴ Professor and Head of department of Neurology, Shri Guru Ram Rai Institute of medical & health sciences Shri Mahant Indires Hospital Dehradun.

⁵ Assistant Professor, department of community medicine, Himalayan institute of medical sciences , Jolly Grant Dehradun.

⁶ ,Professor Department of Neurosurgery, Shri Guru Ram Rai Institute of medical & health sciences Shri Mahant Indires Hospital Dehradun

Abstract:

Introduction-Non-adherence to antiseizure medications is one of the main reasons for the treatment failure and seizure recurrence.

Objective:-Evaluation of adherence and its association with belief about antiseizure drugs in patients with epilepsy were examined

Materials and methods: This was a prospective, cross sectional study in patients suffering from epilepsy in the department of neurology for a period of 6 months. Patient adherence and persistence in long term continuation of treatment was assessed by using the Modified Morisky Adherence Scale and beliefs about medicines questionnaire scale.

Results:A total of 100 patients were enrolled out of which 46% of the patients were adherent, 54 % were non adherent to their medications. GTCS was the commonest seizure (58%) followed by partial seizures (41%) and unclassified seizures (1%). Levetiracetam(37%) was the commonest drug prescribed, followed by valproic acid(24%), carbamazepine(19%), oxcarbazepine(14%), phenytoin(5%), phenobarbitone (1%). Male patients were found to be more adherent to drug therapy as compared to females. (p<0.05).Participants with higher education were highly (73 %) adherent to antiepileptic drugs followed by high school (37%) and primary school 33%). Specific necessity score was significantly more in adherent group as compared to nonadherent group. Patients who believed that antiepileptic drugs do more harm than benefit were significantly more in non-adherent group.

Conclusions:Patient with high educational status, positive attitude and belief toward therapy found to be more adherent to their medication. Assessment of adherence to medication and counselling should be routine part of management for the betterment of health care and quality of life.

Keywords: Epilepsy, adherence, Modified Morisky Adherence Scale, Belief about medication score.

Introduction:

Epilepsy is neurological disorder characterized by recurrent episodes of seizures causing neurobiological, cognitive, psychological, and social consequences.^[1] The annual incidence of epilepsy in India is about 27.3 per 100,000 per year with a prevalence of 5.59 to 10 per 1000^[2]Epilepsy is associated with physical,psychological and social problems.^[3]. The risk of sudden unexpected death is higher in patients with epilepsy as compared to general population.^[4]Prolonged seizures may cause physical injury, disruption of neural networks causing neuronal loss, leading to cognitive impairment.^[5]However, management of epilepsy has been shown to be successful with antiepileptic

agents. Most interesting is that 60% of treated adults stopping taking medication without relapse within 2-5 years of treatment.^[6] Therefore, with appropriate drug management, improved quality of life in epileptic patients can be achieved. Epilepsy has been shown to have significant effects on patient's lives. This is reflected on the ability to work and the standard of living in epileptic patients. Approximately half of epilepsy patients feel that the disorder affects their ambitions and social life.^[7] Patients also admit to missing school or work due to this disorder. Furthermore, these patients also feel that the disease influences their memory.^[8] Children and adolescent with epilepsy also admit that they feel embarrassed about their disorder and feel excluded by their peers.^[9] Employment

opportunity and capability to work for patients with epilepsy are important for self-esteem, self-image and quality of life.^[10]

SeizureControl can be attained through adherence to antiseizure medications. More than half of epilepsy patients have poor seizure control due to non-adherence to medication.^[11] Effects of non adherence have also been linked to other problems. Amongst the effects of medication non adherence is an increased likelihood of an episode of status epilepticus.^[12] In addition, non adherent patients were also more likely to be hospitalized and experience an emergency room admission.^[13]

In view of the state of the disorder, there is also a high rate of road accidents resulting in fracture, head injury and sudden unexpected death in patients with non controlled seizures.^[14]

Medication adherence is therefore important, especially in chronic disease patients. Unfortunately, adherence in these groups of patients has been shown to be poor.^[15, 16] Adherence to medication is affected by various patient factors such as age, duration of disease and co-morbidities.^[15, 17]

Non-adherence to antiepileptic medications has been reported to be high. Studies showed a high prevalence of seizure (21–45%) in patients who did not adhere to their antiepileptic medications.^[18] Patients who are non-adherent to their medication are frequently hospitalized with prolonged lengths of stay, have repeated emergency department visits, and miss school or work frequently because of the seizure effects or out of fear of seizure occurrence.^[19] The direct effect of non-adherence with reducing the quality of life in epilepsy patients however is a concern. So far, studies investigating self-reported adherence in epilepsy have not used validated questionnaires. Therefore, the aim of this work was to identify the level of adherence to medication and perceived belief about medication for epilepsy patients. This study also investigated the extent of non-adherence, associated with poor seizure control which was measured by using a validated self-report questionnaire. We also investigated the relationship between seizure control and beliefs about medication and illness.

MATERIALS AND METHODS

The study was conducted on the patients visiting the outpatient department of neurology of Himalayan institute of Medical College and Hospital, Jolly Grant Dehradun. This was a prospective, cross sectional study enrolling 100 patients suffering from epilepsy. Patients were enrolled after applying inclusion and exclusion criteria. Ethical approval was obtained from the Medical Research and Ethics Committee and

informed consent was taken from all patients before inclusion into the study.

Inclusion criteria:

1. Adults treated for epilepsy with at least one drug was included in the study
2. Patients of both genders in the age group of aged 18 years or older.
3. Patients who were not known to have cognitive impairment or psychiatric illness, without other severe co-morbidities
4. Patients who consented to participate in the current study
- 5.

Exclusion criteria:

1. Inability to understand spoken words due to hearing loss.
2. severe visual impairment hindering reading, Patient information, demographic data, seizure control (more than 1 episode per month, one episode per month, more than one episode per year and seizure free), complexity of medication (one or more medication) was obtained from patient medical records. Patients were then interviewed to assess patient adherence intention. Patient adherence and persistence in long term continuation of treatment was assessed by using the Modified Morisky Adherence Scale^[20, 21] and beliefs about medicines questionnaire BMQ scale.^[22] The Validated 8-item Morisky Medication Adherence Scale (MMAS-8), a self-reporting tool was used to assess the patient's adherence level to antiepileptic drug (AED) therapy.¹⁰ There were 8 questions evaluating the patient's forgetfulness, patient's understanding of the need for continued therapy and whether the patient felt it was inconvenient adhering to a daily medication treatment plan. For questions 1, 2, 3, 4, 6 and 7, a score of zero was given for a positive response whereas a score of one was given for a negative response (Yes = 0; No = 1). Conversely, for item 5, a score of zero was given for a negative response whereas a score of one was given for a positive response (Yes = 1; No = 0). For item 8, a score of one was given for 'Never/Rarely' whereas a score of zero was given for 'Once in a while' / 'Sometimes' / 'Usually' / 'All the time'. The total score of MMAS-8 was 8. A Higher score indicated a higher level of self-reported adherence. Adherence level was categorized as adherent (Score: 8), Non adherent (Score: <8). The beliefs about medicines questionnaire comprises 18 statements, and subjects were asked the extent to which they agree or disagree with the statement on a five-point scale. The questionnaire was divided into two sections, measuring beliefs about medicines in general and beliefs about a specified medication (general and specific sections). The general section of questionnaire consists of the overuse subscale (e.g. "doctors use too many

medicines’), the harm subscale (e.g. ‘‘medicines do more harm than good’’). Subscales assess general perceptions of a) the benefit of medications, b) harm associated with intake of drugs, and c) overuse of prescribed medications by physicians. Specific beliefs about AEDs were assessed by perceived necessity of AEDs and concerns about the negative effects of AEDs. Responses ranked from (1) - strongly disagree’ to (5) - strongly agree

Data was analysed by using SPSS version -20 (Statistical Package for Social Sciences) Descriptive statistics was used to describe demographic and disease characteristics of the patients and their medication adherence scores.

Frequencies and percentages were used for the categorical variables, while means and standard deviations were calculated for the continuous variables. The characteristics of the sample and of the adherent and nonadherent groups were presented. The normality of the data was determined by using one-sample Kolmogorov Smirnov test. Comparison between two groups was done by using Mann Whitney U test in case of non-normally distributed variables whereas Kruskal Wallis test was used for the comparison of more than two groups. The Chi square test was used for the analysis of categorical variables.

Results

Table: 1 Socio demographic Characteristics

Number of patients 100	Frequency and percentage
Male	69%
Female	31%
Mean age	
<35	76%
>35	24 %
Education	
Less than primary	12.1%
High School	64.6%
Higher Education	23.2%
Religion	
Hindu	90%
Muslim	10%
Marital status	
Single	42%
Married	58%
Domicile	
Urban	32 %
Rural	68%
Mean duration of epilepsy	2.22 ±1.41
Type of seizure	
GTCS/Partial/unclassified	58 % / 41% / 1%

Results showed 76% of the participants belonged to the age group <35 years and 24% were of more than 35 years of age, 69% participants were male while 31% were female and majority of the participants (68%) were from rural and 32% were from urban population. Majority of the participants (58%) had generalized tonic-clonic seizure, 41% of the participants had partial seizure 1% had unclassified seizure

Table: 2 Morisky score according to gender and education.

Variable		Morisky Score				Chi-square; p-value
		Non adherent N	Adherent N	Total		
				N	%	
Gender	Male	37	31	68	68.7%	0.002; 0.97
	Female	17	14	31	31.3%	
Education	Less than primary	8	4	12	12.1%	9.86; 0.007
	High School	40	24	64	64.6%	
	Higher Education	6	17	23	23.2%	

Table 2-Results showed that the male participants were more adherent to drug therapy as compared to females. ($p < 0.05$).

According to educational status of the participants 65% of them were of high school followed by 23.2% of higher education and 12.1% were less than primary school. But higher education participants were more (73%) adherent to antiepileptic drugs followed by high school (37%) and less than primary school (33%).

Table: 3 Comparison between adherent and non-adherent groups of patients regarding beliefs about medicines questionnaire scores (BMQ)

Variables	Median		p-value
	(Non-Adherent)	(Adherent)	
Average duration of illness	2.00(3.00-1.00)	2.00(2.50-1.50)	0.67
Specific necessity	19.00(20.00-15.75)	21.00(21.00-20.00)	<0.001
Specific concerns	14.00(16.00-12.00)	13.00(15.50-12.00)	0.74
General overuse	12.00(13.00-10.00)	11.00(12.00-9.00)	0.06
General harm	9.00(11.00-8.00)	8.00(9.00-8.00)	0.01

Statistical Test: Mann Whitney Test

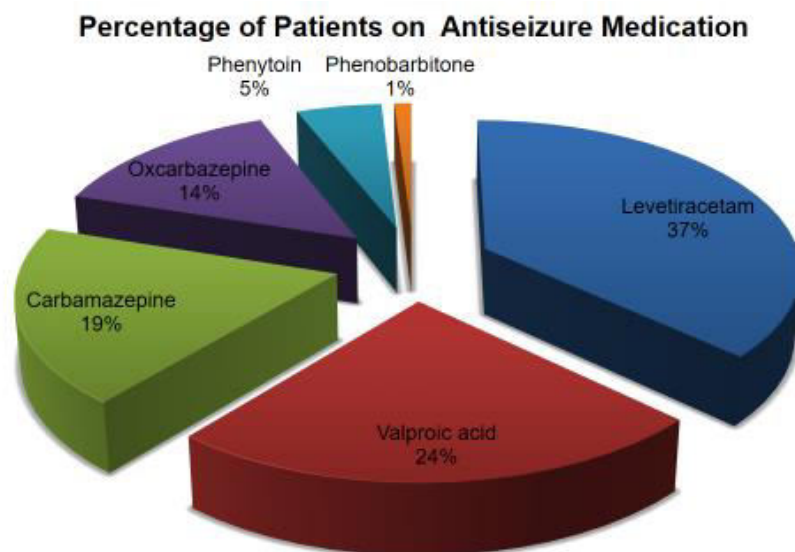
Table 3: Results showed Specific necessity score was significantly more in adherent as compared to nonadherent group. While non adherent group has more score for specific concerns, general overuse of drugs and general harm of drugs.

Table: 4 A comparison in the mean of beliefs about medicines questionnaire scores (BMQ) in both sexes.

BMQ	Total	Male	Female	Pvalue
Specific Necessity	20(18-21)	20(18-20)	20 (17-21)	0.42
Specific Concern	14(12-16)	13(12-15)	14(13-17)	0.05
General Overuse	11(10-13)	11(9-12)	12(10-14)	0.028
General Harm	8(8-10)	8(8-10)	9(8-11)	0.062

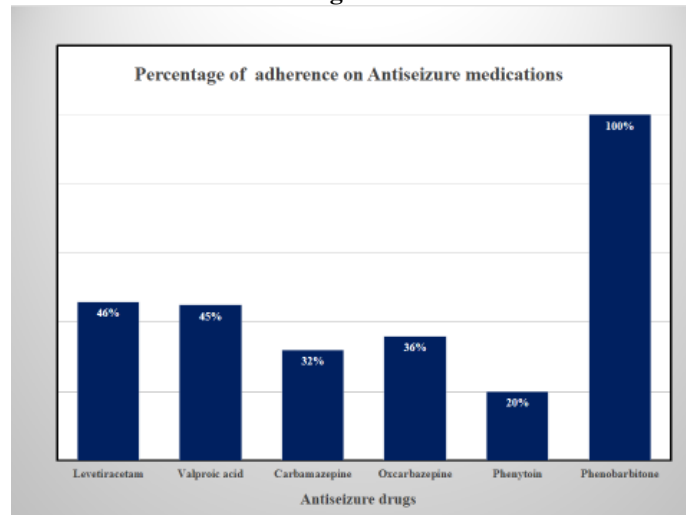
Table 4 :showed there is no significant difference in specific necessity score in both the gender. Female have more specific concern about medication $p=0.05$ general overuse $p < 0.05$ and general harm as compared to males.

Figure 1



Majority of patients were prescribed Levetiracetam (37%) followed by Valproic acid (24%), Carbamazepine (19%), Oxcarbazepine (14%) and Phenytoin (5%).

Figure 2



Discussion

Nonadherence to medication poses difficult issues for all the clinicians in the pharmacological management of conditions which needs long term therapy. High adherence to antiseizure drugs play important role in the successful treatment of epilepsy. Poor adherence to drug therapy is considered as one of the major causes of non-responsiveness to chronic drug therapy such as antiepileptic drugs (Kyngas, 2000).^[23] To suppress epileptic seizure more than 95% adherence is adequately required. Even missing of antiepileptic drug doses once or twice per week may be sufficient to failure of therapy and is responsible for reoccurrence of seizures.^[24] We have classified our patients into Non Adherent and Adherent to their medications according to Modified Morisky Adherence score. There are number of factors which influence patient's adherence to their medications. The primary purpose of this current study was to assess factors influencing medication adherence among epileptic patients and to provide recommendations for the improvement in their healthcare and quality of lives. In this current study, 46% of the patients were adherent, 54% were poorly adherent their medications (Table 2) which need to be improved. Reported patient adherence to drug therapy was different in various studies as 22%^[23], 51.9%^[25] and 41%^[26] while Asadi-Pooyareported 75% of patients compliance to antiepileptic drugs.^[27] These differences in compliance between different studies may be due to different culture, patient's

belief about illness, effectiveness of medication, education and clinician approach to the patient with epilepsy. All these factors influence adherence to the therapy and control of seizure.^[28] The effect of gender was found to be an important contributing factor affecting the medication adherence in this study. Male patients (31.3%) were more adherent to antiepileptic drugs as compared to females (14.1%) $p < 0.05$. Our results were not in agreement with those carried out by Johnbull et al.^[2, 18] (2011) who concluded in his research that there were no demographic differences based on gender between adherent and non-adherent patients. In our study younger age (23.4 ± 12.4) group was found to be more adherent to drug therapy as compared to higher age (33.26 ± 16.34) $p < 0.05$. (Table 1). In our study population consist of the patients with primary school (12.1%), high school (64.6%), and higher education (23.2%). Adherence to medication did not show any significant difference among all the study groups. The mean duration of epilepsy was 1.22 ± 1.41 . The age of disease onset and duration of the disease did not have a significant correlation with the rate of adherence among our patients. In contrast, Kyngas found that the duration of the illness is significantly related to patient adherence.^[23] Good motivation with a positive attitude toward disease and treatment with no fear of complications and no fear of seizures explain good adherence.^[23] The effect of patient beliefs on medication adherence was studied in this current research. It was found that there was positive association between adherence score (MMAS-8) and Belief about specific

necessity score. Patients with positive necessity concerns differential scores were more in adherent patients to antiepileptic drugs as compared to those with negative scores ($p < 0.05$). In addition, patients who believed that antiepileptic drugs benefit more than harm were significantly more in adherent (Tables 3 and 4). Results obtained by Jones et al also found that epileptic patients, who had a greater belief in the need for medication, were significantly more adherent.^[11] It was evident that there was an increase in adherence in patients with stronger beliefs in necessity of treatment as they want to remain seizure free with the help of antiepileptic drugs and also protecting them from becoming worse. Conversely, there was negative association between adherence score and BMQ specific concerns, general overuse and general harm. Patients who believed that antiepileptic drugs do more harm than benefit were significantly higher in non-adherent group. (Table 3)

Non adherent patients have belief about negative impact of medication (specific concerns) like long term effects, dependency on medication, doctor overuse medication to treat them and with low concern about them. Non adherent patients also have belief that medicines most of medicines are addictive, poisons and should be stopped. Patients also had Belief about general overuse of drugs -doctors use too many medications, natural remedies are more are safer than medicines. General harm scores were more in non-adherent compared to adherent patients ($p < 0.05$). (Table 3) In addition, our results suggest that women with epilepsy are less adherent may also have greater concerns about AEDs and more doubts about their personal need for AEDs.^[28] Belief score about specific concern, general overuse and general harm were significant more in females (p value $<$ than 0.05) as compared to males. In current study women believes were more concerned about the negative effects of antiepileptic drugs

Conclusion

Nonadherence to medication is very common among epileptic patients on antiseizure medication and an important factor responsible for treatment failure. Various factors like higher educational status of patient and positive attitude toward therapy can insure high adherence to medication. Belief of patient toward these drugs also play important role to achieve higher adherence. High concern toward negative effect of antiseizure medication negatively impact on adherence. Along with correct diagnosis and appropriate pharmacotherapy and assessment of medication adherence also play important role in management of epilepsy. To improve the quality of life of patients living with epilepsy, adherence

to antiseizure medication needs to be strengthened.

Acknowledgement: Authors would like to thank Himalayan Institute of Medical Sciences for providing the opportunity to conduct the research work. We also indebted to all patients who consented to participate in this study

Conflict of interest -None

We declare that there is no conflict of interest on this research study.

REFERENCES

1. Fisher RS, van Emde Boas W, Blume W, Elger C, Genton P, Lee P, et al. Epileptic seizures and epilepsy: definitions proposed by the International league against epilepsy (ILAE) and the International bureau for epilepsy (IBE). *Epilepsia*. 2005; 46:470-2
2. Banerjee TK, Ray BK, Das SK, Hazra A, Ghosal MK, Chaudhuri A, et al. A longitudinal study of epilepsy in Kolkata, India. *Epilepsia*. 2010; 51:2384-91
3. Devinsky O. Definition and overview of intractable epilepsy. In: Schachter SC, Schomer DL, editors. *The comprehensive evaluation and treatment of epilepsy: a practical guide*. San Diego: San Diego Academic Press; 1997: 86—7.
4. Nobili L, Proserpio P, Rubboli G, Montano N, Didato G, Tassinari CA. Sudden unexpected death in epilepsy (SUDEP) and sleep. *Sleep Med Rev*. 2011 Aug;15(4):237-46.
5. Scott RC. What are the effects of prolonged seizures in the brain? *Epileptic Disord*. 2014 :S6-11..
6. WHO. *Adherence to Long-Term Therapies: Evidence for Action*, 2003.
7. Baker GA, Jacoby A, Buck D, Stalgis C, Monnet D. Quality of life of people with epilepsy: a European study. *Epilepsia* 1997, 38(3): 453-462.
8. Hovinga CA, Asato MR. Association of non-adherence to antiepileptic drugs and seizures, quality of life, and productivity: survey of patients with epilepsy and physicians. *Epilepsy Behav* 2008, 13(2): 316-322.
9. Anderson GD, Kim H, Warner MH. Impact of taking antiepileptic drugs at

- school in a group of children and adolescents. *Epilepsy and Behav* 2000, 1:17-21.
10. De Boer HM. Overview and perspectives of employment in people with epilepsy. *Epilepsia* 2005, 46(1): 52-4.
 11. Jones R.M, Butler J.A , Thomas V.A., Peveler, R.C Preveett, M. Adherence to treatment in patients with epilepsy: associations with seizure control and illness beliefs. *Seizure* 2006, 15 (7): 504-8.
 12. Cramer JA. Mood disorders are linked to health-related quality of life in epilepsy. *Epilepsy Behav* 2002, 3(6): 491-2.
 13. Davis A, Pack A. Initial management of epilepsy. *N Engl J Med* 2008, 359(23): 2499-2500.
 14. Faught E, Duh MS, Weiner JR, Guérin A, Cunnington MC. Nonadherence to antiepileptic drugs and increased mortality: findings from the RANSOM Study. *Neurology* 2008, 71(20): 1572-8.
 15. Islahudin F, Tan SH. Medication knowledge and adherence in nephrology patients. *Int J Pharm Bio Sci* 2013, 3(1): 459-66.
 16. Cramer JA. A systematic review of adherence with medications for diabetes. *Diabetes Care* 2004, 27(5): 1218-24.
 17. Grant RW, Devita NG, Singer DE, Meigs JB. Polypharmacy and medication adherence in patients with type 2 diabetes. *Diabetes Care* 2003, 26(5): 1408-12.
 18. Liu J, Liu Z, Ding H, Yang X. Adherence to treatment and influencing factors in a sample of Chinese epilepsy patients. *Epileptic Disord.* 2013;15(3): 289-94.
 19. Hovinga CA, Asato MR, Manjunath R, Wheless JW, Phelps SJ, Sheth RD, et al. Association of non-adherence to antiepileptic drugs and seizures, quality of life, and productivity: Survey of patients with epilepsy and physicians. *Epilepsy Behav.* 2008;13:316-22.
 20. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986;24:67-74.
 21. Case Management Adherence Guidelines. Case Management Society of America 2004.
 22. Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychol Health.* 1999; 14:1-24.
 23. Kyngas, H Compliance with health regimens of adolescents with epilepsy. *Seizure.*2000. 9, 598-604.
 24. Johnbull, O., Farounb, B., Adeleye, A., Uche, A., Evaluation of factors influencing medication adherence in patients with epilepsy in rural communities of Kaduna State, Nigeria. *Neurosc. Med.* 2011;2 (4), 299-305.
 25. Liu, J., Liu, Z., Ding, H., Yang, X., Adherence to treatment and influencing factors in a sample of Chinese epilepsy patients. *Epileptic Disord;*2013;15, 289-294.
 26. Asadi-Pooya, A.A., Drug compliance of children and adolescents with epilepsy. *Seizure* 2005;14, 393-395.
 27. Miner, P.J, Alexander, J., Ewing, H., Gerace, L., Caregivers' beliefs associated with medication adherence among children and adolescents with epilepsy. *J. Neurosci. Nurs.*2013; 45 (4), 211-218.
 28. Smithson WH, Hukins D, Buelow JM, Allgar V, Dickson J. Adherence to medicines and self-management of epilepsy: a community-based study. *Epilepsy Behav* 2013;26(1): 109-13.