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Adherence to treatment in patients with epilepsy: Associations with seizure control and illness beliefs

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Summary

Objective: This study investigated non-adherence to antiepileptic drug treatment amongst patients with epilepsy in secondary care. The associations between adherence and seizure control, perceptions of illness and medication, anxiety and depression were also examined.
Methods: A cross-sectional study of fifty-four patients with epilepsy were recruited from a hospital epilepsy clinic.
Results: Fifty-nine percent were estimated to be non-adherent to medication. There was a negative correlation between adherence and frequency of seizures. Patients with poorly controlled epilepsy were more anxious, and expected a longer duration of their epilepsy.
Conclusion: Assessment of adherence should be a routine part of management of epilepsy. Further recognition and support should be given to patients who have poor seizure control since they are more likely to be more anxious and have unhelpful illness and treatment beliefs.

Introduction

Epilepsy has a prevalence of between 4 and 10 per 1000 population[1,2] and is associated with physical, psychological and social problems.[3] People with epilepsy have a higher rate of suicide, anxiety, depression, sudden unexplained death and accidental

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death.[4,5] Prolonged seizures may cause physical injury, neuronal death leading to cognitive impairment, and can be fatal.[5]

When treating an individual with epilepsy, there are factors that cannot be modified such as the age of onset, the aetiology of the seizures and the location of the epileptogenic zone. There are also some factors that may be amenable to an intervention to improve outcome. An obvious consideration for the clinician is the choice of medication to prescribe. Despite medication, it has been found that seizures persist in 20—35% of cases.[6] It is necessary therefore to identify other ''modifiable factors'' which could lead to improved seizure control if targeted effectively.

Non-adherence to medication is widespread in chronic disease and is a major problem facing medical practice.[7] Current estimates of non-adherence in epilepsy are similar to those in other chronic illnesses and range from 30 to 50%.[8] This reduces the benefit that could be gained from the medication.[7,9] Poor adherence may be the most important cause of poorly controlled epilepsy.[10] Stanaway et al. found that 31% of seizures were precipitated by non-adherence to medication.[11] If modifable factors associated with non-adherence are understood, then it may be possible to intervene to improve adherence and therefore reduce morbidity caused by recurrent seizures. Existing studies suggest that non-adherence is associated with frequency of administration of medication, age and attitude to taking medication.[12,13] Beliefs about medication and illness are potentially modifiable, can be measured using standardised questionnaires and have been related to adherence in other populations. In addition to beliefs, emotions and coping styles may also influence illness behaviour.[14] A range of theoretical models have been developed to attempt to clarify the relationships between beliefs, attitudes and behaviour, including social learning theory,[15] and the self-regulatory model of Leventhal et al.,[16] which was chosen for the present study.

Adherence is difficult to measure accurately. In epilepsy adherence has been measured by self-report, drug-level monitoring and prescription refill monitoring. Each method has disadvantages. For example, plasma drug levels are altered by pharmacokinetics as well as adherence, require an invasive procedure and only indicate recent adherence. Medication bottles that electronically record every opening are considered to be the most accurate means of measuring adherence.[9] However, a previous study to investigate adherence in epilepsy found this method unreliable.[17] Self-reporting is the simplest measure. Although adherence can be overestimated,[17] particularly due to self-presentation bias,[18] specificity is generally high (87%).[7] George et al.[19] have found that when a valid questionnaire is used (Morisky et al.[20]), self-report scores are accurate with both sensitivity and specificity of over 70%. So far, studies investigating self-reported adherence in epilepsy have not used validated questionnaires.[10,12,21—23] This study aims to investigate the extent to which non-adherence, measured using a validated self-report questionnaire is associated with poor seizure control. We also aim to investigate the relationship between seizure control and beliefs about medication and illness.

Methods

Subjects and procedure

We performed a cross-sectional assessment of self-reported adherence and attitudes to medication. We obtained approval of the study from the local research Ethics Committee. We recruited patients from those registered with a hospital epilepsy clinic. Patients were included if they had a diagnosis of epilepsy, were aged between 18 and 60 years, and were taking at least one antiepileptic drug. Consecutive attenders were asked to participate by the clinic doctor. The researcher (VT) then contacted consenting participants who provided questionnaires to subjects who were asked to complete them and return by post.

Measures

We obtained the age of onset of epilepsy, recent seizure frequency and details of prescribed antiepileptic drugs from the clinical records. Epilepsy was arbitrarily defined as ''well controlled'' if the patient reported less than one seizure per month. Questionnaires of known reliability and validity were used to assess treatment adherence (Morisky et al. questionnaire[20]), beliefs about illness (illness perception questionnaire, IPQ[24]) and treatment (beliefs about medicines questionnaire, BMQ[25]) and psychological symptoms (hospital anxiety and depression scale, HAD[26]). The Morisky scale has four items with minimum score of 0 and maximum of 4. Patients were considered non-adherent if they scored 1 or more. The beliefs about medicines questionnaire comprises 18 statements, and subjects are asked the extent to which they agree or disagree with the statement on a five-point scale. The questionnaire is divided into two sections, measuring beliefs about medicines in general and beliefs about a specified medication (general and specific sections). For our study, items in the specific section were worded to relate to 'antiepileptic drugs'. The

specific section consists of the Necessity subscale (e.g. ''my health at present depends upon my antiepileptic drugs'' and concerns subscales (e.g. ''having to take my antiepileptic drugs worries me''). The general section consists of the overuse subscale (e.g. ''doctors use to many medicines''), the harm subscale (e.g. ''medicines do more harm than good''). The BMQ items in the four subscales have a test–retest reliability of between 0.60 and 0.78 and a Cronbach's alpha of between 0.47 and 0.86.[25]

The illness perception questionnaire has 38 items on a four-point scale. The scale is divided into five subscales: identity (patients attribution of symptoms such as fatigue and headaches to the illness), timeline (perception of duration of illness, e.g. ''my illness will last for a long time''), consequences (perceived negative consequences of epilepsy, e.g. ''my illness has had major consequences on my life''), cure–control (belief that epilepsy can be treated, e.g. ''there is a lot that I can do to control my symptoms'') and cause (the perceived cause of the illness, e.g. ''it was by chance that I developed my illness''). The internal consistence as measured by Cronbach's alpha ranges from 0.73 to 0.82.[24]

Analysis

We used the Chi-squared test, Mann–Whitney test, *t*-test and Pearson's correlation as appropriate. We used non-parametric tests were used due to the small subgroup samples. Statistical Package for Social Sciences (SPSS, Version 10; SPSS Inc., 444 North Michigan Avenue, Chicago, IL, USA) was used for data analysis.

Results

Sample

We invited seventy-five people to participate in the study, of whom 54 (72%) consented. There were no significant age or gender differences between participants and refusers.

Of the fifty-four participants in the study, 25 (46%) were male. The mean age of the participants was 38.2 years (standard deviation (S.D.) 16.1 years). The mean age at diagnosis of epilepsy was 21.8 years (S.D. 19.3) and the mean duration of epilepsy was 18.2 years (S.D. 15.1). The median number of drugs taken each day by the subjects was 2 (inter-quartile range (IQR) 1–2) and the median dosing frequency was 2 (IQR 2–2). Using the accepted criterion of a score of one or more on the Morisky questionnaire indicating non-adherence, 32 patients (59%) were classified as non-adherent to medication. According to our definition of poor seizure control, 31 patients (57%) had poor control (Table 1).

There were no significant differences between well and poorly controlled epilepsy in respect of patient age, gender, age at diagnosis or duration of epilepsy. As expected, patients with poorly controlled epilepsy had significantly more seizures than those with well controlled epilepsy ($p < 0.01$) and were prescribed significantly more medications ($p < 0.01$), although there was no significant difference in dosing frequency. There was no significant overall correlation between adherence and absolute seizure frequency ($r = -0.003$, $p = 0.98$). However, one subject reported over 300 seizures per month which markedly skewed the distribution. When this subject was excluded from the analysis there was a significant positive correlation ($r = 0.344$, $p = 0.01$).

Illness perception and beliefs about medication

Beliefs about medication scores are shown in Table 2.

Patients with poorly controlled epilepsy had a greater belief in the need for medication than well controlled patients (Table 2). There was a non-significant trend for poorly controlled subjects to also

Table 1 Characteristics of patients with well controlled and poorly controlled epilepsy

	Well controlled	Poorly controlled	Test statistic	*p*-Value
Number	23	31		
Mean age (S.D.)	40.8 (18.3)	36.2 (14.4)	$t = 1.03$	$p = 0.31$
Number of males (%)	11 (48%)	14 (45%)	$\chi^2 = 0.04$	$p = 0.85$
Mean age at diagnosis of epilepsy in years (S.D.)	26.6 (22.4)	18.4 (16.3)	$t = 1.60$	$p = 0.13$
Mean duration of epilepsy in years (S.D.)	18.0 (19.5)	17.9 (11.2)	$t = 0.03$	$p = 0.98$
Median number of seizures in last month (IQR)	0 (0–0)	4 (2–12)	$Z = -6.50$	$p < 0.01$
Median number of drugs each day (IQR)	2 (1–2)	2 (2–3)	$Z = -1.90$	$p = 0.05$
Median daily dosing frequency (IQR)	2 (2–2)	2 (2–3)	$Z = -0.20$	$p = 0.10$
Number (%) non-adherent (≥1 on Morisky)	12 (38%)	20 (63%)	$\chi^2 = 1.85$	$p = 0.17$

t = Unpaired Student's t-test statistic, χ^2 = chi squared statistic, Z = Mann–Whitney U statistic.

Table 2 Comparison of beliefs about medicines questionnaire scores between patients with well and poorly controlled epilepsy

	Well controlled	Poorly controlled	Statistical test
Overuse median (IQR)	11 (9—14)	12 (8.8—14.3)	$p = 0.74$, $Z = -0.33$
Harm median (IQR)	9 (8—11)	9 (7.8—10)	$p = 0.97$, $Z = -0.04$
Necessity median (IQR)	18 (14—20)	21 (18—22)	$p = 0.02$, $Z = -2.31$
Concern median (IQR)	13 (11—17)	15 (13—19)	$p = 0.07$, $Z = -1.82$

Table 3 Comparison of illness perception questionnaire scores between patients with well and poorly controlled

	Well controlled	Poorly controlled	Statistical test
Identity median (IQR)	3 (2—6)	5 (4—8)	$p = 0.09$, $Z = -1.69$
Timeline median (IQR)	10 (8—12)	13 (9—15)	$p = 0.03$, $Z = -2.21$
Consequences median (IQR)	23 (20—25)	26 (22—28)	$p = 0.08$, $Z = -1.76$
Cure—control median (IQR)	20 (18—23)	18 (15—21)	$p = 0.13$, $Z = -1.52$

report more concerns with their medication (Table 2).

Illness perception questionnaire scores are shown in Table 3. Compared with the well controlled subjects, those with poor control believed that their epilepsy would last longer. There were no differences in beliefs about symptom profile of the illness, perceived cause of illness, perceived negative consequences of epilepsy or belief that epilepsy can be treated. Poorly controlled patients reported significantly more anxiety than well controlled patients (HAD-A median score 9, IQR 7—12.3 compared to median 6, IQR 5—8, $p = 0.007$).

Discussion

We found that non-adherence to medication is common in epilepsy. We found that patents with poorly controlled epilepsy had beliefs about their epilepsy that were significantly different from those with well controlled epilepsy. They had a greater belief in the need for medication, they expected a greater duration of their illness and they were also significantly more anxious. Our data also suggest that there is a correlation between seizure frequency and non-adherence to medication.

The strength of this study was that for the first time validated questionnaires were used to assess adherence and beliefs about illness and medication in epilepsy. Since poor control was associated with non-adherence, it was surprising that poor control was not associated with less belief in the need for medication. The association with concerns was in the expected direction. Putting these results together, one may conclude that concerns about medication outweigh the perceived need in some patients with epilepsy and this may be associated with higher levels of anxiety. The association between increased psychological morbidity and poor control indicates that patients with poor control are a vulnerable group that may benefit from increased psychological support.

The finding that seizure control is correlated with non-adherence indicates that therapy to promote adherence to medication[27] could be an important part of the treatment strategy provided by a specialist clinic. An approach which focuses on the choice and dose of antiepileptic will have limited success if the prescribed treatment is not adhered to. It is possible that general practitioners refer patients with poor control to secondary care in the belief that they have failed to find a successful drug treatment, when it is in fact more of a problem with adherence. It is not expected that general practitioners will have the time to conduct regular compliance therapy sessions, however a brief assessment of adherence can be made very quickly and with good sensitivity and specificity using the Morisky questionnaire, and it has been shown that health behaviour of patients can be effectively modified in general practice by simple advice.[28] Adherence should be discussed regularly with the patient, and in particular when a treatment seems to fail.

There are however a number of potential weaknesses of the study. Firstly, the sample size was relatively small. Although we found a significant correlation between adherence and seizure frequency, we did not find significant group differences in adherence between people with well controlled and poorly controlled epilepsy. It is likely that significant results were not detected due to an insufficient sample size. We would therefore recommend that future research studies a larger sample. There is a also potential recruitment bias as only 72% of those approached agreed to take part. Although the measures used are all well validated, there is a potential risk of response bias as they rely on

self-reporting. It was not possible in this study to corroborate the reports of adherence by other means which would have added precision to the measures, though at the expense of patient participation and cost. A cross-sectional design cannot determine causality; poor adherence may occur as a result of the severity of the illness or non-responsiveness to treatment. For example, post-ictal confusion or amnesia may result in inadvertent non-adherence. Increased dosing frequency and number of different medications taken in uncontrolled epilepsy would also be expected to affect adherence. Future research could also include measurements of more variables than we measured in this study to explore mechanisms of non-adherence. These may include coping styles, personality types and motivation. Other psychological models could also be investigated.

In secondary care a full assessment of modifiable factors that could be acted on to improve seizure control should be made. Non-adherence to medication may be the single greatest factor in poor seizure control and can be quickly and easily assessed. Adherence assessments should be routine. An inquiry should be made to examine the unhelpful beliefs that the patient may have which interfere with adherence. Given the marked physical, psychological and social dysfunction associated with poorly controlled epilepsy, and the considerable financial impact on health services, psychological input to address adherence may well be a very cost effective addition to the health care provider's armoury. Further studies are needed to evaluate the effect of adherence on seizure control, to evaluate the effect of psychological care in epilepsy, and to assess its impact on adherence, seizure control and distress.

References

1. Anderson VE, Hauser WA, Rich SS. Genetic heterogeneity in the epilepsies. *Adv Neurol* 1986;**44**:59—75.
2. *Brain's diseases of the nervous system*. 10 ed. Oxford: Oxford University Press; 1993.
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 Accademic Press; 1997, p. 86—7.
4. Garnett WR. Antiepileptic drug treatment: outcomes and adherence. *Pharmacotherapy* 2000;**20**(8 Pt 2):191S—9S.
5. Leestma JE, Kalelhar MB, Teas SS. Sudden unexplained death associated with seizures. *Epilepsia* 1984;**25**(84):84—8.
6. Devinsky O. Patients with refractory seizures. *N Engl J Med* 1999;**340**(May (20)):1565—70.
7. Eraker SA, Kirscht JP, Becker MH. Understanding and improving patient compliance. *Ann Intern Med* 1984;**100**(February (2)):258—68.
8. Leppik IE. How to get patients with epilepsy to take their medication. The problem of noncompliance. *Postgrad Med* 1990;**88**(July (1)):253—6.
9. Dunbar-Jacob J, Mortimer-Stephens MK. Treatment adherence in chronic disease. *J Clin Epidemiol* 2001;**54**(December (Suppl. 1)):S57—60.
10. Gomes Mda M, Maia Filho Hde S, Noe RA. Anti-epileptic drug intake adherence. The value of the blood drug level measurement and the clinical approach. *Arq Neuropsiquiatr* 1998;**56**(December (4)):708—13.
11. Stanaway L, Lambie DG, Johnson RH. Non-compliance with anticonvulsant therapy as a cause of seizures. *N Z Med J* 1985;**98**(March (774)):150—2.
12. Loiseau P, Marchal C. Determinants of compliance in epileptic patients. *Epilepsy Res Suppl* 1988;**1**:135—40.
13. Buck D, Jacoby A, Baker GA, Chadwick DW. Factors influencing compliance with antiepileptic drug regimes. *Seizure* 1997;**6**(April (2)):87—93.
14. Lazarus RS. From psychological stress to the emotions: a history of changing outlooks. *Ann Rev Psychol* 1993;**44**:1—21.
15. Bandura A. *Social foundations of thought and action*. Engelwood Cliffs, NJ: Prentice-Hall; 1986.
16. Leventhal H, Meyer D, Nerenz D. The common-sense representation of illness danger. In: Rachman S, editor. *Medical psychology*. New York (NY): Pergamon; 1980. p. 27—30.
17. Cramer J, Vachon L, Desforges C, Sussman NM. Dose frequency and dose interval compliance with multiple antiepileptic medications during a controlled clinical trial. *Epilepsia* 1995;**36**(November (11)):1111—7.
18. Straka RJ, Fish JT, Benson SR, Suh JT. Patient self-reporting of compliance does not correspond with electronic monitoring: an evaluation using isosorbide dinitrate as a model drug. *Pharmacotherapy* 1997;**17**(January—February (1)):126—32.
19. George CF, Peveler RC, Heiliger S, Thompson C. Compliance with tricyclic antidepressants: the value of four different methods of assessment. *Br J Clin Pharmacol* 2000;**50**(August (2)):166—71.
20. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986;**24**(January (1)):67—74.
21. Schmidt D, Reininghaus R, Winkel R. Relevance of poor compliance for seizure control. *Epilepsy Res Suppl* 1988;**1**: 141—6.
22. Peterson GM, McLean S, Millingen KS. Determinants of patient compliance with anticonvulsant therapy. *Epilepsia* 1982;**23**(December (6)):607—13.
23. Long L, Reeves AL, Moore JL, Roach J, Pickering CT. An assessment of epilepsy patients' knowledge of their disorder. *Epilepsia* 2000;**41**(June (6)):727—31.
24. Weinman J, Petrike J, Moss-Morris R. A new method for assessing the cognitive representation of illness. *Psychol Health* 1996;**11**:431—45.
25. Horne R, Weinman J, Hankins M. The development and evaluation of a new method for assessing a cognitive representation of medication. *Psychol Health* 1999;**14**(1):1—24.
26. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;**67**(June (6)):361—70.
27. Kemp R, Hayward P, Applewhaite G, Everitt B, David A. Compliance therapy in psychotic patients: randomised controlled trial. *BMJ* 1996;**312**(February (7027)):345—9.
28. Silagy C, Stead LF. Physician advice for smoking cessation. *Cochrane Database Syst Rev* 2001;(2):CD000165.