# Original article

# Adherence to treatment and influencing factors in a sample of Chinese epilepsy patients

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**ABSTRACT** – *Aim.* To assess adherence to antiepileptic drugs (AEDs) and factors associated with non-adherence in a sample of Chinese patients with epilepsy. *Methods.* A cross-sectional descriptive study was carried out on patients who had no change in treatment regimen over the last six months. Data on adherence to medication and related factors for each patient were gathered using a questionnaire. *Results.* Of a total of 368 patients studied, 48.1% of patients were non-adherent with regards to AEDs. There were no demographic differences (based on gender, age, seizure type, and rural or urban location) between adherent and non-adherent patients. Adherence was positively and significantly correlated with duration of illness (*p*=0.007). The primary reason for non-adherence was forgetfulness or not having medication on hand (69.6%), followed by a negative attitude (12.8%), a bad patient-prescriber relationship (9.5%), side effects (5.4%), inability to buy drugs (1.9%), and other reasons (0.8%). *Conclusion.* The non-adherence of epilepsy patients is common in China. Targeted management programs and communication strategies are necessary to improve adherence to AED treatments in patients with epilepsy and avoid the clinical consequences of poor adherence.

**Key words:** epilepsy, China, adherence, antiepileptic drug

Epilepsy is a common and widespread neurological disorder, affecting people of all ages and socioeconomic classes worldwide (De Boer, 2002). Of those diagnosed with epilepsy, the vast majority are treated with antiepileptic drugs (AEDs) and approximately 70% may become seizure-free once the most effective regime is followed (Eatock and Baker, 2007).

However, approximately a third of patients with epilepsy continue to experience seizures despite the prescription of appropriate doses of AEDs (Hui *et al.*, 2007). Poor adherence to AEDs may be the most important cause of poorly controlled epilepsy (Dunbar-Jacob and Mortimer-Stephens, 2001). The term "adherence" describes the extent to which a patient takes medications, as prescribed with respect to dosage and dosing intervals (Cramer *et al.*, 2008). Non-adherence to treatment is widespread for chronic disease

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and is considered to be a significant problem faced by medical practice (O'Brien *et al.*, 1992).

Non-adherence to AEDs has been reported to be high (Hovinga *et al.*, 2008; Manjunath *et al.*, 2009) and studies have demonstrated a higher prevalence of seizures (21-45%) in those who did not adhere to their AED regimens (Stanaway *et al.*, 1985; Cramer *et al.*, 2002; Manjunath *et al.*, 2009). In addition, poor adherence to AEDs has been reported to increase morbidity and mortality (Faught *et al.*, 2009), as well as decrease quality of life and productivity (Hovinga *et al.*, 2008). Non-adherence was also reported to be associated with reduced mental and emotional well-being, including impaired cognition (Hovinga *et al.*, 2008).

Of the world's 50 million people with epilepsy, 85% live in developing countries (De Boer, 2002). There are approximately 9 million people with epilepsy in China; 6 million with active epilepsy and 0.4 million new cases each year. However, few studies on adherence have been performed in Asian and developing countries (Jin *et al.*, 2008). We therefore undertook a pilot survey of adherence to seizure medication and investigated influencing factors in a population of Chinese epilepsy patients.

## Methods

### Subjects

Patients with epilepsy treated at the Military General Hospital of Beijing People's liberation Army, a public hospital, from October 2009 to January 2012 were included in the study.

Patients who met the following criteria were invited to participate in this study: (1) a diagnosis of epilepsy documented in their medical files; (2) therapy with at least one AED, irrespective of any standard or non-standard treatment; and (3) no change in AEDs in the last six months. Standard treatment was defined according to the International League Against Epilepsy (Glauser *et al.*, 2006), and other medication, such as traditional Chinese drugs, herbs or others, as non-standard treatment.

The patients were arbitrarily divided into four groups according to age: a child group (0-9 years), an adolescent group (10-19 years), an adult group (20-59 years), and an older group (60+ years).

Seizure types were categorised into simple partial seizures, complex partial seizures, generalised tonic-clonic seizures (primary or secondary), and other seizures (*e.g.* absence, myoclonic, tonic, atonic, clonic, and uncertain types).

### Assessment and measures

A questionnaire was sent by post to an unselected, community-based population of patients with epilepsy. The patient survey comprised questions regarding demographics (gender, age, city of origin, etc.), seizure history (type and frequency), current AED treatments, self-reported adherence to medication, and the reasons of non-adherence.

Based on a consensus and published literature supporting a recall period of one month (Doughty *et al.*, 2003), adherence was defined as not missing a dose and non-adherence as missing a dose or stopping treatment in the last month.

### Analyses

All analyses were conducted using SAS software Version 16.0. Continuous variables were expressed as mean±SD. We used the $\chi^2$ and Student's t test to compare adherence between different groups and with other factors; significance was defined as $\alpha<0.05$.

Since all patient data was anonymous, this study did not require ethical approval.

## Results

### Patient and physician characteristics

In total, 382 patients met all study inclusion criteria, of whom 368 (96.3%) agreed to participate in the study. The patients came from all provinces of mainland China. Adult patients represented the largest age group (51.2% of all patients) (*table 1*). Of all patients, 217 (59%) were male and 151 (41%) female. The mean patient age (±SD) was 35.3 (±11.7) years (range: 2-75 years). The onset of epilepsy ranged from the first month of life to 70 years (mean: 15.1±10.7 years). The mean duration of epilepsy was 8.8 (±7.3) years. In total, 57% of the patients were from rural settlements.

Considering all the patients, 5.5% of seizures were simple partial seizures, 33.5% complex partial seizures, 57.9% primary or secondary generalised tonic-clonic seizures, and 3.0% other seizures.

### Rates of non-adherence to AEDs

In our study, 177 (48.1%) patients were categorised as non-adherent and 191 (51.9%) as adherent.

The prevalence of non-adherence was highest (75.0%) among elderly epileptic patients, followed by adolescents (59.3%), adults (50.5%), and children (36.8%). However, there was no significant difference between age and adherence (*p*=0.135, $\chi^2$=5.555), no significant

**Table 1.** The reasons for non-adherence among different age groups.

| Age (years) | No. of patients | Patient adherence (%) | Reasons for non-adherence | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Forgetfulness (%) | Side effects (%) | Negative attitude (%) | Mistrust physician (%) | Unable to buy drugs (%) | Other reason (%) |
| 0-9 | 38 | 63.2 | 47.4 | 26.3 | 10.5 | 15.8 | 0.0 | 0.0 |
| 10-19 | 108 | 40.7 | 61.1 | 3.7 | 30.6 | 1.9 | 1.9 | 0.9 |
| 20-59 | 182 | 49.5 | 75.3 | 3.3 | 5.5 | 13.2 | 1.6 | 1.1 |
| 60+ | 40 | 25.0 | 87.5 | 0.0 | 0.0 | 7.5 | 5.0 | 0.0 |
| Total | 368 | 45.7 | 69.6 | 5.4 | 12.8 | 9.5 | 1.9 | 0.8 |

difference between seizure type and adherence ($p$=0.735, $\chi^2$=1.200), no significant difference in adherence ($p$=0.9) between male and female patients ($p$=0.924, $\chi^2$=0.009), and also no significant difference in adherence between patients from rural or urban settlements ($p$=0.316, $\chi^2$=1.007). However, a significant difference was obtained between adherence and duration of illness ($p$=0.007, $t$=-2.738). Patients with a longer duration of illness had lower adherence rates.

### Factors associated with non-adherence

Of the patients who did not adhere to drugs (69.6%), the primary reason was forgetfulness (65.8%) or not having medication on hand (3.8%), followed by patients' negative attitude towards the therapy (12.8%), a bad patient-prescriber relationship (9.5%), side effects or worry about side effects (5.4%), inability to buy drugs (1.9%), and other reasons such as taste of medication or requirement for drug storage (0.8%). The number of factors associated with non-adherence were different among different age groups (*table 1*).

## Discussion

This is the first published study to investigate the adherence of treatment and related factors in epilepsy patients in China.
Adherence is difficult to measure accurately (Rudd, 1979; Buelow and Smith, 2004). For epilepsy, adherence to medication has previously been measured by self-reporting, drug blood level monitoring, and prescription refill monitoring. Each method has disadvantages (Dunbar-Jacob and Mortimer-Stephens, 2001). Adherence measured by self-reporting may be overestimated (Cramer *et al.*, 1995), but is considered

to be the simplest and least expensive method. In this study, adherence was measured by self-reporting.
In our study, 48.1% of patients were non-adherent to AED treatment. This percentage is almost the same as that reported in other countries, at around 50%: Arab countries (64%) (Sweileh *et al.*, 2011), the United States (29-58%) (Davis *et al.*, 2008; Hovinga *et al.*, 2008; McAuley *et al.*, 2008), and the United Kingdom (59%) (Jones *et al.*, 2006).
In our study, elderly patients had the highest rates of non-adherence (75.0%). This may be due to the fact that elderly patients have more difficulty in following instructions due to cognitive impairment or other physical difficulties, such as problems in swallowing tablets, opening drug containers, handling small tablets, distinguishing colours or identifying markings on drugs (Benner *et al.*, 2002; Jeste *et al.*, 2003; Cooper *et al.*, 2005). However, according to our data, there was no significant difference in rates of non-adherence between the different age groups. Similarly, in the USA, no demographic differences (*i.e.* gender, age) were reported between adherent and non-adherent patients (Hovinga *et al.*, 2008). There was also no significant correlation between adherence rates and geographical location (rural or urban settlement). The main difference with regards to people living in rural or urban locations may be due to education and economic status, although, according to our data, education and economic status were not factors that affected adherence.
The duration of treatment period is also a factor that affected adherence. Acute illnesses are associated with greater compliance (Gascon *et al.*, 2004) and a longer duration of disease may adversely affect compliance (Farmer *et al.*, 1994; Ghods and Nasrollahzadeh, 2003; Dhanireddy *et al.*, 2005). In a study of epilepsy patients, omission of dose was reported to be more

frequent with a longer duration of seizure medication use (Cramer *et al.*, 2002). The long treatment duration might compromise patients' beliefs about medication effectiveness. In our study, the only factor that affected adherence was the duration of treatment period.

Adherence to treatment depends on many factors, and there is no simple explanation to account for non-adherence.

Forgetfulness is a widely reported factor that causes non-adherence to medication or clinic appointments (Ponnusankar *et al.*, 2004; Wai *et al.*, 2005). In our study, forgetfulness was the primary reason for non-adherence in different age groups, with varying degrees. It was most common for elderly patients to forget to take their drugs. Written instructions are better than oral advice for reminding patients to take medication. Physicians should consider prescribing the simplest regimen with the fewest daily doses and tablets, with the expectation of reducing dose omission caused by forgetfulness. Elderly patients should get the necessary help from healthcare providers or family members.

We defined negative attitude as patient unwillingness to take medication, based on perception of the disease or belief, or attitude to medicine, which was the second reason for non-adherence in our study. There were many factors that influenced patients' perception and beliefs with regards to adherence. Patients' knowledge about their disease and treatment is not always adequate and they may lack an understanding of the role of therapy (Ponnusankar *et al.*, 2004), be fearful of dependency on long-term medication (Apter *et al.*, 2003; Bender and Bender, 2005), lack knowledge about the disease and consequences of poor compliance (Alm-Roijer *et al.*, 2004), and may assume that the need for medication is intermittent and thus stop taking the drug in order to see whether medication is still required (Moore *et al.*, 2004). Adherence affected by negative attitude was most apparent in adolescent patients. For adolescents, this period is often marked by rebellious behaviour and disagreement with parents and authorities (Tebbi, 1993). Adolescents typically prefer to live a normal life, similar to their friends, and treatment may make them feel stigmatised (Bender and Bender, 2005) or feel pressure because they are not as normal as their friends or classmates (Kyngas, 1999).

Many studies have reported that side effects may threaten patient compliance (Buck *et al.*, 1997; Grant *et al.*, 2003; Ponnusankar *et al.*, 2004). In our study, the rate of side effects was 5.4%, which is similar to that of Hovinga *et al.* (2008) (9%). For the different age groups, drug side effects were most apparent in the child group (26.3%). This group represents the most important stage of growth and it is therefore understandable why parents were more concerned about side effects. In many cases, parents stopped the drug based purely on worry of possible side effects.

For these reasons, patient education is very important in order to enhance adherence. A poor patient-prescriber relationship is another strong factor which affects patient compliance (Buck *et al.*, 1997; Moore *et al.*, 2004; Gonzalez *et al.*, 2005); good patient-prescriber relationship may enhance adherence (Buck *et al.*, 1997; Schachter, 1999; Schachter, 2000). In order to build a healthy relationship, physicians should not only question patients about seizure frequency and current medication use, but also specifically probe them about adherence (Schachter, 1999; Lowes, 1998). They should give patients a detailed explanation about the disease, treatment regimens (Butterworth *et al.*, 2004), the true side effects, and the importance of adherence, and spend more time with the patients (Moore *et al.*, 2004). Healthcare expenditure is a very important factor for patients with chronic disease. In a report by Hovinga *et al.* (2008), (13)% of all non-adherent patients stopped medication due to financial burden. Today, epilepsy can be treated using more than 15 different AEDs (Bazil and Pedley, 2003). In China, herbal medicine is much cheaper than standard AEDs. In our study, the inability to buy drugs accounted for 1.9% of reasons for non-adherence, however, there were no patients that did not adhere due to financial restriction.

Our study has a few limitations. First, this was not a multiple centre study and the sample size was relatively small, thus limiting the significance of the data. Second, data from hospital-based centres were subject to referral bias. Finally, there was a risk of response bias since the measures relied on self-reporting.

## Conclusion

Medication adherence remains an important issue in epilepsy treatment. The non-adherence of epilepsy patients is common in China. Targeted management programs and communication strategies are necessary to improve adherence to antiepileptic drug treatment for patients with epilepsy and avoid the clinical consequences of poor adherence. □

**Disclosures.**
None of the authors have any conflict of interest to disclose.

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