

Researching on the compliance of epilepsy patients of the Phenobarbital Epilepsy Management Project in a rural area of China

A retrospective study

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Abstract

The aim of this study was to explore the compliance of epilepsy patients in the Phenobarbital Epilepsy Management Project in a rural area of China and its influencing factors, so as to provide the basis for further strategies.

A retrospective study researching on the compliance of epilepsy patients in the Phenobarbital Epilepsy Management Project of Rural China was conducted. The Nan County, Hunan Province as a typical rural China was selected as the study site. We collected the compliance and other relative factors from 2017 to 2019 through the Phenobarbital Epilepsy Management Project data system.

The good compliance patients in the Phenobarbital Epilepsy Management Project in a rural area of China were 98.99% (393/397); only 4 cases had poor compliance. The factors affecting the compliance of epilepsy patients were "adverse reactions of digestive tract symptoms," "how the patient felt physically, mentally, or working and learning ability during this period," and "the ratio of the attack to the previous one."

The rate of good compliance among the epilepsy patients in the Phenobarbital Epilepsy Management Project in a rural area of China was high. More attention to education, patients' psychology, and the curative effect of family members may improve the compliance of patients with epilepsy further.

Keywords: compliance, patients with epilepsy, retrospective study, rural China, the Phenobarbital Epilepsy Management Project

1. Introduction

Epilepsy is a common neurological disease, with seizures of the nature of the disease.^[1] According to a report from the World Health Organization, the epilepsy prevalence in developing

countries and in developed countries were 6.1‰ and 5.0‰, and 80% to 90% of epilepsy patients were in low and middle-income countries, especially in poor rural areas.^[2] In China, many epidemiological surveys showed that the prevalence of epilepsy in China was from 1.43‰ to 8.51‰, with an average prevalence of 7.0‰.^[3] At present, there are 9 million epilepsy patients in China. With 400,000 new patients each year in China, epilepsy has become the second most common disease in neurology.^[4]

Epilepsy has complex seizure performance, specific performance for consciousness, sensory, autonomic nerve, and mental disorders, and other aspects of the attack will seriously affect the patient's health and safety of life quality.^[5] If seizures occur frequently, they can cause severe neurological impairment, or death if they remain epileptic.^[6] Epileptic seizure not only brings physical and mental pain to patients and their families, but also brings relatively large economic burden to medical care, which has gradually become a very serious social problem. Today, more than two-thirds of rural epilepsy patients do not have a reasonable diagnosis and treatment. Studies have shown that, if diagnosed and treated correctly, many people with epilepsy will no longer experience severe seizures.^[7]

Compliance is an important factor affecting the therapeutic effect of patients, especially among epilepsy patients.^[8] On one hand, one of the most common causes of failure in antiepileptic therapy is poor patient compliance, such as not taking medication as prescribed.^[9] On the other hand, the worldly acknowledged treatment of epilepsy is reasonable, long-term, regular use of antiepileptic drugs.^[10] As a common treatment method to control epilepsy, antiepileptic drugs can effectively control the onset of 70% newly diagnosed epilepsy patients; Conversely, drug noncompliance will affect the effective treatment of epilepsy patients and may even lead to treatment failure.^[11] In addition, due to limited medical capacity and other reasons, the proportion of

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epilepsy patients with controllable seizures in China (especially in rural areas) is far lower than the level of 70% to 80% in foreign developed countries, indicating that the overall quality of life of epilepsy patients in China is low and the happiness index is low.^[12] Thus, it is particularly important to explore the causes of poor compliance of epilepsy patients and take intervention measures.^[13]

To alleviate the suffering and social burden of epilepsy patients, World Health Organization launched the “Epilepsy Prevention and Treatment Management Demonstration Project in Rural China,” which includes 2 groups: Phenobarbital Epilepsy Management Project and Valproate Sodium Epilepsy Management Project.^[14] The Nan County, Hunan province as one of the typical rural areas of China, began to implement the “Epilepsy Prevention and Treatment Management Demonstration Project in Rural Areas of China” since 2017.^[15] In view of phenobarbital taking most of the epilepsy treatment this study aim to explore the compliance among epilepsy patients of the Phenobarbital Epilepsy Management Project and its influencing factors by conducting a retrospective cohort study of two years follow-up, so as to provide suggestions for further improving the implementation effect of the Phenobarbital Management Project in the “Demonstration Project of Epilepsy Prevention and Treatment Management in Rural Areas of China.”

2. Methods

2.1. Study population and procedures

2.1.1. Screening of epilepsy patients. Patients with identified convulsive epilepsy were initially screened by trained doctors of rural health centers using a screening diagnostic form, and then all patients screened were reviewed by the neurologists in charge of the project to determine whether the patient should be included in the treatment management group.^[16]

Diagnostic criteria of generalized tonic-clonic seizures were: loss of consciousness; stiff limbs; the whole body tonic, clonic movement; urinary and fecal incontinence; bite the tongue or fall; fatigue, lethargy, headache, and muscle pain after attack. A person with 2 of the first 3 criteria and 1 of the last 3 criteria may be identified as having a convulsive seizure. Rural doctors (including rural health center doctors) are encouraged to have a detailed medical history and to discuss with their superior neurologists whether the diagnosis is correct. Finally by each area neurologist expert and the township (town) hospital physician makes the diagnosis.^[17]

Patients diagnosed with convulsive epilepsy who meet the following criteria may be included in the treatment observation.^[18]

Inclusion criteria were: at least 2 systemic tonic-clonic seizures (including partial seizures secondary to systemic tonic-clonic seizures) occurred in the 12 months before the investigation; the patient and his guardian agree to treatment and sign informed consent form with the township (town) health center responsible for treatment and follow-up.^[19]

Exclusion criteria were: only during pregnancy; the onset is only associated with alcohol or drug reduction; the age of the patient is <2 years' old (or weight is <10 kg); patients with history of Attention deficit and hyperactivity disorder; a history of allergy to phenobarbital (or piertone); the presence of progressive neurological disorders; with heart, liver, kidney disease, or severe hypertension (diastolic blood pressure >110 mmHg or systolic blood pressure >180 mmHg); had 1 (or more) history of epileptic persistent state; patients who were receiving normal antiepileptic drug therapy 1 week before enrollment;

(patients taking phenobarbital can be enrolled and the dosage can be adjusted by follow-up observation); traumatic accompanied by active psychosis.^[20] Patients who meet the inclusion criteria (and are not excluded from the exclusion criteria) and wish to participate may be enrolled for treatment. Antiepileptic treatment should also be considered for patients with other medical conditions or active epilepsy who do not meet the inclusion criteria.^[21] When necessary, local neurologist experts can be consulted to determine the treatment plan. The treatment and management of such patients can be developed in various localities according to the actual situation.^[22]

2.1.2. Follow-up procedure of epilepsy patients. Patients enrolled in the manage project were followed every two weeks for the first two months and every four weeks thereafter to adjust dosage, assess side effects, check patient compliance, and administer medication. The responsible doctor should fill in the “doctor’s follow-up form” carefully for each follow-up visit and distribute the medicine for the next month.^[23] After the patient had been followed up for >8 times (6 months after the enrollment), the patient still went to the rural health center on time every month to get the medicine, but the follow-up chart was changed to be written every 2 months^[24] (Fig. 1).

2.2. Data collection and measurements

The questionnaire was designed by the Epilepsy Project Office of National Health Commission of the People’s Republic of China, which was with good reliability and validity.^[25]

2.2.1. Sociodemographic information. Sociodemographic information includes region, age, sex, occupation, ethnicity, height, weight, and so on. Brief history of epilepsy, seizure, previous treatment, and recent treatment was asked during screening. During the follow-up, the last follow-up time was asked. The present dose of phenobarbital; have you had an episode since the last follow-up visit? The onset is more than before; adverse reactions; judgment of compliance; ask the patient how he or she has been feeling since the last visit. If the patient is taking other antiepileptic drugs irregularly during the week before enrollment, the name and dose of the antiepileptic drugs taken should be noted. If the patient requested or otherwise withdrew from phenobarbital therapy during follow-up, the reason and date of withdrawal should be recorded.

2.2.2. Compliance of patients with epilepsy. Compliance refers to whether the patient is taking medication as prescribed by the doctor. It can be assessed in the following ways: Ask the patient if he took all the pills he took each day, and if he took the full dose on the days he forgot to take the pills; calculate the number of tablets left over: How to calculate the number of tablets left over to determine patient compliance; Whether the patient visits the follow-up physician on time each time; Develop the habit of taking medication regularly, taking simple medications such as after dinner or before bed. So that other people can push the patient to take the medicine; the patient’s blood concentration can be monitored when conditions permit. Repeat the importance of taking medicine as prescribed.^[26]

2.3. Ethics statement

In this study, we use the data recorded in the Epilepsy Management Project database of Nanxian County, Hunan Province. It has been approved by Hunan Provincial Epilepsy

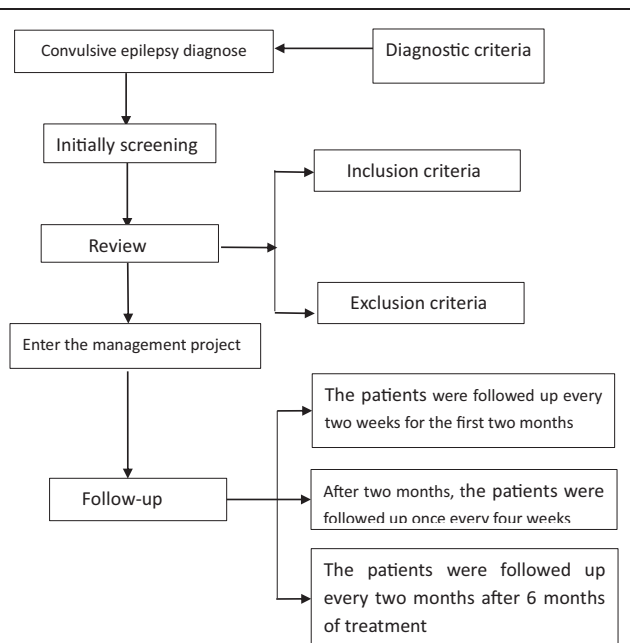


Figure 1. Flow chart of the study. The process of investigation and follow-up for epilepsy patients in this study.

Project Office. All patients in this program were introduced the purpose and significance of the the Epilepsy Management Project of China, and all participants signed the informed consent before their participation.

2.4. Statistical analysis

The data were analyzed by using SPSS V20.0 (SPSS/IBM, Armonk, NY). Data are presented as the number and percentage. The χ^2 test was used to explore differences in compliance with different characteristics. Binary logistic regression analysis was performed to identify risk factors for poor compliance in patients with epilepsy. A physician’s judgment of the patient’s overall compliance (1 = Good compliance and 2 = poor compliance) as the dependent variables. Loss of consciousness at the time of attack (1 = every time I have theta, 2 = nothing and 3 = not every time I have theta), the attack is more than before (1 = only temporary loss of consciousness, no twitch, 2 = loss of consciousness and twitch duration less than before, 3 = no loss of consciousness, only limb twitch and 4 = loss of consciousness and twitch as before), an ataxic reaction occurs (1 = none, 2 = mild, 3 = moderate and 4 = severe), have an adverse reaction to a headache (1 = none, 2 = mild, 3 = moderate, and 4 = severe), hyperkinetic reactions occur (1 = none, 2 = mild, 3 = moderate and 4 = severe), Develop an adverse reaction to a rash (1 = None, 2 = mild, 3 = moderate and 4 = severe), Adverse reactions with gastrointestinal symptoms (1 = None, 2 = mild, 3 = moderate and 4 = severe), and How does the patient feel physically, mentally, or physically during this period of time (1 = None, 2 = mild, 3 = moderate and 4 = severe) were entered as independent variables. The 2-tailed significance threshold was set at $P < .05$ in these analyses.

3. Results

3.1. The characteristic of the study population

A total of 397 patients with epilepsy were screened at the beginning of this study. Among them, there were 240 males and

157 females, with no significant difference in compliance between the sexes ($\chi^2 = 0.190, P = .515$). This study focuses on adults, and the proportion of middle-aged people (19–55) is the largest. There was no significant difference in compliance between different ages ($\chi^2 = 0.347, P = .951$). All the patients were Han nationality, and the most were farmers. The characteristic of the study population are shown in Table 1.

No significant differences in compliance among survey variables were found when studying disease information in patients with epilepsy. Most of the patients had their first seizure in their youth or middle age, and the number of patients with their first seizure <20 years’ old was 208, accounting for 52.4%. The number of patients with first onset between 20 and 40 years’ old was 118, accounting for 29.7%. This indicates that epilepsy is a disease that occurs in a large proportion of young people. 98% of epileptic patients had tonic-clonic seizures <2 times after the last follow-up; 74.5% of patients had <5 attacks in the first year after treatment. The largest percentage of patients with no seizure within 10 months after treatment was 47.4%. All these three points indicate that the patients with epilepsy have achieved good therapeutic effects through drug therapy, and also indicate that the patients have good medication compliance (Table 2).

Table 3 shows the treatment of epilepsy patients. Taking into account the differences between patients with epilepsy, doctors prescribe medications at different doses, with the largest proportion (90.5%) of phenobarbital doses <100 tablets. This suggests that most people with epilepsy do not have serious symptoms. The number of patients who did not take other antiepileptic drugs during the nearly 2 weeks of follow-up was 309 (76.8%); The symptoms of participants were only temporary loss of consciousness after treatment, without a higher propor-

Table 1
The characteristic of the study population.

| Variables | No. of cases (n) | Percentage (%) |
|---------------------|------------------|----------------|
| Sex | | |
| Male | 240 | 60.5 |
| Female | 157 | 39.5 |
| Age, y | | |
| 0–18 | 19 | 4.8 |
| 19–39 | 118 | 29.7 |
| 40–55 | 155 | 39.0 |
| >55 | 105 | 26.4 |
| Nation | | |
| The Han nationality | 397 | 100.0 |
| Occupation | | |
| Farmer | 267 | 67.3 |
| Unemployed | 101 | 25.4 |
| Student | 10 | 2.5 |
| Else | 18 | 4.8 |
| Height, cm | | |
| <100 | 1 | 0.3 |
| 100–150 | 39 | 9.8 |
| 151–170 | 308 | 77.6 |
| 171–190 | 49 | 12.3 |
| >190 | 0 | 0.0 |
| Weight, kg | | |
| <40 | 15 | 3.8 |
| 40–60 | 182 | 45.8 |
| 61–80 | 193 | 48.6 |
| >80 | 7 | 1.8 |

Basic characteristics of 397 patients, such as sex, age, and so on.

Table 2
Disease information of patients with epilepsy.

| Variate | No. of cases (n) | Percentage (%) |
|---|------------------|----------------|
| The no. of tonic-clonic seizures since the last follow-up | | |
| <2 | 389 | 98.0 |
| 2–6 | 7 | 1.8 |
| >6 | 1 | 0.3 |
| Age at first onset (first year of life) | | |
| <20 | 208 | 52.4 |
| 20–40 | 118 | 29.7 |
| 41–60 | 61 | 15.4 |
| >60 | 10 | 2.5 |
| No. of attacks in the last year | | |
| <2 | 141 | 35.5 |
| 2–5 | 155 | 39.0 |
| 6–8 | 31 | 7.8 |
| >8 | 70 | 17.6 |
| How many months have gone by without an attack | | |
| <10 | 188 | 47.4 |
| 10–20 | 12 | 3.0 |
| >20 | 0 | 0 |
| Diagnosis | | |
| Confirm epilepsy meets inclusion criteria | 300 | 75.6 |
| Epilepsy confirmed, but did not meet inclusion criteria | 76 | 19.1 |
| To rule out epilepsy | 21 | 5.3 |
| The onset of type | | |
| Tonic-clonic all over | 341 | 85.9 |
| Absence seizure | 21 | 5.3 |
| Simple partial seizures | 29 | 7.3 |
| Partial onset of systemic seizures | 2 | 0.5 |
| Other systemic seizures | 1 | 0.3 |
| Can't classification | 3 | 0.8 |

The disease conditions of 397 patients with epilepsy, such as the time, frequency, and diagnosis of seizures.

tion of convulsions; 82.9% of the patients felt better physically, mentally, or physically during the time they took the medication. These 3 points indicate that phenobarbital has a better therapeutic effect.^[27] After follow-up, the doctors' comprehensive judgment of adverse reactions after taking drugs was that the number of patients with no adverse reactions as a whole was 327, accounting for 82.4%. This indicates that taking phenobarbital is not only effective, but will not cause too many adverse reactions in patients.^[27] 74.1% of the patients had been diagnosed with epilepsy in the past, and 60.5% of the patients had taken western medicine for treatment and the effect of single treatment was not very good (Table 3).

3.2. The compliance of the study population after the retrospective cohort study of 2 years' follow-up

After the a retrospective cohort study of two years follow-up, there were 393 patients with good compliance, accounting for 98.99%, and 4 patients with poor compliance, accounting for 1.01%.

3.3. Comparison of compliance between different characteristic population

According Table 4, the analysis found that the difference in compliance between patients was not due to the demographic

Table 3
Disease treatment of epilepsy patients.

| Variate | No. of cases (n) | Percentage (%) |
|--|------------------|----------------|
| Phenobarbital dose, mg/day | | |
| <50 | 113 | 28.5 |
| 50–100 | 246 | 62.0 |
| 101–150 | 36 | 9.1 |
| >150 | 2 | 0.5 |
| Have you been taking other antiepileptic drugs in the last 2 wk | | |
| Yes | 88 | 22.2 |
| No | 309 | 76.8 |
| The attack is more than before | | |
| It's just a temporary loss of consciousness, no convulsions | 143 | 36.0 |
| Loss of consciousness and convulsions are less persistent than before | 31 | 7.8 |
| There was no loss of consciousness, only limb twitching | 5 | 1.3 |
| The loss of consciousness and convulsions are as usual | 1 | 0.3 |
| Missing | 217 | 54.7 |
| A doctor's comprehensive judgment of adverse reactions | | |
| Nothing | 327 | 82.4 |
| Mild | 70 | 17.6 |
| How does the patient feel physically, mentally, or physically during this period of time | | |
| Better | 329 | 82.9 |
| No change | 68 | 17.1 |
| Treatment in the municipal hospital | | |
| Yes | 160 | 40.3 |
| No | 160 | 40.3 |
| Treatment in the county-level hospitals | | |
| Yes | 151 | 38.0 |
| No | 179 | 45.1 |
| Treatment in the township hospitals | | |
| Yes | 32 | 8.1 |
| No | 226 | 56.9 |
| Individual doctors | | |
| Yes | 37 | 9.3 |
| No | 223 | 56.2 |
| Has he ever been diagnosed with epilepsy | | |
| Confirmed | 294 | 74.1 |
| Not confirmed | 96 | 24.2 |
| Don't know | 7 | 1.8 |
| A treatment used in the past | | |
| Not treated | 111 | 28.0 |
| Treated | 285 | 71.8 |
| Have you taken any western medicine | | |
| Yes | 240 | 60.5 |
| No | 71 | 17.9 |
| Irregular medication or no treatment | | |
| Irregular medication | 127 | 32.0 |
| No treatment | 85 | 21.4 |
| What kind of instrument have you checked | | |
| Electroencephalogram | 159 | 40.1 |
| CT | 20 | 5.0 |
| Nuclear magnetic resonance | 2 | 0.5 |
| No tests were made | 169 | 42.6 |
| Treatment: never treated | | |
| Yes | 110 | 27.7 |
| No | 287 | 72.3 |
| Reexamination of doctor's conclusions | | |
| Formal treatment | 143 | 36.0 |
| Irregular treatment | 144 | 36.3 |
| Never treat | 26 | 6.5 |

The disease treatment of 397 patients with epilepsy, such as the dosage of drugs taken, whether the performance of improvement after taking the drugs, and so on.

information and disease status of the patients, but the situation of the patients after treatment had an impact on the compliance. However, there was a statistically significant difference in compliance between attack and previous comparison ($P < .05$). The loss of consciousness at the time of attack was statistically significant for compliance differences ($P < .05$). The occurrence of ataxia was statistically significant for the compliance difference ($P < .05$). The adverse reaction of headache was statistically significant for the compliance difference ($P < .05$). The occurrence of hyperactive adverse reactions had a statistically significant difference in compliance ($P < .05$). The adverse reactions with rash were statistically significant for compliance ($P < .05$). The occurrence of adverse reactions with gastrointestinal symptoms was statistically significant for compliance difference ($P < .05$). During this period, the patient's perceived physical condition, mental state, or ability to work and learn had statistically significant differences in compliance compared with the previous period ($P < .05$).

3.4. Risk factors for poor compliance

The results of the binary logistic regression analysis of risk factors for bad compliance are shown in Table 5.

The ratio of the attack to the previous one (OR=9.729, 95% CI:2.240,42.267), adverse reactions of digestive tract symptoms (OR=9.375, 95% CI: 1.460,60.203) and how the patient felt physically, mentally, or working and learning ability during this period(odds ratio=17.053, 95%confidence interval: 2.020–43.938) were more likely to have poor compliance of the

epilepsy patients of the Phenobarbital Epilepsy Management Project.

4. Discussion

4.1. The compliance of the rural China epilepsy patients of the Phenobarbital Epilepsy Management Project was at a high level

Epilepsy is a common chronic disease in neurology department, if adhere to the regular, long-term, timing, quantitative use of antiepileptic drugs, maintain effective blood drug concentration, 80% of the patients can completely control the onset, and irregular medication can reduce the efficacy or aggravate the onset, so good compliance is to ensure the efficacy of antiepileptic drugs basic conditions.^[28] Good compliance includes long-term medication without interruption and regular review as required by the doctor; poor compliance means withdrawal, reduction, refill, or refusal of medication.^[28] In this study, 98.99% of patients with epilepsy consciously took long-term medication as prescribed by the doctor and kept reexamination, indicating that good compliance in this study was at a high level. According to a previous report, the noncompliance of epilepsy patients was as high as 30% to 50%, and higher in China.^[29] However, the noncompliance of epilepsy patients was only 1.01% in this study, which was enough to indicate that the compliance of the rural China epilepsy patients of the Phenobarbital Epilepsy Management Project was very good.

Some reasons for good compliance in the rural China epilepsy patients of the Phenobarbital Epilepsy Management Project may

Table 4
Comparison of compliance among different characteristics of the population.

| Group | Compliance | | χ^2 | P |
|--|------------|-----|----------|------|
| | Good | Bad | | |
| The symptoms that occur during an attack | | | | |
| every time | 214 | 2 | 29.823 | .000 |
| not | 22 | 4 | | |
| not every time | 92 | 0 | | |
| The attack is more than before | | | | |
| It's just a temporary loss of consciousness, no convulsions | 243 | 1 | 212.765 | .000 |
| Loss of consciousness and convulsions are less persistent than before | 66 | 0 | | |
| There was no loss of consciousness, only limb twitching | 8 | 0 | | |
| The loss of consciousness and convulsions are as usual | 2 | 0 | | |
| Ataxia | | | | |
| Not | 391 | 3 | 48.249 | .020 |
| Mild | 1 | 1 | | |
| Have a headache | | | | |
| Not | 391 | 3 | 48.249 | .020 |
| Mild | 1 | 1 | | |
| Hyperactivity | | | | |
| Not | 391 | 3 | 48.249 | .020 |
| Mild | 1 | 1 | | |
| The rash | | | | |
| Not | 392 | 3 | 98.248 | .010 |
| Mild | 0 | 1 | | |
| Gastrointestinal symptoms | | | | |
| Not | 379 | 3 | 14.848 | .018 |
| Mild | 16 | 2 | | |
| How does the patient feel physically, mentally, or physically during this period of time | | | | |
| Better | 252 | 1 | 7.934 | .009 |
| No change | 132 | 6 | | |

The χ^2 test was used to analyze the influencing factors of compliance of patients with epilepsy. The factors with $P < .05$ were the influencing factors.

Table 5
Results of binary logistic regression analysis of risk factors for poor compliance of the epilepsy patients.

| | B coefficient | Wald test | P | OR | 95% CI |
|---|---------------|-----------|------|--------|--------------|
| The ratio of the attack to the previous one | 2.275 | 9.216 | .002 | 9.729 | 2.24–42.267 |
| Adverse reactions of digestive tract symptoms | 2.238 | 5.564 | .018 | 9.375 | 1.46–60.203 |
| Whether the patient lost consciousness during the attack | 2.836 | 6.792 | .009 | 17.053 | 2.02–143.938 |
| How the patient felt physically, mentally, or working and learning ability during this period | −16.885 | 0 | .996 | 0 | 0 |

The influence factors obtained from the χ^2 test analysis were put into the binary logistic regression analysis to further analyze the significance of the influence factors on compliance.

be illustrated. First, the project pays much attention to the training of technical personnel. For example, technical training should be conducted once a year for personnel participating in the project in county and township hospitals according to the requirements of the project. The project gradually improve the professional level of neurologists in charge of the project in county hospitals, expand the professional knowledge of physicians and health care doctors in township hospitals, and further deepen the understanding of the project requirements.^[30] Secondly, the project supports free treatment for epilepsy patients. At the request of the national health department, the Nan County set up an epilepsy outpatient department. The neurologists in charge of the project made home visits and gave epilepsy patients free drug treatment, so as to further improve the curative effect and patients' enthusiasm to adhere to treatment management.^[31] Thirdly, continuous mass publicity and education are through the whole management process. Most of the patients in this project are from rural areas with low education level, poor reception ability and limited access to knowledge. Therefore, publicity and education is particularly important. The Nan County always adhere to carry out epilepsy knowledge education and free consultation activities vigorously, in order to improve the public and patients' families to understand and correct understanding of epilepsy. Various forms of publicity and education should be carried out to make the general public fully understand the importance of the epilepsy prevention and treatment management project, so that more epilepsy patients and their families can actively participate in the project.^[32] Fourthly, the good therapeutic effect comes from phenobarbital. Practice shows that phenobarbital has a significant effect on epilepsy with few side effects and is easy to use. Because patients have fewer side effects and are in much better shape than before, they stick to prescribed medications.^[33] Finally, psychological factors from the project are also effectively. Seeing that the physical condition is getting better day by day, patients can live and work normally, and their confidence in treatment will be continuously enhanced, which is also conducive to the active treatment of patients.^[34]

4.2. Risk factors for bad compliance among rural epilepsy patients of the Phenobarbital Epilepsy Management Project in China

Skacett et al defined compliance as “a procedure whereby a patient's behavior is consistent with the medical guidelines regarding medication, diet, or lifestyle changes.”^[35] The term “compliance behavior” was first translated and used by Professor Ruan Fangfu in China.^[36] He considers compliance to be the extent to which a patient's behavior is consistent with a doctor's prescription for treating and preventing disease. Medication compliance refers to the consistency between the patient's

medication behavior and the doctor's advice. It is an important indicator to evaluate whether the patient is treated according to the doctor's advice, and its level will have a direct impact on the patient's cure rate and control rate.^[37] Logistic regression analysis showed that the factors affecting the compliance of epilepsy patients included: “adverse reactions of digestive tract symptoms,” “whether the patient lost consciousness during the attack,” and “the ratio of the attack to the previous one.”

4.2.1. Adverse reactions of drugs. The mechanism of adverse reactions of antiepileptic drugs is complex, involving multiple systems, including the central nervous system, endocrine system, blood system, cardiovascular system, skin system, among others, which brings great pain to patients, causing some patients to fail to cooperate well in treatment.^[38] Patients receiving long-term or high-dose antiepileptic drug therapy often have different adverse reactions, such as nausea, drowsiness, peripheral neuritis, cerebellar ataxia, anorexia and involuntary movement. Some patients have adverse reactions, and stop the drug without timely medical treatment or drug concentration monitoring.^[39] When patients have some adverse reactions after taking medicine, such as gastrointestinal symptoms, or even worse health than before taking medicine, they may reduce or even stop the medicine because they feel uncomfortable because of taking the medicine, which will lead to poor patient compliance.

4.2.2. Status after taking the drug for a period of time. When the patient compares the symptoms and status during each attack with the previous attack, and finds that the number of attacks is less and less intense, the patient may reduce or stop the drug, leading to poor compliance. If there is no loss of consciousness, the patient may decide that the seizure is not as severe as expected and choose not to take medication for the seizure, which may also affect medication compliance.^[40] After taking medicine as prescribed by the doctor for a period of time, the patient finds that his/her physical condition, mental condition, or ability to work and learn is much better than before, and thinks that his/her condition has improved so much that he/she does not need to continue taking the medicine, which will result in poor medication compliance.

4.2.3. Lack of epilepsy knowledge. Patients with different sex, age, and occupation have different knowledge of the disease. For medical staff with a higher degree of treatment education, they will take the initiative to look up relevant knowledge, and actively cooperate, and have a higher degree of grasp of the disease than those with a lower degree of education.^[41] Patients' lack of understanding of disease knowledge or doctors' orders will affect their compliance. Patients in this study came from rural areas with low education level, poor reception ability, and limited access to knowledge, and the low prevalence of epilepsy knowledge is one of the reasons for poor medication compliance.

4.2.4. Psychological factors and family factors. Due to long-term frequent epileptic seizures, patients cannot live a normal life, work, fear, anxiety and loneliness, and refuse to participate in social activities, employment difficulties and other factors make patients lose confidence in treatment. Epilepsy patients need more support and encouragement from family, relatives and friends for their work, study and quality of life affected due to the frequent seizures.^[42]

4.3. Suggestions on the Phenobarbital Epilepsy Management Project in rural China

Epilepsy as a long-term drug control of chronic diseases, in the treatment process should not only pay attention to the control of the disease attack, more attention should be paid to the improvement of patients' mental health and quality of life. Doctors should communicate with patients patiently, so that patients have the opportunity to vent their feelings of repression; At the same time, patients should be aware of the adverse effects of anxiety and depression, and guide them to face the disease bravely and establish confidence in conquering the disease.^[43] According to the different educational backgrounds of patients, the patients were targeted for publicity and education, explaining the knowledge of epilepsy itself and drugs^[44]; to make patients understand the importance of long-term medication of antiepileptic drugs as prescribed by the doctor, and inform them of the harm of sudden withdrawal of drugs, change of drugs, self-reduction, such as epileptic seizure, epileptic status; explain the drug-related side effects and countermeasures, and change the wrong understanding of drugs by patients and their families.^[45] After the patient is discharged from the hospital, the doctor should follow-up the patient to understand the disease control, medication, and adverse reactions of the patient. Health lectures are held regularly to strengthen patients' understanding of diseases, medicines, and other aspects.^[46]

4.4. Limitations

A limitation of this study is its small sample size, and some self-reported information may introduce bias, so further studies are needed to confirm these findings.

5. Conclusion

The good compliance of epilepsy patients in the Phenobarbital Epilepsy Management Project of rural China was high (98.99%), which was related to China's long-term adherence to publicity and education activities for epilepsy patients. Besides, there were still some factors that affected the compliance level of patients, and we should continue to maintain and increase efforts to promote the prevention and treatment of epilepsy.

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Author contributions

LQ, XF and BL wrote, checked, and revised the manuscript.

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