Seizure 23 (2014) 333–337

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Prevalence and treatment gap of active convulsive epilepsy: A large community-based survey in rural West China

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ARTICLE INFO

Article history:
Received 31 July 2013
Received in revised form 30 November 2013
Accepted 8 January 2014

Keywords:
Prevalence
Treatment gap
Convulsive epilepsy
Rural community

ABSTRACT

Purpose: Active convulsive epilepsy (ACE) impacts patients greatly, especially in low-income countries where patients do not receive appropriate treatment. In the present study, we measured the prevalence and treatment gap (TG) of ACE in rural West China.

Methods: Six rural areas in West China that have a total population of 3,541,319 were selected to conduct prevalence and TG estimates of ACE via a clue survey from 2007 to 2009. Clue survey here is a community-based screening strategy among defined population which requires employed well-trained local physicians//health workers to collect all clues available to discover/identify/recruit patients within a study period. Questionnaire-based interviews were used for the identification of ACE patients, and information was obtained during the survey. Prevalence and TG of ACE were calculated.

Results: A total of 6547 patients with ACE were identified. The estimated prevalence of ACE was 1.8 per 1000 in the general population, with the prevalences in males and females determined to be 2.0 and 1.7, respectively ($p < 0.001$). The TG in the general population was 66.3%, and it was 66.6% and 66.0% in males and females, respectively ($p > 0.05$). The TG figures dropped with advancing age and increased above 30 years of age. Patients aged 60 years or older had the largest TG (77.8%); those with disease course less than 10 years showed a larger TG and those who experienced two to five seizures annually had a significantly larger TG (70.6%). Additionally, only 63.9% of the ACE patients included in the study were aware of the disease and had consulted a doctor.

Conclusions: There exists a large TG of ACE in West China rural areas. Majority of those ever consulted a doctor but failed to receive or adhere to an appropriate treatment program. Management including public education as well as training of local physicians were necessary to fill that gap.

1. Introduction

Epilepsy is one of the most common chronic neurological disorders, affecting nearly 50 million people around the world, 80% of whom live in low-income countries.[1] More than 75% of epilepsy patients in low-income countries do not receive appropriate treatment. The inability of such patients to receive treatment for epilepsy is known as treatment gap (TG).[2] In China, approximately 9 million people are estimated to have epilepsy, with a lifetime prevalence of 7.0 cases per 1000 people. For active epilepsy, the lifetime prevalence is 4.6 cases per 1000 people (with a TG of 63%).[3]

In 1997, as part of the Global Campaign Against Epilepsy launched by the World Health Organization (WHO) in cooperation with the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy, a project that included an epidemic survey, an intervention trial, and an educational program was initiated to study epilepsy in China.[4] In 2000, another large-scale project supported by the government was launched in the northern and eastern rural areas of China to identify and manage active convulsive epilepsy (ACE) in these communities. During that period, two major studies that focused on an efficacy assessment of phenobarbital and on premature mortality due to epilepsy were published.[5,6] In 2005, a project with the same protocol and design was extended to the rural areas of West China. Our previous report on the causes of death from ACE was based on that project.[7] As of this writing, the epidemiologic data on epilepsy have been

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1059-1311/$ – see front matter.
http://dx.doi.org/10.1016/j.seizure.2014.01.007

primarily obtained from that study. The present study discusses the prevalence and TG of ACE based on the previous extended project. Although some epidemiological data on this topic has been reported in northern and eastern areas of China in the past ten years.[3] However in western rural areas of China, no special report referring to prevalence and TG has been issued. This study provides a detailed discussion of the epidemiological features of the prevalence and TG of ACE based on a large rural community-based survey in West China.

2. Methods

The Institutional Ethics Committee of West China Hospital provided ethical approval of the project. All participants provided written consent to participate in the project, and consent was given by guardians for children (age < 18 years).

Six rural areas in West China with a total population of 3,541,319 were selected to estimate the prevalence and TG of ACE via a clue survey (Fig. 1). Clue survey here is a community-based screening strategy among defined population which requires employed well-trained local physicians//health workers to collect all clues available to discover/identify/recruit patients within a study period. A total of 211 local communities (towns/villages) and 541 local primary care physicians were involved in this project. From 2007 to 2009, all six areas completed the screening process successively. The screening procedure was limited to one year for each area, and the study targeted members of the population who were older than two years of age.

Prior to screening, an operational model of a network for managing patients with ACE was established to guarantee the successful completion of the survey.[8] Such a network depends on all existing primary health organizations in which the local, well-trained primary care physicians were involved. First, free epilepsy clinics were established in each local community. To ensure that ACE patients in the overall population were aware of the disease, a training program for primary care physicians and public information dissemination, which included distribution of informational materials, telecasts, and free community medical consultations, was implemented. By clue survey, possible patients with ACE were exposed from main four sources: (1) possible ACE cases visiting the free epilepsy clinics; (2) cases reported by the visitor with epilepsy or other diseases in clinic, and further interviewed by the local primary care physicians; (3) suspected cases provided by local mayor of the village, anti-epidemic stations, health centers, mental hospital etc., (4) cases collected by local primary care physicians when they went down to the villages. After recording the a possible ACE patient based on clinic visits and witnesses' clues, a face-to-face interview using a standard diagnostic panel with proven reliability and validity[5] was conducted by local primary care physicians to formulate an initial diagnosis of ACE. Each local primary health organization was responsible for screening the hidden patient from the local community via the clues. An door-to-door survey, although ideal, was impractical in such vast rural areas. The clue-trace method was regarded as the optimal manner in which to find these patients because rural patients with similar diseases were likely to share their treatment experience with each other. Even if patients did not know each other personally, they were likely to know about people with similar diseases in the neighboring areas. The witnesses could tell the local primary care physicians about the seizures. Additionally, relatives of the patients could visit clinics for consultation. After the initial diagnosis of ACE made by the primary care physicians, supervising neurologists were assigned to each community to identify and screen those suspected positive cases. Patients with diseases mimicking epilepsy or patients with partial seizures were excluded from the study. Finally, information was collected and delivered to the provincial Centers for Disease Control (CDC), where the data were checked and stored. In addition, a questionnaire for primary care physicians was formulated to assess their ability to identify patients who may potentially suffer from ACE (Additional Table 1). Five hundred and twelve (94.6% of total) primary care physicians participated in this investigation, and their average score was 8.6 ± 2.8, which represents competent diagnoses.

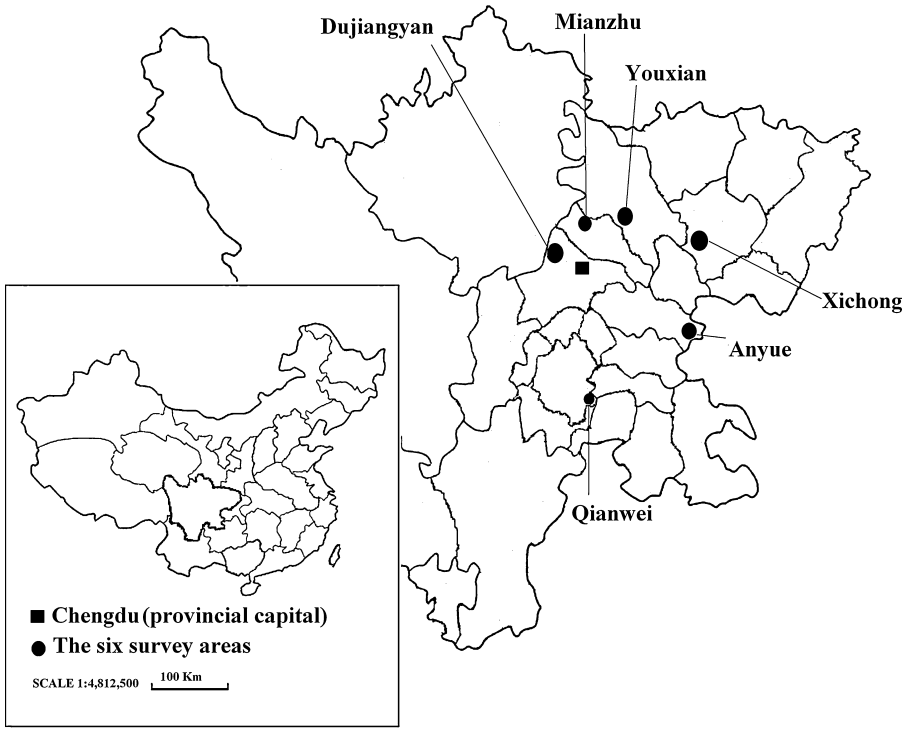

Fig. 1. Administrative map of the Sichuan province of China highlighting the six survey areas.

Table 1
Demographics of ACE patients ($n = 6547$).

	Mean (SD) or n (%)
Study population	
Male	3606 (55.1)
Female	2941 (44.9)
Age (years)	34.8 (16.1)
Age group (years)	
2–14	719 (11.0%)
15–44	4176 (63.8%)
45–59	1170 (17.9%)
≥60	482 (7.3%)
ACE traits	
Age of onset (years)	18.3 (14.6)
Disease course (years)	16.5 (12.2)
Seizure frequency (per year)	23.4 (38.6)

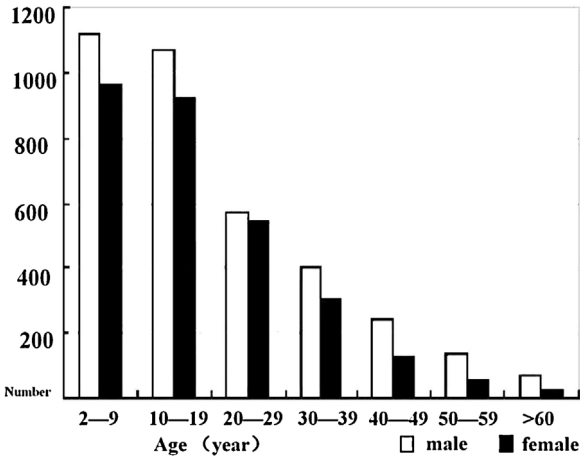

Fig. 2. Distribution of ACE in different onset age.

A person with ACE was defined as someone who had experienced more than one identified, unprovoked convulsion within the 12 months immediately prior to screening. A person was considered "untreated" if he had not received antiepileptic drug (AED) treatment or Chinese traditional treatment (such as acupuncture and herbal medicines) in the month prior to identification of ACE. Appropriate treatment is the regular treatment of ACE according to national standards, which primarily involves prescribing AEDs and rarely includes surgery, when feasible. TG refers to the ratio of the number of patients with ACE who are not receiving appropriate treatment to the number of all patients with ACE screened in a given period of time, expressed as a percentage. The given time was defined as the month prior to the identification of ACE, within which the receipt of appropriate treatment by a patient is determined.

The data were analyzed using SPSS 17.0 software for Windows. Chi square tests were used to explore the different frequencies and rates of gender, age, prevalence and TG in different groups. Statistical significance was set at $p < 0.05$.

3. Results

Six areas in West China were involved in the survey, and 6547 patients with ACE were identified (Table 1). Among the ACE patients, the ratio of males to females was 1.23, compared to a ratio of 1.08 in the overall population ($p < 0.001$). The number of ACE patients was found to decrease as the age of onset increased. At the age of 20, the number of ACE patients suddenly decreased (Fig. 2). The majority of ACE patients (4075, 62.6%) had an onset age of less than 20 years old.

The prevalences and TGs of ACE in the six study areas are provided in Additional Tables 2 and 3. The prevalence of ACE was 1.8 per 1000 in the general population, and the prevalences in males and females were 2.0 and 1.7, respectively ($p < 0.001$). The TG in the general population was 66.3%, and the TG were 66.6 and 66.0 in males and females, respectively ($p > 0.05$).

Tables 2 and 3 show the prevalence and TG of ACE at different ages. Prevalence increased as age increased, peaking (2.7 per 1000) from ages 30 to 39 and declining gradually to 0.4 in the oldest age group (>80 years old). The prevalence varied between genders ($p < 0.05$) in the 10–19 age group and in those older than 59 years of age. In the population with ACE, TG figures dropped with advancing years and increased after 30 years of age. Differences in TG between genders were found in the following age groups: 10–29 years old and 70 to 79 years old ($p < 0.05$).

Table 4 shows the TG information grouped according to age, disease course, and seizure frequency. The table also provides a comparison between subgroups within each group. In terms of age group, patients aged 60 years or older had a larger TG (77.8%) with a significant difference compared with other age groups. Patients under the age of 15 had the second largest TG (71.2%) with a statistically significant difference. In the disease course group, the TG in the subgroup of 2–9 years was greater than that in the subgroup of over 9 years; however, no significant difference was found for the TG between the latter group (≤1 year) and the others. In the seizure frequency group, those who experienced two to five seizures annually had a significantly larger TG (70.6%) than those who experienced more than five seizures. Additionally, almost no difference in TG was observed between genders in each group.

This survey found that 63.9% of the ACE patients included in the study were aware of the disease to some extent and consulted a doctor, whereas 36.1% of the ACE patients were not aware of the disease and did not see a doctor.

Table 2
Prevalence (‰) of ACE in different age brackets.

Age group (years)	Screening population Total (Male/Female)	Total	Male	Female	p-Value
2–9	512677 (273514/239163)	349 (0.7)	197 (0.7)	152 (0.6)	0.246
10–19	545753 (287535/258218)	976 (1.8)	576 (2.0)	400 (1.5)	<0.001
20–29	581910 (296086/285824)	1030 (1.8)	502 (1.7)	528 (1.8)	0.168
30–39	647672 (332382/315290)	1750 (2.7)	931 (2.8)	819 (2.6)	0.115
40–49	458424 (238852/219572)	1156 (2.5)	625 (2.6)	531 (2.4)	0.181
50–59	378851 (200609/178242)	805 (2.1)	454 (2.3)	351 (2.0)	0.050
60–69	243818 (127973/115845)	349 (1.4)	234 (1.8)	115 (1.0)	<0.001
70–79	133685 (6436169324)	118 (0.9)	78 (1.2)	40 (0.6)	<0.001
≥80	38529 (14356/24173)	14 (0.4)	9 (0.6)	5 (0.2)	0.036
Total	3541319 (1835668/1705651)	6547 (1.8)	3606 (2.0)	2941 (1.7)	<0.001

Table 3
TG (%) of ACE in different age brackets.

Age group (years)	Total	Male	Female	*p*-Value
2–9	73.9	76.0	71.1	0.296
10–19	66.9	70.5	61.8	0.004
20–29	61.5	64.5	58.5	0.047
30–39	65.3	63.5	67.3	0.096
40–49	65.4	63.5	67.6	0.145
50–59	65.4	64.5	66.7	0.514
60–69	78.8	77.8	80.9	0.507
70–79	79.0	73.4	90.0	0.036
≥80	42.9	33.3	60.0	0.334
Total	66.3	66.6	66.0	0.565

Table 5 shows that 33.7% of ACE patients received appropriate treatment, but few used new AEDs. In all of the patients, 27.7% did not receive any treatment.

Table 5
Treatment of ACE.

Treatment	*N* (%)
Regular AEDs	2204 (33.7)
Old AEDs	2089 (31.9)
Phenytoin	984 (15.0)
Phenobarbital	560 (8.6)
Carbamazepine	677 (10.3)
Valproate	360 (5.5)
New AEDs	175 (2.7)
Inappropriate treatment	2531 (38.7)
Irregular AEDs	1002 (15.3)
Chinese herb	1507 (23.0)
Acupuncture	227 (3.5)
Folk empirical prescription	810 (12.4)
Untreated	1812 (27.7)

New AEDs include Oxcarbazepine, Lamotrigine, Topiramate, etc. Note that one patient could use more than one therapy, which could include both appropriate and inappropriate treatments. We categorized those who received regular AEDs and another inappropriate treatment (irregular AEDs was not included) in the regular AEDs group.

4. Discussion

The present study estimates the prevalence of ACE and the TG using a clue survey method based on large communities because of the limited manpower and financial resources of the study. However, a door-to-door survey would have been an ideal method for this study. The prevalence of ACE (rather than partial seizures) was selected for the study not only because ACE has severe physical effects that deserve attention but also because establishing a clinical diagnosis for ACE is easier than establishing one for partial seizures. When diagnosing partial seizures, other disease entities mimicking epilepsy, such as psychogenic non-epileptic seizures, would be difficult to exclude.

A slight increase in the prevalence of epilepsy among males is commonly reported. However, the prevalence of convulsive epilepsy has rarely been studied. From the few published reports on the subject, the male-to-female ratio varies from 0.71 to 1.29.[6,9] Our findings confirmed an increased male-to-female ratio among ACE patients (1.23). Global disparities are present in the prevalence of epilepsy. At the beginning of this century, one epidemiological survey on China showed that the lifetime prevalence of epilepsy was 7 cases per 1000 people.[3] Prior to that study, the lifetime prevalence of epilepsy was found to be between 3 and 5 cases per 1000, and 4.4 cases per 1000 is often cited.[10] Wang's study on the prevalence of active epilepsy suggested a prevalence of 4.6 cases per 1000 people.[3] To date, epidemic data on the prevalence of ACE in China have yet to be reported. Considering that partial epilepsy contributes to more than half of epilepsy cases in the general population, the data 1.8 for the prevalence of ACE is to some extent consistent with Wang's estimate for active epilepsy, although the value might be underestimated. Methodological differences could directly lead to underestimation and it is also possible that patients with active partial and secondary generalized seizures were excluded from this estimation. Of course whether the prevalence is low in the area studied need further investigations. The literature suggests that the incidence and prevalence of epilepsy is highest in the elderly.[11] Among seizure types, partial epilepsy is known to occur most frequently in the elderly, and the incidence of general epilepsy remains low. In the present study, the prevalence of ACE was found to peak during the ages of 30–39 years and declined until reaching the lowest value of 0.4 cases per 1000 in the elderly. Based on those figures, we can deduce that a number of ACE patients may experience remission or die before reaching old age, which can partially explain the low prevalence of ACE in the elderly. Another important factor that may contribute to the poor physical status of the elderly is that they may have been unable to provide accurate information for diagnosis. Additionally, living alone or in a remote location decreases the likelihood of neighbors having witnessed an episode and makes it more difficult for patients to travel to receive treatment. Thus, further studies are necessary to examine this phenomenon.

Table 4
TG (%) comparison in different groups.

Group	Total TG	Male TG	Female TG	*p*-Value
Age group (years)				
2–14[a]	71.2	73.9	67.2	0.051
15–44[b]	64.1	64.2	64.0	0.887
45–59[c]	66.5	65.7	67.5	0.515
≥60[d]	77.8	75.4	84.5	0.080
Disease course group (years)				
≤1[a]	69.3	66.8	74.5	0.175
2–4[b]	72.4	73.9	70.1	0.230
5–9[c]	68.3	71.7	63.8	0.006
10–19[d]	64.6	63.5	65.9	0.254
≥20[e]	64.4	64.0	64.9	0.627
Seizure frequency group (n/year)				
2–5	70.6	70.1	71.4	0.569
6–11	65.7	66.9	64.2	0.324
12–23	65.8	65.6	66.0	0.851
≥24	63.1	63.7	62.4	0.538

Comparison between subgroups of age: $p^{ab} < 0.001$, $p^{ac} = 0.033$, $p^{ad} = 0.011$, $p^{bd} < 0.001$, $p^{cd} < 0.001$.
Comparison between subgroups of disease course: $p^{bd} < 0.001$, $p^{be} < 0.001$, $p^{cd} = 0.041$, $p^{ce} = 0.029$.
Comparison between subgroups of seizure frequency: $p^{ab} = 0.004$, $p^{ac} = 0.002$, $p^{ad} < 0.001$.
Only those with $p < 0.05$ were listed.

According to one systematic review, the worldwide TG for epilepsy is estimated to be approximately 56%, and more than 90% of these cases occur in developing countries.[12] In China, a door-to-door epidemic survey found a TG of 63% for active epilepsy.[3] Our survey indicated a TG of 66.3% for ACE, which is consistent with the previous study conducted in other areas of China. To our knowledge, there are few detailed studies on the TG for epilepsy. The present study addresses the research gap and provides an overview of the subject.

In general, differences in TG between genders were not found. However, for patients aged 10–19 years, more females received appropriate treatment, whereas for patients aged 70–79 years, more males received appropriate treatment. In addition, the lowest TG was observed in females in the 20–29 age group. This may be because females of childbearing age receive more medical attention, but gradually lose this attention as they age. By contrast, adult males received slightly more appropriate treatment.

However, no significant difference was found between the sexes. In the past, the main labor force in rural China was composed of adult males who played a central role in the family. Compared with women, adult males received greater medical attention. However, the recent situation reflected in this study implies that both genders in the family enjoy almost equal status.

The ILAE concluded that the determinants of TG are diagnostic and therapeutic deficits, economic conditions, cultural beliefs, and distance from health facilities.[13] These factors were not included in our research due to the original design of the project. Nevertheless, the present study describes other factors such as age, disease course, and seizure frequency. The elderly population with ACE had the largest TG in the present study, followed by children. This result suggests that these underserved populations may not be receiving enough care due to their physical and psychological vulnerability. We observed that patients who have had epilepsy for less than one year showed no difference in TG compared to others. Ten years appeared to be a watershed period that was lower than the period where TG remained high and vice versa. Inadequate understanding of the disease and the absence of timely medical treatment may explain why a substantial number of patients fail to receive the early treatment that is essential to ensure maximum remission of seizures. Seizure frequency appeared to influence the TG. After experiencing five seizures per year, patients generally opted to seek treatment, although appropriate treatment is not always guaranteed in rural areas. Epilepsy in numerous patients who experience a lower frequency of seizures may progress into chronic epilepsy without timely treatment. New AEDs are rarely used because a majority of patients cannot afford the medication. In addition, Chinese herbal medicine, which has not proven effective, comprises the majority of ''inappropriate treatment''. In this study, numerous patients who participated in the investigation did not receive or adhere to an appropriate treatment program, which reflects the need for public education as well as the training of local physicians.

Limitations

Reporting on the prevalence using a subset of patients from a much wider pool of people with all forms of epilepsy without a meticulous etiological diagnostic work up affected the scientific cache.[14] The clue survey used for the estimation of prevalence had its weakness and limitations. On one hand, it might fail to screen out all patients with ACE and underestimate the prevalence in those areas. On the other hand, such method was focused on the ACE and unable to detect all forms of epilepsy. According to the rules of epilepsy project, our cohort lose the information of those with age less than two years. Also in the present study, diagnosis was mainly based on the clinical situation. Laboratory tests, electroencephalogram, and imaging examinations were rarely applied which might affect a definite diagnosis. As regard to TG, considering the purpose of the project is to identify and manage those patients with ACE, complete information were not required to obtain, thus factors associated with TG were unable to recognize. In the future, a door-to-door survey is needed for the accurate estimation of the prevalence. Also exploring potential factors related to TG are benefit for the better management of epilepsy.

Acknowledgements

We sincerely thank all of the participants in this project and all of our colleagues in the local primary heath care centers for their cooperation. We also thank the experts at the CDC of Sichuan province for their assistance.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.seizure.2014.01.007.

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