Epilepsy & Behavior 78 (2018) 20–24

Contents lists available at ScienceDirect

Epilepsy & Behavior

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

Active epilepsy prevalence, the treatment gap, and treatment gap risk profile in eastern China: A population-based study

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ARTICLE INFO

Article history:
Received 29 August 2017
Revised 14 October 2017
Accepted 15 October 2017
Available online 21 November 2017

Keywords:
Eastern China
Active epilepsy
Prevalence rate
Treatment
Risk factors

ABSTRACT

We measured the prevalence of active epilepsy and investigated the treatment gap and treatment gap risk profile in eastern China.

This was a cross-sectional population-based survey conducted in Zhejiang, China, from October 2013 to March 2014. A total 54,976 people were selected using multi-stage cluster sampling. A two-stage questionnaire-based process was used to identify patients with active epilepsy and to record their demographic, socioeconomic, and epilepsy-related features. Logistic regression analysis was used to analyze risk factors of the treatment gap in eastern China, as adjusted for age and sex.

We interviewed 50,035 people; 118 had active epilepsy (2.4‰), among which the treatment gap was 58.5%. In multivariate analysis, failure to receive appropriate antiepileptic treatment was associated with higher seizure frequency of 12–23 times per year (adjusted odds ratio = 6.874; 95% confidence interval [CI] = 2.372–19.918), >24 times per year (adjusted odds ratio = 19.623; 95% CI = 4.999–77.024), and a lack of health insurance (adjusted odds ratio = 7.284; 95% CI = 1.321–40.154).

Eastern China has relatively lower prevalence of active epilepsy and smaller treatment gap. Interventions aimed at reducing seizure frequency, improving the health insurance system should be investigated as potential targets to further bridge the treatment gap.

1. Introduction

Epilepsy is a chronic neurological disease characterized by recurrent, unprovoked seizures. Approximately 50 million people worldwide are diagnosed with epilepsy, with nearly 80% being in the low- and middle-income countries [1]. In China alone, more than 6.5 million people have active epilepsy [2], constituting nearly 5‰ of the total Chinese population.

Despite the high prevalence, patients with epilepsy receive insufficient attention. A systematic review found that 40–50% of people with active epilepsy in China did not receive adequate treatment [2], an issue known as treatment gap. Untreated or irregularly treated epilepsy poses a significant threat to the individual, their family, and even society, whether economically, physically, or psychologically. Consequently, the Commission on Asian and Oceanian Affairs research task force has listed the study of treatment gap as high priority in epilepsy research, including more complete documentation of treatment gap and the identification of the underlying determinants and characteristics of areas with large treatment gap [3]. While some studies have investigated the prevalence of local treatment gap [4], little is known about its risk profile. The risk factors of treatment gap, however, are of utmost significance due to its value in policymaking and intervention designs.

Characterized by a wide geographic span and high economic heterogeneity, China is also varied in terms of the prevalence and characteristics of epilepsy. To date, studies on the prevalence and treatment gap of epilepsy in China have mainly focused on inland rural areas and western areas [2,5–7]. Consequently, data on the prevalence and treatment gap of active epilepsy in eastern China and urban and coastal areas are lacking. Accordingly, we investigated the prevalence and treatment gap of active epilepsy in Zhejiang, an eastern coastal province in China, and analyzed the treatment gap risk profile.

2. Methods

2.1. Study area and study population

Zhejiang is marked by a relatively high level of economic status and urbanization. The total population includes 54,980,000 people: 35,190,000 people (64%) in the urban areas and 19,790,000 people

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https://doi.org/10.1016/j.yebeh.2017.10.020
1525-5050/

(35.99%) in the rural districts. Economically, the gross domestic product per capita of Zhejiang is 68,331 yuan per person (US$11,033). The average per-head disposable income is about 29,774.99 yuan per year (US$4432.65), ranking third among China's 33 first-level administrative divisions. Zhejiang is also the third largest exporter in China [8].

The participants enrolled in this study were registered residents of Zhejiang who either lived there or had temporarily left for <1 year. The Human Research Ethics Committee of the Second Affiliated Hospital of Zhejiang University reviewed and approved this study (Registration No: 2013–032). All participants provided written informed consent to participate in the study.

2.2. Study design

This was a population-based cross-sectional study conducted from October 2013 to March 2014. In this study, multi-stage cluster sampling was used. Five of 11 cities in Zhejiang were selected as study sites, as they represented different geographic and economic scenarios within the province. One village or community was considered a cluster, and one cluster was selected from each city through random cluster sampling, with the probability proportional to size. Within each cluster, participants were selected via simple random sampling. The sample size for the study was estimated using Epi Info version 3.1.1 using the formula for the population survey; the 95% confidence interval (CI), 0.1% expected degree of margin of error (d), design effect of 5, and expected prevalence of 0.3% were obtained from a systematic review [4]. Hence, a total 54,976 participants were selected for our study. The sample size was proportionally allocated to the selected clusters based on the total population of the village or community.

2.3. Procedures

We used a two-stage process to identify and ascertain cases of active epilepsy. The screening questionnaire was based on World Health Organization (WHO) screening questionnaires previously used in China and on the International Community-based Epilepsy Research Group (ICBERG) screening instrument [9], adjusted according to the recently published standards for epidemiologic studies and surveillance of epilepsy [10].

In the first stage, local health workers performed door-to-door surveys with a screening questionnaire. Healthcare professionals from the Centers for Disease Control and Prevention and neurology specialists were responsible for standardizing and training the interviewers participating in the data collection. For each visit, face-to-face interviews were performed, especially with the head of the family. Children and the elderly were interviewed through the family members responsible for their care. Phone interviews were used for those who worked outside the home. The minimum response rate for the door-to-door recruitment was 90%.

In the second stage, epilepsy specialists performed door-to-door investigations with a more specialized questionnaire in participants with suspected epilepsy from the first stage. This questionnaire contained more questions, including those related to the respondent's demographic details (age and sex), social characteristics (education and marital status), socioeconomic data (living area and health insurance), and epilepsy-related features (description of the first seizure, etiology of epilepsy, seizure frequency, duration of epilepsy and treatment). Neurological examinations were also performed during the interview. If present, the brain imaging and electroencephalography results were also recorded.

2.4. Operational definitions

Epilepsy was defined as having ≥2 epileptic seizures, unprovoked by any immediate identified cause. Individuals with only febrile seizures or only neonatal seizures were excluded [11].

Active epilepsy was defined as having ≥2 unprovoked seizures in the previous year [12]. The prevalence of active epilepsy was defined on the time point of January 1, 2013.

Treatment gap of active epilepsy was defined as the difference between the number of people with active epilepsy and the number of people whose seizures are being appropriately treated in a given population at a given point of time, expressed as a percentage [12].

Appropriate treatment of active epilepsy requires regular management of recurrent seizures according to international standards, which mainly involves antiepileptic drugs and/or rarely includes surgery, and includes the identification and management of underlying causes [12].

Patients with epilepsy were considered treatment-naïve if they were not receiving any antiepileptic treatment (neither traditional medicine nor antiepileptic drugs) for active epilepsy.

2.5. Statistical analysis

Data were double-entered. Statistical analysis was performed using SPSS version 17.0. The quantitative variables are presented as the mean and standard deviation. The qualitative variables are described in the form of frequency and percentage.

Univariate associations for failure to receive appropriate antiepileptic treatment were investigated using logistic regression adjusted for age and sex. Variables with $p < 0.1$ and potential predictors according to previous studies [4,5,7] were included in a multivariate logistic regression model. In the multivariate model adjusted for age and sex, variables with $p < 0.05$ were retained in the final model.

3. Results

3.1. General information

The epidemiological survey included 54,976 people as the study population, among which 50,035 were interviewed and considered valid responders (Fig. 1). The response rate was 91.01%. There were 26,119 males (52.2%) and 23,916 females (47.8%) in the sample; the male:female ratio was 1.09:1.

3.2. Prevalence and treatment gap of active epilepsy

The diagnosis of active epilepsy was confirmed in 118 people (prevalence of active epilepsy, 2.4 per 1000) (Table 1). Table 2 lists the general characteristics of the people with active epilepsy. The treatment gap in the general population was 58.5% (Fig. 2). People who failed to receive appropriate antiepileptic treatment included those who were treatment-naïve and those who received inappropriate antiepileptic treatment. Scenarios of the latter included taking antiepileptic drugs irregularly, stopping the medications themselves, or taking Chinese traditional medicine instead.

3.3. Risk factors of failure to receive appropriate antiepileptic treatment

We studied eight variables as potential risk factors of failure to receive appropriate antiepileptic therapy (Table 2). Of these, three had univariate $p \leq 0.10$ and were included in the multivariate logistic regression model. Multivariate analysis showed that people with active epilepsy were more likely to receive inappropriate antiepileptic treatment or be treatment-naïve if they had no health insurance and higher seizure frequency (Table 3).

4. Discussion

As the first door-to-door survey of epilepsy in eastern China, this study broadens epidemiologic understanding of active epilepsy in China as a whole. Moreover, as one of the few studies to describe the risk profile of epilepsy treatment gap in developing countries, our