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Risks of probable SUDEP among people with convulsive epilepsy in rural West China

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ABSTRACT

Purpose: This study aimed to examine the risk factors of probable sudden unexpected death in epilepsy (SUDEP) among patients with convulsive epilepsy in rural communities.
Method: A total of 35 cases with identified probable SUDEP were recruited in the study and compared with three survival controls that were sex and age matched from the same cohort for each case. Three healthy controls per case were chosen as a control group. Risk factors were analyzed using the logistic regression model. The odds ratio (OR) was calculated to determine the risk or protective effect.
Results: The following three factors significantly increased the risk of probable SUDEP: early-onset age of seizures (≤10 years vs. >10 years) with an OR of 6.8 (95% CI: 1.5–32.6), high seizure frequency at baseline (>10 years vs. ≤10 years) before regular phenobarbital treatment with an OR of 5.9 (95% CI: 2.2–16.6), and experiencing one or more seizures (vs. seizure-free) in the month prior to probable SUDEP with an OR of 9.5 (95% CI: 3.0–30.1).
Conclusion: Lack of seizure freedom before and during regular antiepileptic drug treatment increase the risk of probable SUDEP. Special attention should be given to patients with early convulsive epilepsy-onset, and the proper control of convulsive seizures is critical for the prevention of probable SUDEP.
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1. Introduction

Sudden unexpected death in epilepsy (SUDEP) refers to sudden death with or without evidence of seizure among seemingly healthy individuals with epilepsy; by definition, SUDEP is not attributed to trauma, drowning, status epilepticus, or other known causes [1,2]. Recent clinical studies have focused on SUDEP, and public and political recognition of this condition has increased [2]. The overall incidence rate of sudden death is more than 20 times higher in patients with epilepsy than in the general population [3] and varies depending on the study population [1]. In general epilepsy populations, incidence rate of SUDEP is low, and in individuals with chronic refractory epilepsy the rate is higher and highest in epilepsy surgery candidates [1]. A previous review [2] concluded an incidence of SUDEP per 1000 patient-years was 0.09–2.65 in community samples, 1.2–5.9 in tertiary care epilepsy centers, and 6.0–9.3 among patients evaluated for or treated with surgery or vagus-nerve stimulation for epilepsy.

The few existing epidemiological surveys suggest that the frequency of tonic–clonic seizures could be the most prominent factor affecting SUDEP [4–7]. Additional risk factors include the lack of antiepileptic drug (AED) treatment, frequent changes in therapy with AEDs, AED polytherapy, early adulthood, epilepsy of long duration, and mental retardation [6,8–10,4]. To the best of our knowledge, studies on the risk of SUDEP in China and other low-middle income countries are lacking. In the present study, we determined the risk factors of probable SUDEP in a rural community sample with convulsive epilepsy in West China on the basis of an established network of epilepsy management [11]. The network is under unified leadership of the public health administration departments, who liaise with medical institutions and disease control and prevention organizations to foster local communities to participate. The results of this study may provide insights into the probable SUDEP of patients in our region and possible prevention against probable SUDEP.

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2. Methods

2.1. Study sites and study population

This study explored the characteristics of probable SUDEP in a population with convulsive epilepsy in rural communities of West China. As part of an epilepsy management program, 16 target counties (Fig. 1) covering a population of 10.5 million individuals in rural West China were selected to undergo a convulsive epilepsy screening followed by pragmatic phenobarbital (PB) monotherapy at the primary care level from May 2005 to December 2013. The Sichuan University Ethical Standards Committee on Human Experimentation provided ethical approval of the project. All participants or guardians for children aged <18 years provided their written informed consent.

2.2. Patient selection

Project background and operation procedures were elaborately illustrated in previous reports [12–15]. In accordance with the rural management program, patients with convulsive epilepsy in each target county were identified at the first year and received PB intervention during follow-up. In these programs, primary health-care physicians provided the initial diagnosis of active convulsive epilepsy among participants, which was later confirmed by supervising neurologists (2–4 supervising neurologists from tertiary hospital were assigned to each target area) in accordance with strict criteria. In this study, patients with convulsive epilepsy were defined as (age, >2 years) those satisfying following diagnosis criteria [16]: major criteria: (1) Loss of consciousness; (2) Rigidity; (3) Generalized convulsive movements; minor criteria: (1) Bitten tongue or injury sustained in falling; (2) Urinary incontinence; (3) Post-seizure fatigue; (4) Drowsiness; (5) Headache or muscle aches (positive diagnosis requires at least two major criteria and at least two minor criteria). The exclusion criteria were as follows: (1) provoked seizures only; (2) age under two years at the time of recruitment; (3) presence of a learning disability or an active psychiatric condition; (4) presence of a progressive neurological condition; (5) presence of cardiac, hepatic, or renal disorders, or severe hypertension; (6) status epilepticus alone; (7) current medication possibly affecting PB usage. Three healthy controls per case were chosen as a control group.

2.3. Follow-up procedures

Each participant was required to collect a one-month supply of PB in designated clinics; thus, monthly follow-up was conducted to

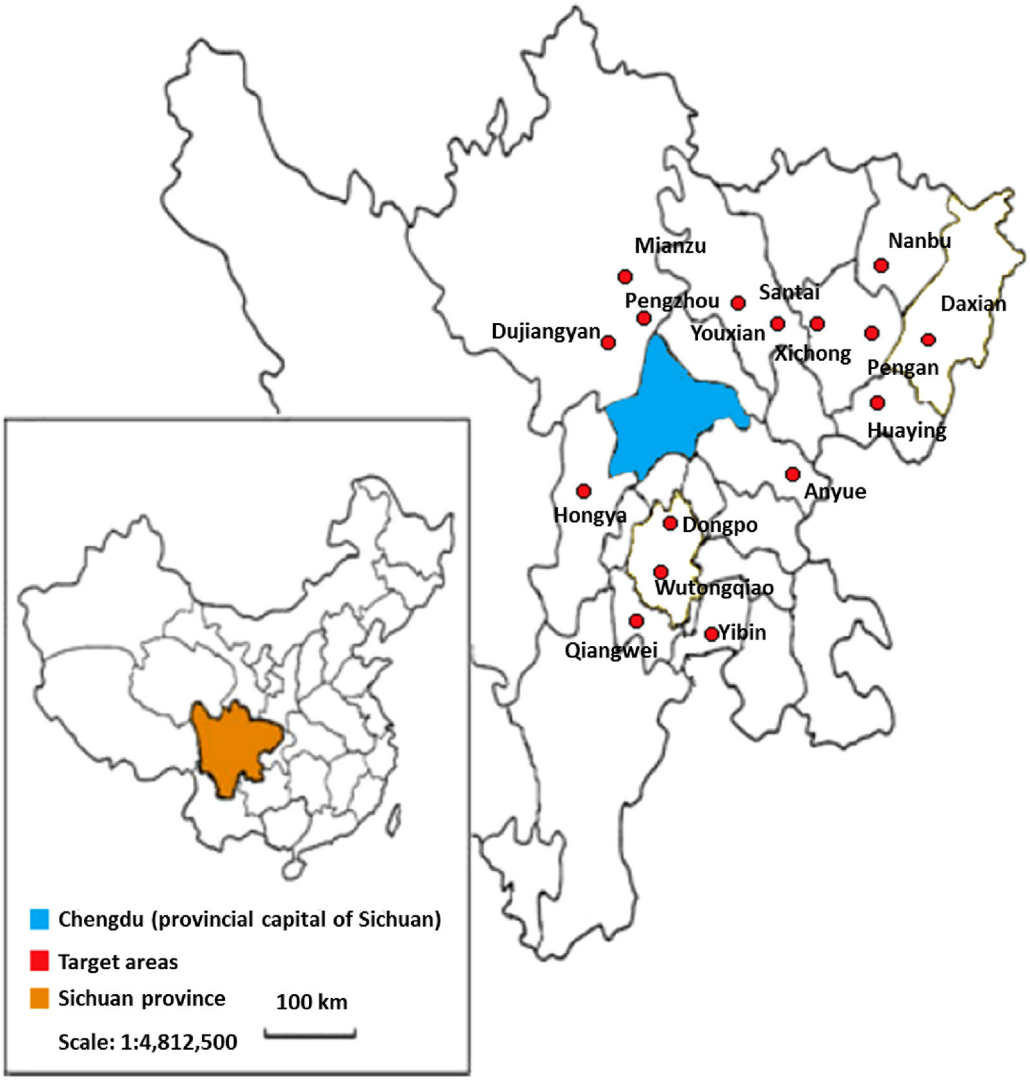

Fig. 1. Study target areas.

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