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Smoking prevalence and seizure control in Chinese males with epilepsy

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ABSTRACT

Smoking has a negative effect on most diseases, yet it is under-investigated in people with epilepsy; thus its role is not clear in the general population with epilepsy. We performed a retrospective pilot study on males with epilepsy to determine the smoking rate and its relationship with seizure control using univariate analysis to calculate odds ratios (ORs) and also used a multi-variate logistic regression model. The smoking rate in our sample of 278 individuals was 25.5%, which is lower than the general Chinese population smoking rate among males of 52.1%. We used two classifications: the first classified epilepsy as generalized, or by presumed topographic origin (temporal, frontal, parietal and occipital). The second classified the dominant seizure type of an individual as generalized tonic clonic seizure (GTCS), myoclonic seizure (MS), complex partial seizure (CPS), simple partial seizure (SPS), and secondary GTCS (sGTCS). The univariable analysis of satisfactory seizure control profile and smoking rate in both classifications showed a trend towards a beneficial effect of smoking although most were not statistically significant. Considering medication is an important confounding factor that would largely influence seizure control, we also conducted multi-variable analysis for both classifications with drug numbers and dosage. The result of our model also suggested that smoking is a protective factor. Our findings seem to suggest that smoking could have a potential role in seizure control although confounders need exploration particularly in view of the potential long term health effects. Replication in a much larger sample is needed as well as case control studies to elucidate this issue.

1. Introduction

Cigarette smoking is a worldwide health problem. Given its high prevalence among the population, many studies have been done over the years regarding its health effects. In some diseases, smoking has negative effects, while in others, for example in inflammatory bowel diseases [1,2], it can be a protective factor.

Some aspects of smoking in people with epilepsy have been investigated. Most studies considered the general prevalence rate of smoking in people with epilepsy rather than the effect of smoking [3–8]. In several studies the smoking rates in people with epilepsy were always higher than in the general population, with rates ranging from 21.8% to 38.8% [3–8]; the smoking rate in people with epilepsy is also higher than in most other chronic diseases [6]. The smoking rate was even higher in people with drug resistant epilepsy [9]. A recent study, however, showed the rate was dropping [10].

Some reports suggest that smoking or nicotine can have negative effects on seizures and epilepsy [11–15]. There are studies concluding that children of women who smoke have a higher rate of febrile seizures [13,14,16], although other studies did not confirm this [17,18]. Women with epilepsy have been shown to have an increased risk of premature contractions and premature birth [19,20]. Self-reported seizure triggering factors suggest that smoking may be a trigger factor with other factors such as medication withdrawn and sleep deprivation [21]. Poor adherence to a medication regimen may co-occur in adolescents [22]. In a prospective study of a nurse cohort followed for more than 20 years, current cigarette smoking was associated with an increased risk of seizures (RR 2.60, 95% CI 1.53–4.42), and past smoking was associated with an increased risk of epilepsy (RR 1.46, 95% CI 1.01–2.12) [23]. Smoking may also influence drug concentrations in serum. Several studies suggest that smokers may have lower serum drug concentrations than non-smokers while taking the same drug (such as lamotrigine (LTG) due to smoking related hepatic enzyme changes [24]. Nicotine, a main component in cigarettes, has also been shown to lower the seizure threshold in animals [11].

Conversely, nicotine has been confirmed as being protective and as having a treatment effect in rare hereditary epilepsy (autosomal dominant nocturnal frontal lobe epilepsy [ADNFLE]). The most specific mutated genes in ADNFLE are related to functioning of the nicotinic acetylcholine receptor [25,26]. People with epilepsy in families with ADNFLE who smoked or used nicotine patches had better overall seizure

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control than those who did not [25]. However, a study about sporadic nocturnal frontal lobe epilepsy was unable to determine the role of smoking [26]. Another study showed that nicotine patch use in video EEG monitoring increased the duration of hospitalization of people with epilepsy as fewer seizure events were captured [27]. Thus there is some circumstantial evidence for smoking and nicotine to have a beneficial effect on seizure control.

Data from 2015 suggest that the general smoking rate in the Chinese population is 27.7% (52.1% in males and 2.7% in females) [28]. Smoking rates among people with epilepsy in China have not been recently ascertained. We aimed to investigate the role of smoking in people with epilepsy in China.

2. Materials and methods

We have an established clinical databank for people with epilepsy in our center. The data bank should include data on all those who routinely attend. Data included contact information and demographics such as name, sex, age, education profile, marriage status and number of children. Recorded clinical data included diagnosis, EEG, neuroimaging, seizure types, current seizure frequency, medication profile and epilepsy phase (Table 1).

The establishment of the databank was approved by the West China Hospital Ethics Committee and written consent was always provided by individuals before data were collected.

In November 2015, we contacted by telephone males in the databank inquiring about their smoking status (as below). Only those in the databank prior to November 2014 were contacted as to avoid including individuals with newly diagnosed epilepsy. Only males were included in this pilot study as most smokers in China are males. We excluded people with a history of poor adherence and those whose final diagnosis was not epilepsy. We also excluded newly diagnosed patients (hard to evaluate their seizure control in a short time) and symptomatic epilepsy.

We collected data on smoking status as – never-smoker, current smoker (at least 1 cigarette per day in past 6 months), and former smoker (smoking stopped by the time of the study). For smokers and former smokers the number of years smoking was recorded. We also performed the Fagerström Test of Nicotine Dependence (FTND) on the current smokers [29]. This includes 6 questions, and we calculated the nicotine dependence level of individuals by adding the grade of all items together. Smokers with a total grade lower than 6 were considered as having a low to moderate nicotine dependence level and those with grade equal or higher than 6 were considered as having a high nicotine dependence level.

2.1. Epilepsy classification

Individuals were classified based on clinical judgment as having focal or generalized epilepsy, and by the dominant seizure type. Focal or generalized epilepsy included categories such as temporal lobe epilepsy, frontal lobe epilepsy, parietal lobe epilepsy, occipital lobe epilepsy and generalized epilepsy. For dominant seizure types, individuals were grouped as having generalized tonic clonic seizures (GTCS), myoclonic seizures (MS), simple partial seizures (SPS), complex partial seizures (CPS) and secondarily generalized tonic clonic seizure (sGTCS).

Table 1
Definition of different phases of an individual with epilepsy.

Active phase	Individuals have had a seizure within the previous year and are changing their medication
Maintenance phase	a. Seizures have stopped and no medication changes have taken place within the previous year (Type 1) b. Individuals have had a seizure within the previous year but have had no medication change (Type 2)
Medication reducing phase	Individuals reducing their medications
No medication phase	Individuals who have reduced and subsequently stopped their medications

2.2. Smoking rate and seizure control

For simplicity, we classified seizure control profile into satisfactory seizure control and unsatisfactory seizure control. We excluded individuals in the Type 2 maintenance phase who had seizures within a year without medication change because the reasons for not changing their medication were complicated. They may be less affected by their seizures and decided not to increase the dose of medication or they could have drug resistant epilepsy or they may be having seizures frequently but refused to take more medication for worrying side effects. These two situations were not considered either satisfactory or unsatisfactory seizure control. Satisfactory seizure control was defined as type 1 maintenance phase, reduced medication phase and no medication. Unsatisfactory seizure control was defined as being in the active phase.

All our data were processed in SAS version 9.4 (SAS Institute, Cary, NC, USA). The smoking rate was calculated based on the whole cohort and both classifications. For different categories within a classification, we also compared the difference of smoking rate by chi-square to establish whether smoking rate is different between categories.

The seizure control profile under each category of classification was compared by calculation of odds ratios [OR]. For example, in temporal lobe epilepsy using the focal or generalized epilepsy classification, we calculated the number of individuals who smoke with satisfactory seizure control, those who smoke with unsatisfactory seizure control, those who do not smoke with satisfactory seizure control and those who do not smoke with unsatisfactory seizure control; thus we could generate an OR and also identify its statistical significance. We did the same for all categories in 2 different classification systems.

2.3. Multi-variable analysis for smoking and epilepsy

The control profile in an individual is primarily based on antiepileptic drugs (AEDs), thus medications were considered as confounding factors in our analysis. We simply categorized the number of medications as equal or less than 2 medications and more than 2 medications. Furthermore, we considered comparative dosages of their medications as small or large using definitions of daily drug dosage (DDD) among different AEDs by WHO (see Table 2).

We performed multiple logistic regression analysis model based on medication numbers, dosage levels, age of the patient (between different ages of patients, the smoking rate can be different), their smoking status as yes or no and separately using both classification methods. We calculated the coefficients and evaluated whether smoking is a protective factor for seizure control in people with epilepsy.

Table 2
Definition of small and large dosage for a patient based on medication number and dosage for each medication.

	Small dosage	Large dosage
Only 1 medication	≤50%DDD	>50%DDD
2 medications	a. Both ≤50%DDD b. 1 ≤ 50%DDD	a. Both >50% DDD
3 medications	a. All ≤ 50% DDD b. 1 > 50% DDD Other 2 ≤ 50%DDD	a. 2 > 50% DDD b. All >50%DDD
4 medications	a. All ≤ 50%DDD b. 1 > 50%DDD Other ≤50%DDD c. 2 > 50%DDD Other 2 ≤ 50%DDD	a. 3 > 50%DDD, 1 ≤ 50%DDD b. All >50%DDD