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Analysis of the Q-T Dispersion and T Wave Alternans in Patients with Epilepsy

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Abstract

Objectives: There is a high rate of sudden death in epilepsy patients, part of which is sudden cardiac death. By investigating ECG T wave alternans and Q-T dispersion changes of epilepsy patients, we may predict the possibility of the occurrence of sudden death and provide basis for clinical prevention. **Methods**: Selecting 587 cases of epilepsy patients as the study group, 672 same period cases of healthy persons as the control group; Analyzing the effect of epilepsy on ECG T wave alternans and Q-T dispersion with the standard 12 lead ECG. **Results**: The study group had a significantly prolonged Q-T dispersion and an increased incidence of T wave alternans than that of the control group; Compared with other seizure types, tonic clonic seizure and absence seizure had a significantly prolonged Q-T dispersion and an increased occurrence rate of T wave alternans. **Conclusions**: Epilepsy patients ECG T wave alternans and Q-T dispersion has higher abnormal rate, and are prone to sudden cardiac death; Routine ECG(RECG) T wave alternans and Q-T dispersion changes can provide guidance for clinical prevention of sudden unexpected death in epilepsy (SUDEP).

Keywords

Epilepsy, T Wave Alternans, Q-T Dispersion

1. Introduction

Sudden unexpected death in epilepsy is an unexplained death that occurs to epilepsy patients without the prior expectations, with or without witnesses, non trauma or drowning cases; it may be associated or not associated with seizures, except status epilepticus, no autopsy lethal toxicity and anatomical factors [1]. SUDEP is the fatal complication of epilepsy, accounting for 7.5% - 17% of death in patients with epilepsy [2]. Causes of SUDEP are quite complex, of which part

of the patient is sudden cardiac death. The main cause of sudden cardiac death is ventricular arrhythmia, especially ventricular fibrillation, while the exception of T wave alternans and Q-T dispersion is extremely easy to cause ventricular fibrillation. So we analyzed the changes of T wave alternans and Q-T dispersion (QTd) in RECG of epilepsy patients who were diagnosed in our hospital from January 2011 to December 2015, as to provide early prediction index for the prevention of sudden death in epilepsy; and now it is reported as follows.

2. Data and Methods

2.1. Case Selection

Select 687 cases of epilepsy patients hospitalized in our hospital from January 2011 to December 2015 as study group. All the cases were in accordance with the classification of the International League against Epilepsy [3]. All the cases are generalized seizures and diagnosed by history, EEG or/and MRI, and symptomatic epilepsy is excluded. Select same period 672 cases of healthy persons as control group.

2.2. Method

All patients accepted Synchronous routine 12 lead ECG test on the 1st day. QTd calculation: measuring the QT interval; determine the end point at the intersection of the T wave descending and the baseline, at the T-U low when U wave exists. Each lead takes the average value of three consecutive QT intervals as the QT interval of this lead; correct QT dispersion (QTcd) according to the heart rate, the difference between QTmax and QTmin is QTd [4]. Calculation of T wave alternans: in the same lead T wave amplitude difference 0.1 mv is T wave alternans; calculate the incidence of T wave alternans.

Ambulatory EEG detection was performed in all patients. Electrodes installation used the International 10 - 20 system for EEG electrode placement: the vertex as the center, respectively draw straight line to the divide (10 aliquots) in the temporal side; then sagittal line bisection point is the radius of concentric circle; determine the electrode placement according to the intersection point, and place reference electrode on the mastoid; there is a total of 21 electrodes. Record video and EEG data 24 hours.

Brain MRI: Before examination, patients should be in quiet and rest for 15 minutes; Using Philips 1.5T MRI scanner to make orientation map in coronary, sagittal and transverse three directions at the same time with fast imaging sequence; determining scanning baseline, scanning method and scanning range on the positioning films. Imaging ranges from OMBL to the vertex of the skull. Routinely carried out cross section T1WI, T2WI, sagittal or coronal T1WI. Imaging space is 10% - 50%. Imaging layer thickness is 5 - 10 mm; matrix (128 × 128) - (512 × 512).

2.3. Statistical Analysis

QTd results were expressed by average ± standard deviation ($x \pm s$) ; Using rank

sum test to compare the study group and the control group; Seizure types were compared by variance analysis and comparison between two groups was made by using q test; Comparison of the incidence of T wave alternans was made with X^2 test, $P < 0.05$ with statistical difference.

3. Results

The 687 cases in the study group and 672 cases in the control group were all included in the statistics, no omission. Of the study group 448 cases were male, 239 cases were female, age 3/12 - 88 year old, average age (47.25 ± 14.31) years old. There are 159 cases of tonic seizures, 127 cases of clonic seizures, 294 cases of tonic clonic seizures, 79 cases of absence seizures and 28 cases of atonic seizures. Of in the control group male 417 cases, female 255 cases, age 7 - 76 years old, the average (52.7 ± 24.62) years old. Two groups have no statistical difference in age and gender ($P > 0.05$), see Table 1.

T wave alternating rate of two groups: T wave alternans occurred rate of the study group increases; For study group, T wave alternans occurred rate after seizure increases than before ; Compared with other seizure types, tonic clonic seizures and absence seizures has a significantly prolonged Q-T dispersion and an increased T wave alternans occurred rate ($P < 0.01$), see Table 2.

QTd of two groups: Q-T dispersion of the study group is significantly prolonged than that of the control group; For the study group, Q-T dispersion after the seizure is significantly prolonged than before; Tonic clonic seizure and absence attack, compared with other seizure types, their Q-T dispersion is significantly prolonged ($P < 0.01$), as shown in Table 3.

4. Discussion

Epilepsy patients have a high rate of sudden death. In addition to seizures, drugs and other affecting factors that cause sudden death, cardiogenic sudden death is also a major factor [5], and even arrhythmia caused by epileptic seizures occur before epilepsy attacks itself [6]. A main reason for the sudden cardiac death induced by seizures is ventricular fibrillation. Strzelczyk A. [7] demonstrates that derangements in autonomic function and TWA are highly prevalent after sGTCS in patients with chronic uncontrolled epilepsy. Further studies are warranted to investigate the value of TWA for risk stratification in epilepsy patients

Table 1. Comparison of basic information between the study group and the control group.

	total	average age	gender	
			male	female
The study group	687	47.25 ± 14.31	448	239
The control group	672	52.7 ± 24.62	417	255
P value		P > 0.05	P > 0.05	

Table 2. Comparison of the incidence of T wave alternans between the study group and the control group.

	T wave alternans	without T wave alternans	total
The study group	215	472	687
Tonic seizures (A)	14	145	159
Clonic seizures (B)	10	117	127
Tonic clonic seizures (C)	137	157	294
Absence seizure (D)	48	31	79
Atonic seizures (E)	6	22	28
The control group	19	653	672
Total	234	1125	1359

	T wave alternans	without T wave alternans	Total	χ^2	P
The study group	215	472	687		
The control group	19	653	672	193.151	<0.01
Total	234	1125	1359		

	χ^2	P
A with B	0.08	0.778
A with C	66.328	<0.01
A with D	73.951	<0.01
A with E	3.972	0.046
B with C	58.525	<0.01
B with D	67.341	<0.01
B with E	4.553	0.033
C with D	4.995	0.025
C with E	6.561	0.01
D with E	12.793	<0.01

for sudden cardiac death and SUDEP. If effective predictions of the likelihood of ventricular fibrillation can be made, advance prevention will reduce the mortality of patients with epilepsy. Ventricular fibrillation is more often induced by cardiac electrical repolarization abnormalities [8], and heart rate variability, Q-T dispersion, T wave alternans [9] in 12 lead ECG can be used to directly observe the cardiac electrical repolarization abnormalities. While heart rate variability needs dynamic ECG monitoring which takes longer, Q-T dispersion and T wave

Table 3. Comparison of QTd of the study group and the control group ($\bar{x}$ ± s; ms).

	QTd
The study group	58.37 ± 15.54
Tonic seizures (A)	47.61 ± 14.12
Clonic seizures(B)	48.79 ± 14.58
Clonic seizures(C)	67.42 ± 19.71
Absence seizure(D)	64.29 ± 19.33
Atonic seizures(E)	45.52 ± 13.67
The control group	32.65 ± 11.23

	QTd	Z	P
The study group	58.37 ± 15.54	168.351	<0.01
The control group	32.65 ± 11.23		

	Z	P
A with B	0.3256	0.732
A with C	69.567	<0.01
A with D	88.751	<0.01
A with E	0.7645	0.043
B with C	54.453	<0.01
B with D	78.097	<0.01
B with E	5.156	<0.01
C with D	4.897	<0.01
C with E	12.476	0.01
D with E	21.543	<0.01

alternating, conventional ECG is able to interpret; so we choose two parameters on RECG, T wave electric alternating and Q-T dispersion, as the observation index. We retrospectively analyze the correlation between epilepsy and abnormal electrical activity of the heart, and provide guidance for the clinical prevention of epilepsy sudden death.

It is found in our results that epilepsy patients have a higher incidence of abnormal electrical activity of the heart. There are 1,173 cases of the primary epilepsy patients, of which 363 cases T wave alternans occur, accounting for 30.9%; and there is a significant difference between the two groups. As for seizure types, tonic clonic onset and absence seizures are more common, and Q-T dispersion of these epilepsy patients significantly prolonged compared with the control

group, which further illustrates that the seizures would inevitably lead to abnormal cardiac electrical activity, resulting in ventricular arrhythmia, and eventually leading to sudden death in patients with epilepsy. Abnormal cardiac electrical activity caused by epileptic seizures should be the result of multiple factors. First, the abnormal electrical activity which causes epilepsy and the abnormal electrical activity of heart have common electrophysiological basis. Hyperpolarization activated cyclic nucleotide-gated ion channel gene family (HCN) mutations can cause seizures; HCN is related to the generation of cations (K+, Na +)-activated Ib depolarization current, and the current can activate atrioventricular node and the sinoatrial node [10]. Hartmann found the first sodium channel gene SCN5A which can prolong the QT interval of ECG and lead to bradycardia even cardiac arrest, and thus epilepsy sudden death. It is located on chromosome 3p24, and was previously considered only expressing in the myocardium, but by using the method of in situ hybridization and PCR techniques its mRNA is also found in the limbic system such as piriform cortex and amygdala. The gene mutation can lead to sodium influx extension and cell depolarization, which is presented as the seizures in the central nervous system, as the prolongation of the QT interval, tachycardia and ventricular fibrillation in the ECG [11]. Due to the common basis of ionic channels and that hypoxia and electrolyte imbalances of epileptic seizures also affect the electrical activity of the heart, tonic clonic seizures have a high incidence of abnormal electrical activity of the heart. Secondly, the location of central epileptic foci impacts the electrical activity of heart. Temporal lobe is the source of 70% of seizures bradycardia or cardiac arrest, and frontal lobe of 30%. And insular lobe epilepsy is more prone to abnormalities of cardiac electrical activity. Insular cortex is the cortical area of cardiovascular activity. The left and the right insular lobe have different effects on cardiovascular activities; left insular cortex is related to parasympathetic effect, while right insular cortex is associated with sympathetic activity. The insular cortex epilepsy damaged the coordinate relationship of cardiac sympathetic-vagus nerve and left the cardiac activity in an unstable state. It is also the reason for what shows in our results that the T wave alternans incidence and Q-T dispersion anomalies are different from that of other seizure types, as absence seizure is more often the temporal lobe epilepsy.

There are some limitations of our study. First of all, EEG abnormal rate of our study was lower than that of the peers [12]. It's mainly because that we only counted the T wave alternans and Q-T dispersion, while other ECG abnormalities were not included in the statistics, thus causing some deviations .So the comprehensive judgment is needed in future analysis. Second, autonomic dysfunction can be studied via other methods, such as heart rate variability and changes of blood pressure; but these methods request a longer observing time and some special analysis software. Since our purpose is to provide a fast and effective predictor for grassroots medical staff, we take the choice of T wave alternans and Q-T dispersion, hoping to replace the application of heart rate varia-

bility and blood pressure changes.

In short, the prolongation of Q-T dispersion and the occurrence of T wave alternans have prompted severe autonomic dysfunction in patients with epilepsy who are prone to sudden cardiac death, which needs to be paid attention in the post processing. There is a close relationship between ECG T wave alternans and Q-T dispersion changes and the bleeding site of patients who are in the acute phase of cerebral hemorrhage. When these parts are bleeding, we should pay attention to observing the ECG changes to avoid the occurrence of acute cardiovascular events.

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