Electrocardiographic changes in patients with refractory epilepsy

Mohammad Zare, Mehri Salari, Marzieh Tajmirriahi, Mohammad Saadatnia, Rasul Norouzi
Department of Neurology, Isfahan Neurosciences Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Background: Epilepsy is the second most common type of chronic neurological disease. Its diagnosis carries an excess mortality, which is 2-3 times higher than that of general population. Mortality rates are increased among patients with uncontrolled seizures. The aim of this study was to characterize the electrocardiogram (ECG) changes during pre-ictal, ictal and post-ictal states in pharmaco-resistant epilepsy patients. Materials and Methods: This retrospective study conducted by Department of Neurology and Department of Cardiology of Isfahan Medical University from September 2008 to December 2012, patients with medically refractory epilepsy who underwent standard pre-surgical assessment from Epilepsy ward of Kashani hospital in Isfahan city were recruited in this study. Results: The heart rate (HR) varied significantly throughout the record. Significant difference in HR was identified between ictal and pre-ictal periods ($P = 0.000$), furthermore, the difference between ictal and pre-ictal HR (mean $= 63.867 \pm 0.061$, $P = 0.000$), ictal and post-ictal HR (mean $= 38.833 \pm 0.067$, $P = 0.003$), and between pre- and post-ictal HR (mean $= 25.033 \pm 0.089$, $P = 0.000$), was significant. Conclusion: ECG monitoring should be a part video- (electroencephalography) EEG monitoring to identify serious cardiac abnormalities, particularly in patients with refractory epilepsy.

Key words: Electrocardiography, epilepsy, electrocardiogram monitoring

INTRODUCTION

Epilepsy which is the second most common chronic neurological condition affects approximately 0.5-2% of the population.\[1\]

Its diagnosis carries an excess mortality, which is 2-3 times higher than that of general population.\[2\] Mortality rates are increased among patients with uncontrolled seizures.\[3,4\] The most frequent cause of death in epilepsy is sudden unexpected death.\[3\] Incidence of Sudden Unexplained Death in Epilepsy (SUDEP) is between 3.5 and 9.3 per 1000 person-years in refractory epilepsy\[3,4\] and at least 12% of patients with childhood epilepsy and no terminal 5 year remission will die of SUDEP by the age of 40 years.\[1,2\] Certainly, most SUDEP victims are young adults with a mean age at the time of death of about 35 years.\[4-6\]

The observed SUDEP is usually triggered by a seizure through mechanisms, which are not clear yet,\[3\] seizure activity can disrupt normal physiological regulation and control of cardiac activity;\[7\] the most common heart activity changes is tachycardia;\[8\] however, bradychardia, deviation of RR intervals\[9\] and long QT\[10\] have also been reported. Most studies have shown changes in cardiac autonomic parameters occur in more than 90% of patients with complex partial and generalized tonic-clonic seizure;\[9\] therefore, cardiovascular changes have received the most attention in SUDEP, but previous data could not find neither certain changes, which are related to SUDEP nor predictor parameters.

In this paper, we attempt to characterize the electrocardiogram (ECG) changes during pre-ictal, ictal, and post-ictal states in pharmaco-resistant epilepsy patients to evaluate the prevalence of this variability and to identify the suspected parameter through, which those who are at higher risk for SUDEP cab is predicted.

MATERIALS AND METHODS

Study design
This retrospective study conducted by Department of Neurology and Department of Cardiology of Isfahan Medical University, patients with medically refractory epilepsy who underwent standard pre-surgical assessment from Epilepsy ward of Kashani hospital in Isfahan city were recruited in this study from September 2008 to December 2012. Video EEG monitoring was carried out using conventional scalp recording (10-20 system) and simultaneously ECG recording from lead II; to minimize environmental electrical noise and to provide patient comfort and
mobility, all wires were tied together, poor quality ECG was not included in this study. Exclusion criteria were prior history of cardiac disease in patients and family membranes. Patients were observed for 1-2 days and if seizure did not happen, anti-epileptic drugs were reduced for those patients who had seizure, seizure was identified by neurologist based on EEG and video recordings.

After asking for permission from ethic committee, we analyzed the EEG, ECG, and video recording of 30 patients who were admitted from January to December of 2011, the study was inclusive for all ages.

**Electrocardiogram analysis**

The ECG as well as EEG records were visually screened; the ECG data were divided in three epochs: Pre-ictal, ictal, and post-ictal periods.

The heart rate (HR) calculation was done during short-time period (30 s) in the 1 min before seizure onset, during ictal phase, and post-ictal by PR intervals.

The PR interval measurements were made by mean PR interval during 3 phases mentioned above.

The QT and PR intervals were measured from 3-5 successive ECG complexes in all 3 periods (pre-ictal, ictal, and post-ictal), QT intervals were calculated using the following formula: QTc = QT/RR\(^{1/2}\).

All of the measurements were done manually by cardiologists; besides, the recorded ECG screened for any abnormality such as T-invert and wide QRS.

**RESULTS**

A total of 30 patients with retractable epilepsy with available video EEG data were included and the subject gender was 15 males and 15 females. The age range was 5 years to 45 years, with a mean age of 23.77 years. About 66.7% of patients were right handed; 26.7% of them have positive family history for seizure, and 20% had history of febrile convulsion in childhood. Complex partial seizures were the dominant seizure types in 26 patients. Two patients suffered from primary generalized epilepsy. Lenox was the dominant type of seizure in one patient. Finally one patient had Juvenile Myoclonus Epilepsy. All patients experienced at least one episode of seizure.

In MRI analysis of patients, 70% of them had lesion: 40% mesial temporal lobe sclerosis, 20% hypopampal atrophy, 6.7% had cerebral cyst, and 3.3% had cavernous angiomia. Furthermore, 77.42% of lesions were in right side, 23.80% were in left side, and 4.76% were in both sides.

The HR varied significantly throughout the record. There was a trend for tachycardia during ictal phase, which returned to the baseline in post-ictal phase. Significant difference in HR was identified between ictal and pre-ictal periods \((P = 0.000)\), also, the difference between ictal and pre-ictal HR \(\text{[mean = 63.867 ± 0.061, } P = 0.000]\), ictal and post-ictal HR \(\text{[mean = 38.833 ± 0.067, } P = 0.003]\), and pre- and post-ictal HR \(\text{[mean = 25.033 ± 0.089, } P = 0.000]\), was significant \(\text{[Figure 1]}\).

Total of 64.3% patients had seizure duration more than 10 years; however, there was no significant difference between disease duration and ECG changes.

The other parameter is shown in Table 1.

![Figure 1: Heart rate changes during each phase](image)

<table>
<thead>
<tr>
<th>ECG parameter</th>
<th>PR-interval</th>
<th>QT-interval</th>
<th>Heart rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (mm)</td>
<td>P value</td>
<td>Mean (mm)</td>
</tr>
<tr>
<td>Comparison between</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-ictal</td>
<td>0.167±0.029</td>
<td>0.000</td>
<td>0.407±0.033</td>
</tr>
<tr>
<td>Post-ictal</td>
<td>0.150±0.037</td>
<td>0.000</td>
<td>0.384±0.049</td>
</tr>
<tr>
<td>Pre-ictal</td>
<td>0.140±0.045</td>
<td>0.000</td>
<td>0.369±0.061</td>
</tr>
<tr>
<td>Pre-ictal, ictal</td>
<td>Difference =0.027±0.061</td>
<td>0.000</td>
<td>Difference =0.037±0.052</td>
</tr>
<tr>
<td>Ictal, post-ictal</td>
<td>Difference =0.010±0.067</td>
<td>0.091</td>
<td>Difference =0.015±0.0477</td>
</tr>
<tr>
<td>Pre-ictal, post-ictal</td>
<td>Difference =0.017±0.0893</td>
<td>0.000</td>
<td>Difference =0.023±0.033</td>
</tr>
</tbody>
</table>

ECG=Electrocardiogram
The difference between ECG changes and other factors such as age, sex, type of seizure, and duration of seizure were not significant.

DISCUSSION

Addressing the issue of cardiac changes during ictal phase is challenging, and previous studies have shown different results. Greene et al. showed there is no significant difference in the HR during seizure activity, however, other reported a transient increase in HR in the ictal phase. The expected consequence of seizure activity is an increased HR due to sympathetic discharge and likewise the major finding of our study was that cardiac rhythm abnormalities occur during or after seizure activity in patients with refractory epilepsy.

Mesial temporal structures have a profound effect on HR and therefore, temporal lobe epilepsy are most likely to be associated with cardiac rhythm changes and this is in agreement with our finding, which most types of seizures were Temporal lobe epilepsy (TLE).

Additional study is desired to explore to research the exact relation between seizure activity and cardiac rhythm.

Studies in adults demonstrated that a higher number of seizure activities were associated with tachycardia. This implied that the sympathetic discharge in complex partial seizures is usually dominant over the parasympathetic. Our finding was compatible too and there was a trend for tachycardia during ictal phase.

The consequence of a sustained tachycardia during epileptic seizures could be a ventricular tachycardia and sudden death. This is especially, significant for individuals underlying cardiac disease. These results suggest the possibility of increase SUDEP during seizure period, which is introduced by previous studies.

In conclusion, ECG monitoring should be a part video-EEG monitoring to identify serious cardiac abnormalities, particularly, in patients with refractory epilepsy. Patients with ictal cardiac arrhythmias should be referred to a cardiologist for a complete cardiac evaluation for underlying cardiac substrate.

REFERENCES


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