ORIGINAL ARTICLE

Cardiac Troponin Levels Following Complicated and Uncomplicated Epileptic Seizures

Rahime Eskandarian, a Nabiolah Asghari, b Mahbobeh Darban, c and Raheb Ghorbani d

a Department of Cardiology, b Department of Neurology, c Department of Internal Medicine, and d Department of Social Medicine, Fatemieh Hospital, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran

Received for publication April 19, 2011; accepted August 12, 2011 (ARCMED-D-11-00200).

Background and Aims. Cardiac troponins are tests with high sensitivity and specificity and selective biomarkers for diagnosis of acute myocardial infarct. Epilepsy is one of the common neurological diseases that presents as recurrent seizures. This study was designed to assess the troponin levels in patients with complicated and uncomplicated seizures.

Methods. Included in the study were hospitalized patients in Fatemieh Hospital, Semnan, Iran who were referred due to seizures with normal ECG and echocardiography and without critical features of cardiac diseases. Based on the results of pulse oximetry, K, urine analysis and CPK, patients were divided into two groups: complicated and uncomplicated.

Results. Thirty patients with complicated seizures and 30 additional patients with uncomplicated seizures were investigated; 53.3% of both groups were male. The mean (±SD) age of patients with complicated and uncomplicated seizures were 43.4 ± 15.5 and 44.7 ± 21.5 years, respectively (p = 0.789). The mean (±SD) troponin I level in patients with complicated seizure was 0.61 ± 0.26 ng/mL, whereas it was 0.41 ± 0.30 ng/mL in control group (p = 0.005). In none of the patients was troponin level higher than the normal value.

Conclusions. Although troponin I is considered as a sensitive and specific marker for diagnosis of cardiac tissue injury, association between its increasing plasma levels with complicated seizures was shown. Troponin I level perhaps may be used as a risk factor in patients with complicated seizures. © 2011 IMSS. Published by Elsevier Inc.

Key Words: Troponin I, Seizure, Complicated seizure, Risk factor.

Introduction

Acute coronary syndrome (ACS) is considered as a critical phase of cardiac diseases that can result in increasing the risk of cardiac infarct and sudden death. Cardiac troponins are highly specific and sensitive tests and are selective biomarkers for diagnosis of acute myocardial infarction (AMI) (1–3). Meanwhile, it has been proven that some neurological diseases such as subdural hematoma and brain ischemia affecting myocardial cells result in reversible myocarditis and a subsequent rise in troponin levels (4). Epilepsy is one of the common neurological diseases that presents as recurrent seizures at various times (5). Seizures, as in other situations with stress and increase in coronary flow, can lead to atherosclerotic plaque rupture, resulting in ischemia and ACS. It appears that seizure, as a stress-inducing agent, can cause ACS (6–8). There are several controversial studies regarding the association between troponin and epileptic seizures (9–15). For example, in a case report study, increasing troponin levels after epileptic seizure have been shown (9). In most of the studies, troponin levels after uncomplicated seizures have been reported to be in the normal range; however, the same results have been shown in regard to this issue (10–14). In another study with 20 rats, seizure was induced using electricity. Troponin level increased significantly than...
before the seizure (12). Brobbey et al. reported the increased troponin I values in a patient after generalized tonic-colonic seizure. The patient’s catheterization and echocardiography were normal (9). Colugnati et al. in a study of 11 patients found increased troponin I in three cases (13). We designed and carried out this study due to the scarce literature regarding troponin level in patients with noncomplicated seizures (10,11) as well as the fact that the relationship between troponin levels and complicated or noncomplicated seizures has not been assessed.

Materials and Methods

In this study among hospitalized patients in Fatemieh Hospital, Semnan, Iran, those who were referred due to seizure were enrolled in the study. All patients provided informed consent before being enrolled in the study. History, physical examination and ECG were then done. If ECG was normal, echocardiography was performed by a cardiologist. Patients with normal ECG and echocardiography and without critical features of cardiac diseases were entered into the next stage of study. A 5-cc venous blood sample and urine were taken from each patient on the sixth and tenth days after seizure (blood concentration of troponin increased 2–6 h after myocardial injury and decreased after 10 days) (16) and were sent to the laboratory in order to measure troponin I, creatinine, potassium (K), CPK levels and urine myoglobin level. Meanwhile, pulse oximetry was performed for all patients in order to assess complicated seizures. Troponin I was measured using ELISA and Diplus Kit (Monobind Inc., Lake Forest, CA) and awareness system (stat fax-2010) with precision: CV = 2.45%, δ = 0.05, sensitivity = 95% and specificity = 100%. Levels >1.3 ng/mL were considered as positive. All samples were assessed in a single laboratory.

Patients were divided into two groups based on the results of pulse oximetry, K, urinanalysis and CPK: complicated and uncomplicated. Complicated epilepsy causes one or more systemic complications including the following (15):

1. Hypoxia without history respiratory disease (PO₂ <60, O₂ Sat <90)
2. Respiratory or lactic acidosis (pH <7.37)
3. Hypoglycemia
4. Hypotension (SBP <100)
5. Hyperkalemia (K >4.5)
6. CPK >1000
7. Myoglobinuria

Troponin I level was compared between groups. Inclusion criterion of the study was that all patients were >12 years old and with epileptic seizure. Exclusion criteria of the study were pregnancy, simultaneous renal diseases, mental retardation, recent or previous ischemic heart diseases, progressive cerebral disorders and respiratory disease. All data were registered using a special questionnaire designed for this study.

Statistical Analysis

Results were reported as mean ± standard deviation (SD) for quantitative variables and percentages for categorical variables. The groups were compared using Student t-test for continuous variables and χ² test (or Fisher’s exact test if required) for categorical variables. Finally, in order to assess the simultaneous effects of variables on troponin level, linear regression analysis was done. All statistical analyses were performed using SPSS v.13.00 (SPSS Inc., Chicago, IL); p <0.05 was considered statistically significant.

Results

There were 30 patients with complicated seizures (case group) and 30 patients with uncomplicated seizures (control group) enrolled in the study. Potassium, CPK levels and urine myoglobin level were normal in all patients. Patients with complicated seizures had hypoxia (decrease in arterial O₂ saturation to <90%).

About 53.3% of both groups were male. Mean age, mean age at the time of the first seizure, mean duration from onset of seizure to study recruitment, serum creatinine level, and serum K of the patients with complicated and uncomplicated epilepsy were not statistically significant (p >0.05) (Table 1). Echocardiography was performed in all cases and results were normal in all patients with mean ejection fraction (EF) of 54.73% ± 1.53. Wall motion abnormalities were also absent in all cases. In addition, no arrhythmias and ischemic ECG changes were found.

All study patients had grand mal (generalized tonic-colonic) seizures. Half (50.0%) of the patients with complicated seizure and 60% of the uncomplicated group had a history of two or more seizures (p = 0.436). The mean troponin I level in patients with a first seizure (27 patients) was 0.47 ± 0.29 ng/mL, whereas this value was 0.55 ± 0.29 ng/mL in patients with two or more seizures, which was not significantly different (p = 0.277). The mean ± SD troponin I level in patients with complicated seizures was 0.61 ± 0.26 ng/mL, whereas this was 0.41 ± 0.30 ng/mL.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Complicated Mean</th>
<th>Complicated SD</th>
<th>Uncomplicated Mean</th>
<th>Uncomplicated SD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.4</td>
<td>15.5</td>
<td>44.7</td>
<td>21.5</td>
<td>0.789</td>
</tr>
<tr>
<td>Age of first seizure (years)</td>
<td>38.8</td>
<td>17.3</td>
<td>40.3</td>
<td>21.9</td>
<td>0.774</td>
</tr>
<tr>
<td>Duration from onset of seizure to recruit in study (min)</td>
<td>43.4</td>
<td>6.9</td>
<td>43.7</td>
<td>8.0</td>
<td>0.891</td>
</tr>
<tr>
<td>Serum creatinine level (mg/dL)</td>
<td>0.86</td>
<td>0.18</td>
<td>0.84</td>
<td>0.17</td>
<td>0.585</td>
</tr>
<tr>
<td>Serum potassium (K) level (mg/dL)</td>
<td>4.15</td>
<td>0.12</td>
<td>4.18</td>
<td>0.11</td>
<td>0.336</td>
</tr>
</tbody>
</table>
in the control group. This difference was statistically significant ($p = 0.005$) (Table 2). None of the patients had a troponin I level higher than normal value.

In order to assess the simultaneous effects of the mentioned variables on troponin I level, linear regression analysis was performed. Among these variables only type of epilepsy (complicated or uncomplicated) had a significant effect on serum troponin I level ($F [1, 85] = 8.58$, $p = 0.005$). Patients with complicated seizures had an average 0.21 ng/mL troponin I level higher than patients with noncomplicated seizures (Table 3).

### Discussion

Although troponin is considered as a sensitive and specific marker for diagnosis of cardiac tissue injury, an association has been demonstrated between increased plasma levels and some nonischemic cardiac diseases such as cardiomypathy, myocarditis and noncardiac diseases including subarachnoid hemorrhage, subdural hematoma, brain stroke, septicemia, and renal disease (17–21).

The results of the present study showed that the mean serum troponin level in patients with complicated seizures is significantly higher than uncomplicated seizures, whereas troponin level was not higher than normal range in both groups of patients. Epileptic seizure in complicated or uncomplicated patients did not cause increased troponin level higher than the normal limit. This result has been shown in other studies (10,11,13). In some studies and also in studies in rats, serum troponin level had a considerable elevation without evidence of cardiac ischemia (9,12,14).

In a case report by Parvuca-Codrea et al., troponin I levels increased after seizure but repeated assessment showed cardiac ischemic events after seizure in this patient (5).

Higher mean troponin I levels in complicated patients in this study may be a reason for negligible injury of cardiac tissue during seizure (18). In justifying this issue, two probable mechanisms should be mentioned that can lead to myocardial cell injury during seizure: 1) generalized tonic-colonic seizure leads to severe physical activity in patient and contraction of skeletal muscles in tonic stage leads to increasing the cardiac after load. This leads to a temporary imbalance in supply and cardiac tissue demand that can condition myocardial cell injury (14). 2) Neural-hormonal factors play roles in damage to myocardial cells such as what happens during brain hemorrhage or brain stroke. Imbalance in autonomic nervous system with increase in sympathetic nervous system and release of large amounts of catecholamine in blood during seizure may have destructive effects on cardiac tissue. These neural-hormonal stresses and increasing myocardial wall tension with catecholamine effect lead to troponin release due to cardiac cell wall damage (14). It seems that, in our study, the mentioned mechanism had more effects on damage to myocardial tissue compared to uncomplicated patients due to hypoxia in complicated seizures.

Meanwhile, it is proposed that patients should be evaluated for other probable factors that affect cardiac tissue injury during seizure such as respiratory and metabolic acidosis so that at-risk patients can be diagnosed in order to apply preventive strategies for epilepsy-related complications. In several studies it has been confirmed that hypochloremic lactic acidosis happens subsequent to generalized seizure (19,20) and respiratory acidosis in prolonged seizures make the patient susceptible to cardiac arrhythmia and hypotension (21).

It appears that seizure itself is not responsible for the increase in serum troponin level (10,11,13). If cardiac troponin increases to higher than its normal limit in an epileptic patient, the probability of an ischemic cardiac event should be considered (5). Moreover, in patients with seizures and increased troponin level, the probability of neural events such as brain stroke, subarachnoid hemorrhage or subdural hematoma should be considered (9). However, higher troponin level in patients with complicated seizures in this study may be due to negligible injury to cardiac tissue that leads to releasing troponin in the serum by increasing the permeability of cardiac cell membrane. Increase of troponin level can be seen in negligible damage of cardiac tissue without necrosis and acute ischemia (22,23) and also has been recognized as an important risk factor in many diseases such as unstable angina (24,25).

The study limitation was uncollected data regarding outcome in patients who had complicated seizure; therefore, assessment of the relationship between troponin levels and outcome was not possible.

In conclusion, cardiac troponin I may be used as a risk factor in patients with seizure. Using troponin level as a screening method in patients with complicated seizures needs further studies.

### Acknowledgments

This study was supported by funds from the Research Deputy of Semnan University of Medical Sciences. This paper is extracted from the above text.
from the thesis of Dr. Mahboobeh Darban (resident of internal medicine).

References