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Electrocardiographic, Cardiac Enzymes, and Magnesium in Patients With Severe Acute Pancreatitis

ABSTRACT

Severe acute pancreatitis (SAP) can lead to multiple-organ dysfunction syndrome (MODS). Electrocardiographic (ECG), cardiac enzyme, and serum magnesium abnormalities occur after SAP. Electrocardiographic and cardiac enzyme abnormalities are described as variables in SAP patients, which contribute to the effects of MODS. Hypomagnesemia is also closely associated with ECG abnormalities; therefore, hypomagnesemia was also considered to be a variable in this study. A consecutive series of 54 patients admitted within 72 hours after SAP occurred was studied. A standard 12-lead ECG, cardiac enzyme, and serum magnesium measurement were routinely performed at admission. Linear correlation was used to analyze the relationship between hypomagnesemia and sinus tachycardia. The nonparametric binomial test was used to analyze dichotomized dependent variables (premature beat, atrial fibrillation, ST-segment depression, abnormal T wave, and long QT interval). Hypomagnesemia was present in 15 patients (28%), who subsequently had sinus tachycardia. There was a significant negative relationship ($-1 < r < 0$) between hypomagnesemia and sinus tachycardia ($p < .05$). There were 14 (17%) premature beat, 7 (8%) atrial fibrillation, 21 (25%) ST-segment depression, 18 (21%) abnormal T wave, and 17 (31%) long QT-interval events in 54 SAP patients. Hypomagnesemia is a reason for ECG abnormalities. Electrocardiographic and cardiac enzyme abnormalities are considered to be transitory variables that are present in patients with SAP.

Acute pancreatitis (AP) is a common disease. About 25% of the individuals with AP will develop severe or life-threatening complications (Hartwig, Werner, Muller, Uhl, & Buchler, 2002). In AP, the acute inflammatory process of pancreas is associated with variable involvement of pancreatic and peripancreatic tissue. Severe acute pancreatitis (SAP) is associated with organ failure and local complications

such as necrosis and pseudocyst formation (Werner, Feuerbach, Uhl, & Buchler, 2005). Progression of the disease can lead to multiple-organ dysfunction syndromes (MODS), including pulmonary, cardiovascular, renal, and other systems. The reported incidence of organ failure in SAP varies from 28% to 76%, and the resulting mortality ranges from 28% to 69%. The occurrences of organ dysfunction and progressive organ failure have a major impact on outcome (Bai et al., 2007).

The cardiovascular system may be affected in all stages of AP with abnormalities of cardiac rhythm, contractility, and vasomotor tone of peripheral vessels (Yegenswaran, Kostis, & Pitchumoni, 2011). Acute pancreatitis is associated with a number of metabolic abnormalities such as hypokalemia, hypomagnesemia, and hypocalcemia, which may cause hemodynamic changes. Variations in patients with SAP have electrolyte disorders at admission that are related to SAP severity. Electrocardiographic (ECG) changes mimicking acute myocardial infarction in patients with AP have been reported in the literature (Khairy & Marsolais, 2001). Electrocardiographic abnormalities in AP patients have been described as ST-segment deviations

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and T-wave inversions, which mimic acute myocardial infarction. Around 50% of AP patients present ECG abnormalities due to electrolytes (Pezzilli, Barakat, Billi, & Bertaccini, 1999; Rubio-Tapia, Garcia-Leiva, Asensio-Lafuente, Robles-Diaz, & Vargas-Vorackova, 2005). Magnesium depletion, in general, is associated with changes in the ECG. Peaking of T waves has been described with modest magnesium loss, whereas more severe magnesium depletion can lead to prolongation of the PR and QT intervals, progressive widening of the QRS complex, and diminution of the T wave.

This study was undertaken in 54 hospitalized SAP patients with ECG and myocardial enzyme changes. Serum magnesium levels were reviewed for patients to establish a relationship between hypomagnesemia and the occurrence of ECG abnormalities in SAP patients.

Methodology

Sample

The study population consisted of 54 patients with SAP who were managed in the department of gastroenterology, gastroenterology surgery, and intensive care unit in the affiliated hospital of Ning Xia Medical University from January 2009 to March 2011. A consecutive series of 54 patients admitted within 72 hours after SAP was prospectively reviewed. All enrollment patients were diagnosed with SAP according to the Atlanta criterion (shock; systolic blood pressure < 90 mmHg; pulmonary insufficiency, $\text{PaO}_2 < 60$ mmHg; renal failure, creatinine level >2 mg/dL after rehydration; and gastrointestinal tract bleeding, >500 mL/24 hours). Acute Physiology and Chronic Health Evaluation (APACHE) II scores were also estimated as described previously (Bradley, 1993; Knaus, Draper, Wagner, & Zimmerman, 1985; Rocha et al., 2009). This time frame was chosen because the most pronounced ECG changes occur during the first 72 hours. At the same time, approximately one third to one half of the deaths in SAP occur during the first week as a result of progressive organs failure MODS (McKay, Evans, Sinclair, Carter, & Imrie, 1999).

An ECG was routinely done at admission, as was blood sampling, which included measurement of cardiac enzyme and magnesium by an American Beckman automatic biochemistry analytical instrument. For study purposes, the first ECG recording was used as well as data from the initial blood samples. Hypomagnesemia was defined as a serum magnesium level of 0.70 mmol/L. The study was approved by the NIngXia Committee on Research Ethics for the Protection of Human Subjects.

Statistical Analysis

The SPSS 10.5 package program (SPSS, Chicago, Illinois) was used to perform statistical analyses. The relation between serum magnesium and sinus tachycardia was

assessed with linear regression in which ECG abnormalities were taken as the dependent variable. The nonparametric binomial test was utilized to assess for dichotomized dependent variables (premature beat, atrial fibrillation, ST-segment depression, abnormal T wave, and long QT interval). A value of $p < .05$ was considered to be statistically significant.

Results

Patient Characteristics

Fifty-four patients were enrolled according to the Atlanta diagnosis criterion of SAP. Their mean age was 56 years (range = 34–78 years). Thirty-nine were male and 15 were female. The causes in SAP was (1) only alcohol ($n = 23$), (2) only gallstones ($n = 15$), (3) both alcoholic and gallstones ($n = 11$), and (4) idiopathic ($n = 5$). Of these, 32 patients had respiratory failure, 12 patients had acute renal failure, and 12 patients had both respiratory and renal failure (Table 1).

Electrocardiographic and Cardiac Enzyme Abnormalities

The patients' ECG findings were analyzed for ST-segment depression, T-wave abnormalities, QT interval, and arrhythmia. Cardiac enzyme included aspartate aminotransferase (AST), lactate dehydrogenase (LDH), creatine kinase (CK), creatine kinase MB (CK-MB), and troponin I (see Tables 2 and 3).

Serum Magnesium and Heart Rate

The linear correlation statistics were used to analyze the relationship between serum magnesium and heart rate (Figure 1). The results showed that low serum magnesium was related to the sinus tachycardia. Adjustment for age and gender did not essentially influence the relation.

Discussion

Severe acute pancreatitis is a commonly encountered and frequently occurring disease that harms the pancreas as well as other organs. Multiple-organ dysfunction syndrome and multiple organs failure are believed to be the main reasons for high mortality in SAP (Takeyama, 2005). Acute respiratory distress and acute renal failure are the most common complications. Cardiac-specific biomarkers and an ECG facilitate the diagnosis in specific circumstances (Korantzopoulos et al., 2005). In this study, focus was directed to the changes of ECG, cardiac enzymes, and serum magnesium in SAP patients.

Electrocardiographic Abnormalities and Hypomagnesemia

Systemic inflammatory response syndrome (SIRS) is the occurrence of at least two of the following criteria:

TABLE 1. Patient Characteristics ($N = 54$ Patients With Severe Acute Pancreatitis)

	<i>n</i> (%)
Age (years)	
30–40	10 (18%)
41–50	12 (22%)
51–60	20 (37%)
61–70	8 (15%)
>71	4 (8%)
Gender	M:F ratio = 3.08:1
Males	39 (73%)
Females	15 (27%)
Causes	
Only alcohol	23 (42%)
Only gallstones	15 (29%)
Alcohol and gallstones	11 (21%)
Idiopathic	5 (8%)
Organ systems failing	
Single etiology	
Pulmonary	32 (60%) (12 without ventilation, 20 with ventilation)
Renal	12 (23%) (7 without dialysis, 5 with dialysis)
Two etiologies	
Pulmonary and renal	12 (23%)
Death	6 (11%)

fever greater than 38.0°C or hypothermia less than 36.0°C, tachycardia greater than 90 beats/minute, tachypnea less than 20 breaths/minute, leucocytosis greater than $12 \times 10^9/L$, or leucopenia less than $4 \times 10^9/L$ (Dellingler et al., 2008). In this study, SIRS were associated with 88% of SAP patients. The SIRS in SAP is thought to be secondary to the release of mediators from the pancreas and adjacent tissues responsible for initiating and propagating the SIRS in remote organs (Gupta, Rajani, Primrose, & Johnson, 2001). Systemic inflammatory response syndrome, which induced SAP, was one of the reasons for ECG abnormalities such as sinus tachycardia.

Hypomagnesemia is associated with concomitant metabolic changes, coronary artery spasm, and ECG abnormalities (Fox, Ramsomair, & Carter, 2001). In

TABLE 2. Electrocardiographic (ECG) Abnormality in 54 Patients With Severe Acute Pancreatitis

ECG Characteristics	ECG Abnormality, <i>n</i> (%)	ECG Abnormality and Hypomagnesemia	<i>p</i> ^a
Premature beat	14 (17%)	8 (15%)	.001
Atrial fibrillation	7 (8%)	4 (7%)	.027
ST-segment depression	21 (25%)	9 (17%)	.004
Abnormal T wave	18 (21%)	11 (20%)	.000
Long QT interval	17 (31%)	10 (19%)	.005 ^a

^a*p* is based on the nonparametric binomial test.

this study, there were 15 SAP patients (27%) with the lower level of serum magnesium less than 0.7 mmol/L. At the same time, all patients with hypomagnesemia had sinus tachycardia. There was a significant negative relation ($-1 < r < 0$) between hypomagnesemia and sinus tachycardia through linear correlation statistics ($p < .05$). Electrolyte abnormalities were believed to be the main reason for subsequent ECG abnormalities, which occurred frequently (around 50%) in patients with pancreatitis (Patel, Movahed, & Reeves, 1994). Long QT interval, abnormal T waves, and ST-segment depression have been described with modest magnesium loss.

Of patients enrolled in this study, 17% had premature and 8% had atrial fibrillation. ST-segment depression and abnormal T-wave morphology were also discovered in 25% of SAP patients. There were no fatal cardiac arrhythmias. ST-segment and T-wave abnormalities were followed to ensure adequate recovery after organ perfusion. There was no indication that myocardial ischemia or infarction had occurred in SAP patients. Electrocardiographic changes return to normal once the patient recovers from SAP. This result was the same as related reports (Patel et al.,

TABLE 3. Cardiac Enzyme Abnormality in 54 Patients With Severe Acute Pancreatitis

Biochemistry Markers	<i>n</i> (%)
Aspartate aminotransferase > 100 IU/L	21 (39%)
Lactate dehydrogenase > 200 IU/L	32 (60%)
Creatine kinase > 180 U/L	19 (35%)
Creatine kinase MB > 0.3	9 (17%)
Troponin I	2 (4%)

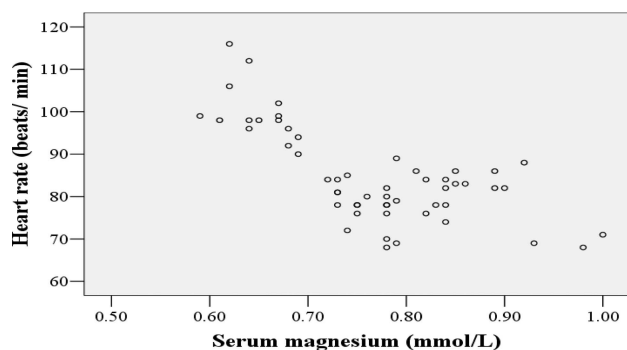


FIGURE 1. The relationship between serum magnesium and heart rate in patients with severe acute pancreatitis. There was a significant negative relation ($r = -.604$, $-1 < r < 0$) between hypomagnesemia and sinus tachycardia through linear correlation statistics ($p < .05$).

1994; Van de Walle, Gevaert, Gheeraert, DePauw, & Gillebert, 2006). Electrocardiographic abnormality is considered to be transitory in SAP patients.

Several cases were noted with ECG ST-segment depression suspected to be related to acute thoracoabdominal pain. This finding may lead to a vasculocardiology consultation and coronary angiography or thrombolytic therapy. There is a need to have a dynamic state to observe the ECG and cardiac enzyme changes.

Cardiac Enzyme Abnormalities

The level of serum enzymes that may arise from the heart was more frequently helpful than the ECG in evaluating the extent of cardiac damage and in predicting mortality in patients with myocardial infarction (Mayer et al., 1999). Cardiac enzyme markers including AST, LDH, CK, CK-MB, and troponin I were detected in this study after admission. Patients with SAP were frequently found to have higher levels of AST and LDH. Twenty-one of patients (39%) had values of AST > 100 U/L and 32 patients (60%) had values of LDH > 200 IU/L. Serum LDH and AST are derived not only from cardiac and skeletal muscle but also from liver and other tissues. Lactate dehydrogenase and AST are considered less helpful as indicators of myocardial damage and cannot be used as single indicators of myocardium injury.

Shinzeki et al. (2008) reported that the increase in LDH reflects cellular injuries. Lactate dehydrogenase has been reported to be a sensitive indicator of pancreatic necrosis (Isogai, Yamaguchi, Hori, & Kaneoka, 1998; Uhl, Buchler, Malfertheiner, Martini, & Beqer, 1991). In this study, six SAP patients who died were noted to have had a high level of LDH. The positive rate (LDH > 700 IU/L) was 65%, and the mortality rate of positive patients was 30% (Ogawa et al., 2002).

Of 54 patients, 19 (35%) had serum levels of CK that were greater than the normal level and 9 (17%) had serum levels of CK-MB that were greater than the normal level. Expressions of CK and CK-MB were not unique to the heart. They were found in skeletal muscle and the gastrointestinal tract. Thus, elevated CK-MB levels can occur because of analytical problems, trauma, rhabdomyolysis, myopathies, or renal failure (owing to a myopathy), or during the peripartum period (Babuín & Jaffe, 2005). As a result, CK and CK-MB cannot solely be utilized to judge myocardium injury.

Troponin assays are not only more sensitive but also more specific than CK-MB assays. Troponin I is considered the gold standard for detection of myocardial injury. In this study, two patients had elevated troponin I and the outcome was death. There were variables that were similar in the prior cases mentioned, which also had mortality as an outcome. The first similarity noted was the extent of pancreas necrosis on computer tomographic scan of the abdomen within 48 hours after admission. The second noted similarity was the extent of organ failure to both lungs and kidneys. The third noted similarity was aged men. There is a correlation between the extent of necrosis and organ failure (Garg et al., 2005).

In a recent study, the age of the patients and comorbidity were shown to be strong predictors of multiorgan failure and early death (Frey, Zhou, Harvey, & White, 2007). At present, all studies are consistent in acknowledging the fact that elevation of cardiac troponin carries prognostic significance (Collinson & Gaze, 2005). The disagreement within the literature concerns whether the troponin elevation is an independent risk predictor or whether it is an organ system failure marker. If the latter, it would be expected to be a dependant variable within an organ system failure score and therefore a univariate predictor rather than a multivariate predictor. There are published data to support both arguments (Wu et al., 2004). In spite of these arguments, the researchers believe that it is necessary to monitor the dynamic changes with ECG and cardiac enzyme SAP patients. These markers should be associated to estimate the severity and mortality of SAP, not only one factor.

Summary

In patients with SAP, lower serum magnesium concentrations are associated with ECG abnormality. The advice for clinical practice in patients with ECG changes after SAP is to measure serum magnesium. The principle of the initial treatment of SAP is monitoring vital signs, adequate fluid and electrolyte replacement, and nutritional support. Magnesium therapy might be worthwhile and should be the focus of further study.

There is a need for further evidence to prove ECG and cardiac enzyme abnormalities as potentially serious cardiac complications or clinical outcome. Further recommendations are to monitor ECGs, cardiac enzymes, and serum magnesium to prevent any fatal arrhythmia taking place during the first week of admission in SAP. ❖

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