Comparison of Creatine Kinase Activity and Myoglobin Blood Level in Acute Myocardial Infarction Patients

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Abstract

The aim of this prospective study was to evaluate and compare the relative increase of serum myoglobin level and total creatine kinase (CK) activity in acute myocardial infarction (AMI) patients (n=36). We measured serial changes in total CK activity and myoglobin serum level in three-time periods (6-9 hours, 24 hours and 6-7 days) from chest pains onset. Myoglobin peaked during the first 6-9 hours but total CK reached its peak activity after 24 hours from AMI symptoms onset. Results of this study showed that as non-specific cardiac marker myoglobin had better sensitivity and earlier rise in serum than total CK activity in AMI patients. Rapid kinetic of myoglobin level is important for its utility as marker for re-infarction diagnosis. Early myoglobin increase in serum is important for early triage of AMI patients and early "ruling out" of AMI diagnosis if there is no evidence of its elevation in circulation.

KEY WORDS: myoglobin, creatine kinase, acute myocardial infarction

Introduction

Diagnosis of AMI is based on clinical features, (presence of risk factors), electrocardiogram (ECG) changes and levels of cardiac biomarkers. Necrotic cells of heart muscle release a variety of enzymes and proteins that can be measured in peripheral blood. Intracellular concentration, fractional release and normal serum levels determine the relative increase of a marker molecule in blood (1). Biochemical testing for the AMI diagnosis is rapidly changing from traditional enzymatic assay to immunoassay of more sensitive markers (2). Serial measurement of biochemical markers is now accepted universally as an important determinant in "ruling in" or "ruling out" of AMI diagnosis. "Rule in" of AMI diagnosis requires a high diagnostic

specificity while "rule out" a high diagnostic sensitivity of cardiac marker (3). For many years, CK (E.C.2.7.3.2.) was used together with ECG to confirm the presence of myocardial infarction. The physiological role of CK enzyme is maintenance of an adequate store of high-energy phosphorylated creatine, which is used to restore adenosine triphosphate (ATP) levels depleted during muscle contraction. Elevation in total CK is not specific for myocardial injury, because the most of CK is located in skeletal muscle and elevations are possible from variety of non-cardiac conditions (4, 5, 6). Peak levels of CK typically occur from 12-24 hours after the onset of chest pain and decline to normal by about 3 days. Myoglobin was the first serum cardiac marker that was not an enzyme or an isoenzyme. It is relatively small (17, 8 kDa) heme protein and transports oxygen within muscle cells. Myoglobin constitutes about 2 % of muscle protein in both skeletal and cardiac muscle (7). Because of its low molecular weight, myoglobin is rapidly released into the circulation and is the first marker to rise after an AMI. Very little free myoglobin circulates as result of natural protein turnover. Serum myoglobin levels are elevated in conditions unrelated to AMI, such as skeletal muscle, neuromuscular disorders, renal failure, intramuscular injection, strenuous exercise and in presence of various toxins and drugs (8, 9). During the course of a myocardial infarction, myoglobin escapes from the ischaemic cardiac muscle and can reach levels 5-10 times from normal during the first 5-18 hours. It is rapidly removed from circulation, filtered through the glomerular membrane of the kidney, and excreted in the urine (10). Rapid kinetic of myoglobin serum level is important for its utility as marker for reperfusion (11) and re-infarction diagnosis (12). Myoglobin precedes the total creatine kinase serum elevations. The diagnosis of AMI might be made earlier if serum myoglobin levels are measured.

Objective

The aim of this prospective study was to evaluate and compare the relative increase of serum myoglobin level and total CK activity in AMI patients. We analyzed their relative increase and window-time duration in serum. We have made effort to detect the time of the highest diagnostic significance in AMI diagnosing by measuring total CK activity and myoglobin serum concentration.

Patients and Methods

PATIENTS

The prospective study included 36 patients with confirmed AMI diagnosis (20 males and 16 females, age range 54 -75 years). They were randomized in three groups according to the time from the chest pains onset: group I (6-9 hours); group II (24 hours) group III (6-7 days). Control group represented a healthy subjects (n=12; 6 males and 6 females).

METHODS

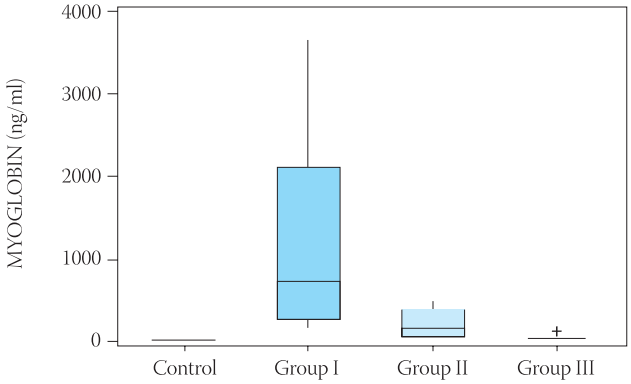
Venepuncture was performed on each patient and blood samples were drawn within 6-9, 24 hours and 6-7 days after the onset of chest pains. Samples were centrifuged at 4000 r.p.m. for 10 minutes to separate the serum and it was used immediately for the measurement of total CK activity and myoglobin serum concentration. The Ethical Committee of our institution approved the protocol of this study. Myoglobin was measured with the Abbott immunoassay system (Microparticle Enzyme Immunoassay) using AxSYM analyzer. The upper reference limit was 116 ng/ml. Total CK activities in serum were measured at 30°C with N-acetylcysteine-activated reagents (Chronolab) used Flexor analyzer. The upper reference limit was 1,78 μkat/l.

STATISTICAL ANALYSIS

The data were evaluated statistically by using Kruskal-Wallis test and post-hoc Tukey test. Variable are described in terms of summary statistics (median, first and third quartile, minimum and maximum). Significance was assumed at a probability value of $p<0,05$.

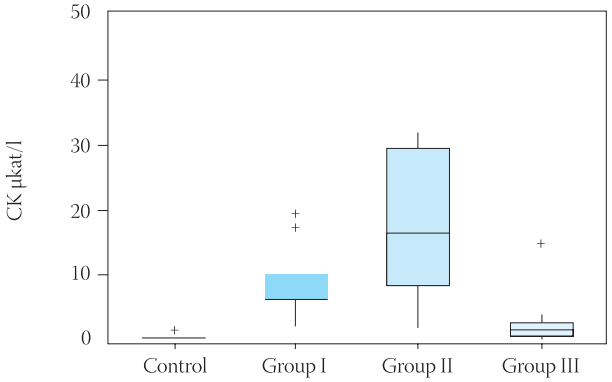
Results

Median age of patients included in study was 61 varying from 54 to 75. Myoglobin peaked during the first 6-9 hours from onset of ischaemic symptoms (Figure 1.). Kruskal-Wallis test showed statistically significant difference in all groups ($H=38,640$; $p<0,00001$). Post-hoc Tukey test showed significant difference between group I and II versus control group ($p<0,01$). There was no difference between group III and control group $p>0,05$. Post-hoc Tukey test showed statistically significant difference $p<0,01$ between group I and III. Total CK reached its maximum value 24 hours from ischaemic symptoms onset (Figure 2.) Kruskal-Wallis test showed statistically significant difference in all groups ($H= 32,906$; $p<0,00001$). Post-hoc Tukey test showed significant difference between group II and I versus control group ($p<0,01$). There was no difference between group III and control group. Difference between group I and III was $p<0,05$ and group II and III $p<0,01$. We compared relative increase of serum myoglobin level



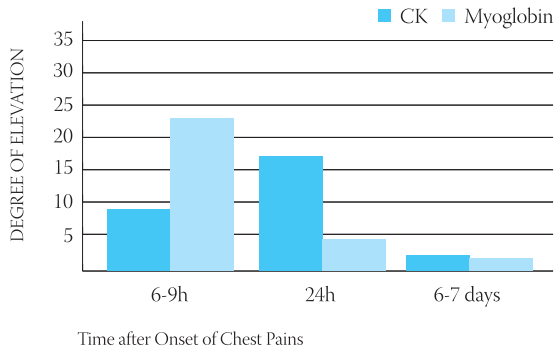
Horizontal lines indicate 25%-quartile (Q1, inferior end of the line) and 75%-quartile (Q3, upper end of the line) of the median value. The middle horizontal line represents median value. Vertical lines indicate distance between minimal and maximal values. + indicates extreme values in the group. Myoglobin concentration is expressed in ng/ml.

FIGURE 1. Myoglobin serum level of AMI patients group I, II and III



Horizontal lines indicate 25%-quartile (Q1, inferior end of the line) and 75%-quartile (Q3, upper end of the line) of the median value. The middle horizontal line represents median value. Vertical lines indicate distance between minimal and maximal values. + indicates extreme values in the group. Total CK activity is expressed in µkat/l.

FIGURE 2. Total CK serum activity of AMI patients group I, II and III



Columns show elevation degree of median serum myoglobin concentration and total CK activity values in all AMI patients groups (after 6-9, 24 hours and 6-7 days) versus median myoglobin serum concentration and total CK activity values of control group.

FIGURE 3. The comparison of total CK activity and myoglobin serum level in AMI patients

and total CK activity in AMI patients (Figure 3.) in three time periods from AMI symptoms onset. Myoglobin median value within 6-9 hours was 31-times higher than median value of healthy control group. In the same time, CK activity in serum was 12,5-times higher than control. After 24 hours from symptom onset myoglobin blood level represented as median value is 7,29-times higher than control. In this time CK had a higher sensitivity than myoglobin because its median value was 23,7-times higher than control. In AMI patients of group III (after 6-7 days) levels of both markers returned to normal range.

DISCUSSION

Acute myocardial infarction, as the most complicated form of acute coronary syndrome, is one of the leading

causes of mortality in the world. Biochemical markers had essential importance in "ruling in" or "ruling out" of AMI diagnosis. Insufficient sensitivity of specific cardiac markers in early hours from ischaemic symptoms onset requires using non-specific markers that have higher sensitivity compared to specific markers. Myoglobin was introduced as an early marker, but most studies have not compared it to total CK. The total CK is a simple, fast and inexpensive test that is available for usage on many laboratory instruments. From a physiologic point of view, CK and myoglobin are similar. They are both cytoplasmic proteins and both depend on gender, race and age. Myoglobin is low molecular weight protein (17,8 kDa). Its half-life is 1-3 hours when glomerular filtration rate is normal (13). Molecular weight of CK is about 80 kDa and its half-life is approximately 36 hours (13). In our investigation we obtained wide variation of levels of observed two markers in single patient groups. Vary ranges of marker in heart tissue content cause difference in blood levels of marker among patients. Swaanenburg and co-workers found significant differences in the content, expressed per gram wet weight tissue, in the right and left ventricles for troponin I, troponin T, myoglobin and α-hydroxybutiric acid dehydrogenase (14). Different myocardial infarction size between patients can be one of the causes of vary blood levels of both markers in single AMI groups (15). Myoglobin peaked during the first 6-9 hours from onset of ischaemic symptoms. Our results showed that myoglobin serum concentrations, in some patients of group II, were not in the reference range. It points on slower myoglobin elimination from circulation and is caused by a possible large infarction or renal insufficiency (16, 17). During the first 6-9 hours CK showed elevation of activity but reached its maximum 24 hours from ischaemic symptoms onset. Extreme values of myoglobin concentration and total CK serum activity in groups can be caused by non-cardiac conditions (18,6). Results of this study showed greater elevation degree of myoglobin concentration in serum after 6-9 hours from onset of AMI symptoms in comparison with CK serum activity. After 24 hours blood myoglobin level shows rapid myoglobin elimination from circulation except in some patients with large infarction or renal insufficiency. According to our presented results, we consider myoglobin as more sensitive marker then CK. Lim and co-workers had the same result in their investigation (19). Better sensitivity and earlier rise of blood myoglobin is caused by its higher heart tissue content, lower molecular weight and shorter blood half-life in comparison with CK.

Conclusion

This prospective study showed that myoglobin, as non-specific cardiac marker, had earlier rise and better sensitivity in AMI patients compared to total CK activity. Early myoglobin increase in serum is important for early triage of AMI patients and early "ruling out" of AMI diagnosis if there is no evidence of its elevation in circulation. Myoglobin is favorable marker of reperfusion for its rapid kinetic. Rapid myoglobin release-kinetic is important for its utility as marker for re-infarction diagnosis. Myoglobin measurement should be used together with cardiac specific marker measurement for finally AMI diagnosing, because of its poor cardiac specificity.

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