Impact of plasma neutrophil gelatinase-associated lipocaline level on early outcome of a patient with ST-segment elevation myocardial infarction

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Article History:
Received on: 15.03.2019
Revised on: 22.06.2019
Accepted on: 26.06.2019

Keywords:
Neutrophil gelatinase-associated lipocaline, ST-elevation myocardial infarction, atherosclerosis

ABSTRACT
In patients with the atherosclerotic arteries, Neutrophil gelatinase-associated lipocaline (NGAL) may play a part in vascular remodeling and the instability of atherosclerotic plaques. Patients with angiographically documented coronary artery disease have significantly higher levels of serum NGAL compared with persons with normal coronary arteries. This study aims to determine the short term prognostic value of NGAL serum levels in a patient with acute ST-segment elevation myocardial infarction. This study enrolled twenty patients with acute ST-elevation myocardial infarction (STEMI) and twenty healthy subjects as control. Serum NGAL level was compared between the patients and control and then correlated with early outcome of the patients. There was a significant elevation of serum NGAL in STEMI patients compared with control, and significant relationship was observed between admission serum NGAL early complications and mortality. High NGAL level associated with poor outcome in STEMI patients and can be used as initial indicator for close monitoring of high-risk patients.

INTRODUCTION
The atherosclerotic disease can now be defined as a chronic inflammatory disease with phases of cyclical activities of varying size in different individuals. In other words, a subject may be suffering from atherosclerotic plaques of different severity, with the variable extent of inflammation, different degree of activation of inflammatory cells, and different plaque composition. Inflammatory cells (foam cells and T lymphocytes) are present in the early stages of atherogenesis (Ross, 1999).

The usual initial event in acute myocardial infarction is the atheromatous plaque rupture and thrombus formation. Inflammatory mediator including C-reactive protein (CRP), cytokines, interleukins, and activated neutrophils, are involved in the development and rupture of the plaques (Smith et al., 2006) (Ikonomidis et al., 2012).

Neutrophil gelatinase-associated lipocalin (NGAL) is one of the lipocalin proteins that participate in ligand transport. Human NGAL was first isolated in 2003 by Mishra et al. inside the specific granules of neutrophils (Mishra et al., 2003).
rrial infections (Schmidt-ott et al., 2007). However, NGAL is highly affected by various pathological conditions, making it a useful biomarker of various disease states. It is one of the sensitive markers of acute renal injury, because of rapid release after tubular damage. However, a recent evidence highlights an important role for NGAL in cardiovascular diseases like myocardial infarction and heart failure. (Buonafine et al., 2018).

When NGAL binds with the matrix metalloproteinase-9 (MMP-9) results in the formation of a complex that plays an important role in atherosclerotic plaque erosion and thrombus formation (Hemdahl et al., 2006). The process involves the degradation of several components of the basement membrane, including type I gelatin and collagen types I, IV, V and XI (Triebel et al., 1992).

In patients with the atherosclerotic arteries, NGAL may play a part in vascular remodeling and the instability of atherosclerotic plaques (TeBoekhorst et al., 2011).

NGAL both in the free-form and in combination with MMP-9 have been detected in atherosclerotic plaques of the arterial media, and the concentration of NGAL/MMP-9 complex was higher in the plaques with intramural hematoma and central necrosis. Patients with angiographically documented coronary artery disease have significantly higher levels of serum NGAL compared with persons with normal coronary arteries (Hemdahl et al., 2006) (Kalousek et al., 2006).

This study aims to determine the short term prognostic value of NGAL serum levels in patient with acute ST-segment elevation myocardial infarction (STEMI).

PATIENTS AND METHODS

This is study enrolled twenty patients with acute STEMI, who were admitted to CCU in Al-Sader teaching hospital, between July 2018 and November 2018. Males comprised (75%) of the entire study population, patient’s age ranged from 40 to 71 years, with a mean of (51.6 ± 9.4). The study also included twenty healthy subjects as control, aged 51.4 ± 10.6 years, and 20% were male.

Diagnosis of acute STEMI was based on clinical picture (chest pain start within 24 hr), typical ECG changes, and positive serum troponin I. Exclusion criteria were history of heart failure, renal impairment, systemic infection, malignancy, and pancreatitis.

Blood samples were collected from venous access for NGAL determination and stored at below zero degree centigraide for subsequent processing using ELISA method at the bioelisa-reader ELX800 device using the Human Lipocalin-NGAL kit (bioassay technology laboratory, Cat. No.E1719Hu). Applying the four-parameter calculation method, a standard curve was established, and the results were calculated based on this curve in terms of ng/ml.

The studied patients were admitted to C.C.U, treated according to ACS guidelines and followed for an average of 5 days for early complications and death. All patients were subjected for daily history, clinical examination, ECG, and echocardiography. Informed consent was taken from the patients or their first-degree relatives.

Statistical Analysis

SPSS® Software (version 23.0 for Linux®) was used to perform statistical analysis. Comparison of study groups was carried out using the chi-square test for categorical data and using Student’s t-test and Mann-Whitney U test for continuous data. Correlations were assessed using Spearman’s rank-order correlation for ordinal variables, and Pearson’s product-moment correlation coefficient for continuous variables.

RESULTS AND DISCUSSION

Level of neutrophil gelatinase-associated lipocalin (NGAL) has been compared between patients with STEMI and healthy control, and there was a statistically significant difference (P-value < 0.001).Table 1

| Group          | NGAL level ng/ml | P-value         |
|----------------|------------------|-----------------|
| STEMI patients | 109.37 ± 250.40  | 11.64 – 1105.59 < 0.001 |
| Control (n=20) | 4.39 ± 3.39      | 0.16 – 11.64    |
| Mann-Whitney U test = 0.50, P < 0.001 |

Early complications and mortality of STEMI patients during the follow-up period were reported in the Table 2. There was a significant relationship between the level of NGAL and incidence of complications and mortality rate (P-value = 0.002), and (P = 0.003) respectively. Table 3

In this study, we did compare the relation between NGAL level and an ejection fraction of the STEMI patients, and there was a statistically significant re-
Table 2: Early complications and mortality rate among STEMI patients.

| Type of the complications | Number | Percentage |
|---------------------------|--------|------------|
| Cardiogenic shock         | 2      | (10%)      |
| Cardiac standstill        | 1      | (5%)       |
| Ventricular Fibrillation (VF) | 2   | (5%)       |
| Pulmonary Edema           | 3      | (15%)      |
| Ventricular Tachycardia   | 1      | (5%)       |
| Hypotension + Bradycardia | 1      | (5%)       |
| Frequent ventricular ectopic | 1    | (5%)      |
| All causes mortality      | 3      | (15%)      |

Table 3: The relation between NGAL level and early complications among STEMI patients

| Complications | NGAL level ng/ml | P-value |
|---------------|------------------|---------|
| Mean          | SD               |         |
| Yes (n=11)    | 180.58 326.43    | 0.002   |
| No (n=9)      | 22.34 14.91      |         |
| Mann-Whitney U test = 8.00, P = 0.002 |

Table 4: The relation between NGAL level and mortality rate among STEMI patients

| Mortality | NGAL level ng/ml | P-value |
|-----------|------------------|---------|
| Mean      | SD               |         |
| Yes (n=3) | 428.72 474.62    | 0.003   |
| No (n=17) | 29.53 19.26      |         |
| Mann-Whitney U test = 1.00, P = 0.003 |

The most important cause of coronary thrombosis and ischemic heart disease include myocardial infarction is the rupture of atheromatous plaque. Inflammation has a key role in the mechanism of atherosclerosis and plaque instability. In this study, we found a significant rise in serum NGAL level in STEMI patients compared with control subjects. 

(Zografos et al., 2009) observed a significant elevation of NGAL level in a patient with coronary artery disease and also detected a significant correlation between NGAL levels and the severity of the coronary disease.

In another study by (Choi et al., 2008) who compared 49 CAD patients with 42 age and gender-matched control subjects, also demonstrated a significant correlation between NGAL level and CAD, and the suggest that the measurement of serum NGAL levels may be a useful bio marker for assessing CAD risk.

In the present study also there was significant relation between NGAL level and early complications and mortality rate in STEMI patients. A meta-analysis study by Fan Y1 and (Fan and Zou, 2019) concluded that STEMI patients with high NAGL levels had higher risk of mortality and major adverse cardiovascular events (MACEs).

Finally, in the current study there was inverse relationship between serum NGAL level and ejection fraction measured by echocardiograph for STEMI patients along their stay in the CCU.

(Alvelos et al., 2013) studied the prognostic value of serum NAGL level in patients with acute heart failure, and found poor short term prognosis in patients with acute heart failure and high NAGL level, in the form of mortality rate and re-hospitalization.

CONCLUSION

High NGAL level associated with poor outcome in STEMI patients and can be use as initial indicator for close monitoring of high-risk patients.
CONFLICT OF INTEREST
The authors declare that they have no competing interests.

FUNDING SOURCE
University funding was provided for: data collection, analysis, and interpretation; trial design; patient recruitment. No public funding was received.

ACKNOWLEDGEMENTS
The authors would like to thank volunteers and all the participants in this study for their kind permission and cooperation, time, understanding and efforts which made this study possible, and also appreciate the staff of the Al-Sadder Teaching Hospital / CCU.

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