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The endogenous intoxication phenomenon in patients with Q-Myocardial infarction

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Abstract
The aim of this study was to exam of inflammation level in patients with STEMI and arterial hypertension (AH) by evaluation of endogenous intoxication phenomenon. We observed of 130 patients with STEMI with or without AH. The level of endogenous intoxication measured by sorption ability of erythrocytes (SAE) method was similar in STEMI patients with or without AH, but was higher than in control group. The moderate correlation between SAE and resting HR was established in patients with STEMI and without essential AH. In STEMI patients without AH we observed the moderate direct correlation between SAE and some Echocardiography parameters (see table 5): EDS (r_s= 0.55, p<0.001), ESS (r_s= 0.52, p<0.001), EDV (r_s= 0.50, p<0.001), ESV (r_s= 0.53, p<0.001) and LVEF (r_s= 0.40, p=0.012).

Keywords: Myocardial infarction, inflammation, endogenous intoxication

1. Introduction
Over the past decades, mortality and morbidity from cardiovascular diseases (CVD) have declined in several developed countries, whereas they appear to have increased substantially in many developing countries [1, 2]. The mortality, incidence, and clinical presentation of CVD tend to vary greatly over the time. ST-segment elevation myocardial infarction (STEMI) is one of the common causes of cardiac admission at emergency departments and currently accounts for the high burden on health care services [3].

At present time there are a lot of risk factors caused of myocardial infarction (MI). The most relevant finding of the INTERHEART study was the determination of 9 risk factors that accounted for over 90% of the population attributable risk of the first acute MI. Moreover, those factors were easily measured and collected by standardized electronic data capture forms, and were considered potentially modifiable, which included the following by decreasing odds ratio: raised ApoB/ApoA1 ratio (3.25), current smoking status (2.87), psychosocial factors (2.67), diabetes (2.37), history of hypertension (1.91), abdominal obesity (1.12), alcohol consumption (0.91), regular physical activity (0.86), and daily consumption of fruits and vegetables (0.70), indeed all factors being significantly associated with acute MI (p<0.0001 for all risk factors and p = 0.03 for alcohol) [4].

In the 1980s and 1990s, experimental evidence derived predominantly from large animal studies suggested that postinfarction inflammation may accentuate ischaemic myocardial injury in the reperfused heart; thus, inhibition of inflammatory signals was considered a potentially promising therapeutic target [5]. In the infarcted heart, sudden necrosis of a large number of cardiomyocytes results in release of their intracellular contents and initiates an intense inflammatory reaction. Several distinct, but overlapping, pathways play a role in activation of postinfarction inflammation. Necrotic cardiomyocytes (CM) and damaged extracellular matrix release danger signals (DAMPS) triggering the complement cascade and activating TLR/IL-1 signalling. Resident mast cells degranulate and release preformed pro-inflammatory mediators, whereas activation of endothelial cells and fibroblasts results in induction of chemokines and cytokines. Leucocytes are recruited in the infarcted heart through activation of a multistep adhesion cascade. Circulating neutrophils are captured by the activated endothelium and roll on the endothelial surface through interactions that involve the selectins. Neutrophils 'sense' chemokines immobilized on the endothelial surface and exhibit integrins activation. Firm adhesion of the leucocyte to the endothelium follows through interactions that involve integrins and ICAM-1. Transmigration of the neutrophils across the endothelial layer is a complex process that involves the JAMs, ICAM-1 and VE-cadherin. After extravasation into the infarct, neutrophils play an important role in clearance of the tissue from dead cells and matrix debris [6-9].

The aim of this study was to exam of inflammation level in patients with STEMI and arterial hypertension (AH) by evaluation of endogenous intoxication phenomenon.

2. Material and Methods: We observed of 130 patients with STEMI. The validation of MI was based on information on medical history, symptoms, electrocardiograms, and cardiac enzymes. STEMI was diagnosed by a cardiologist when new or presumed new ST-segment elevation ≥1 mm (≥2 mm in V1 to V3) was seen in any location in two or more contiguous leads or new left bundle branch block was found on the index or qualifying electrocardiograms with ≥1 positive cardiac biochemical marker of necrosis, including cardiac troponin measurements.

All observed patients were divided into two groups: with essential AH (70 persons) and without AH (60 persons).

30 apparently healthy persons were included into control group.

Resting heart rate (HR), systolic (SBP) and diastolic blood pressure (DBP) were measured due current recommendations.

Echocardiography was performed at baseline and within 6 months. All measurements were made according to the recommendations of the American Society of Echocardiography (ASE) and the European Association of Echocardiography [10].

The endogenous intoxication was evaluated by method of sorption ability of erythrocytes [11].

The results were reported as mean ± standard error of mean or median with interquartile range (whenever the data did not appear to have normal distribution) for the quantitative variables, and the categorized variables were summarized as frequencies and percentages. The groups were compared using the Student's t-test or Mann-Whitney U for the continuous variables, and the $\chi 2$ test for the dichotomous variables. This study was done with the power of 90%. P values of 0.05 or less were considered statistically significant. All the statistical analyses were carried out via Statistica 12.0 (StatSoft, Tulsa, OK, USA).

The study was performed in accordance with the Helsinki Declaration and Good Clinical Practice Guideline. The study was approved by the local ethics committee and written informed consent was obtained from all patients.

3. Results and Discussion: The average age of all observed patients with STEMI was (64,96±12,94) years. Among all patients 78 persons (60.0 %) were males.

No differences between HR were observed in both groups (see table 1): (80.73±2.95) bpm – in patients without AH and (79.39±1.43) bpm – in patients with essential AH (p=0.65). But we founded of blood pressure inequality: SBP was (125.0±1.58) mm Hg and (161.69±2.91) mm Hg relatively (p<0.001), and DBP – (81.12±2.39) mm Hg or (94.60±1.60) mm Hg (p<0.001).

Table 1: The main hemodynamic parameters in patients with STEMI

Parameters (M±m)	STEMI (n=60)	STEMI + AH (n=70)	p
HR, bpm	80.73±2.95	79.39±1.43	0.65
SBP, mm Hg	125.0±1.58	161.69±2.91	<0.001
DBP, mm Hg	81.12±2.39	94.60±1.60	<0.001

Notes: STEMI - ST-segment elevation myocardial infarction, AH – essential arterial hypertension, HR – heart rate, SBP – systolic blood pressure, DBP – diastolic blood pressure

The level of endogenous intoxication measured by sorption ability of erythrocytes (SAE) method was similar in STEMI patients with or without AH (see table 2), but was higher than in control group - (24,56±0,58) % (p<0,01).

Table 2: The level of endogenous intoxication in patients with STEMI

Parameters (M±m)	STEMI (n=60)	STEMI + AH (n=70)	p
SAE, %	40.89±0.72	39.88±0.43	0.21

Notes: STEMI - ST-segment elevation myocardial infarction, AH – essential arterial hypertension

No differences in Echocardiography parameters were observed in both groups' patients with STEMI (see table 3).

Table 3: The Echocardiographic parameters in patients with STEMI

Parameters Me [IQR]	STEMI (n=60)	STEMI + AH (n=70)	p
Left atrium diameter, cm	3.91 [3.4; 4.3]	3.87 [3.5; 4.2]	0.54
EDS, cm	5.14 [4.7; 5.8]	5.16 [4.65; 5.5]	0.76
ESS, cm	3.95 [3.4; 4.3]	3.79 [3.25; 4.15]	0.99
EDV, ml	138.73 [102.0; 167.0]	130.11 [102.0; 147.0]	0.88
ESV, ml	72.47 [48.0; 83.0]	60.02 [41.0; 70.5]	0.77
Septal thickness, cm	1.12 [0.9; 1.3]	1.18 [1.0; 1.28]	0.88
Stroke volume, ml	65.07 [48.0; 79.0]	67.53 [56.0; 79.0]	0.23
LVEF, %	49.73 [48.0; 52.0]	54.0 [49.0; 58.0]	0.55

Notes: STEMI - ST-segment elevation myocardial infarction, AH – essential arterial hypertension, ESS - end-systolic size, EDS - end-diastolic size, ESV - end-systolic volume, EDV - end-diastolic volume, LVEF - ejection fraction of left ventricle

The moderate correlation between SAE and resting HR was established in patients with STEMI and without essential AH: r=0.40, p=0.012 (see table 4).

Table 4: The correlation between SAE and main hemodynamic parameters in patients with STEMI

Parameters	STEMI (n=60)	STEMI + AH (n=70)	p
HR	r=0.40, p=0.012	r=0.12, p=0.19	0.047
SBP	r= -0.04, p=0.87	r= -0.06, p=0.5	0.46
DBP	r= -0.03, p=0.91	r=0.04, p=0.69	0.48

Notes: STEMI - ST-segment elevation myocardial infarction, AH – essential arterial hypertension, HR – heart rate, SBP – systolic blood pressure, DBP – diastolic blood pressure, SAE - sorption ability of erythrocytes

In STEMI patients without AH we observed the moderate direct correlation between SAE and some Echocardiography parameters (see table 5): EDS (r_s= 0.55, p<0.001), ESS (r_s= 0.52, p<0.001), EDV (r_s= 0.50, p<0.001), ESV (r_s= 0.53, p<0.001) and LVEF (r_s= 0.40, p=0.012).

Table 5: The correlation between SAE and main Echocardiographic parameters in patients with STEMI

Parameters	STEMI (n=60)	STEMI + AH (n=70)
Left atrium diameter	r_s= 0.08, p=0.62	r_s= -0.09, p=0.33
EDS	r_s= 0.55, p<0.001	r_s= 0.16, p=0.12
ESS	r_s= 0.52, p<0.001	r_s= 0.11, p=0.22
EDV	r_s= 0.50, p<0.001	r_s= 0.16, p=0.12
ESV	r_s= 0.53, p<0.001	r_s= 0.09, p=0.38
Septal thickness	r_s= 0.06, p=0.72	r_s= -0.11, p=0.29
Stroke volume	r_s= -0.13, p=0.44	r_s= 0.12, p=0.26
LVEF	r_s= 0.40, p=0.012	r_s=-0.09, p=0.36

Notes: STEMI - ST-segment elevation myocardial infarction, AH – essential arterial hypertension, ESS - end-systolic size, EDS - end-diastolic size, ESV - end-systolic volume, EDV - end-diastolic volume, LVEF - ejection fraction of left ventricle, SAE - sorption ability of erythrocytes

In our study we established that STEMI is accomplished by endogenous intoxication. This phenomenon is not depended from essential AH. These results are in accordance with small trial where 56 patients with acute Q-wave MI were observed [12]. Blood levels of creatine phosphokinase (KK), total and effective albumin (TA, EA), middle-mass molecules (MMM), white blood cells (WBC), and WBS subpopulations were measured. On this basis, albumin binding reserve (ABR), toxicity index (TI), intoxication coefficient (IC), WBC intoxication index (WBC II) were calculated. Increased toxemia levels were observed through the whole study period. WBC, WBC II, KK levels peaked in the first 1-2 days of MI. TI and MMM levels were constantly increased (for at least 2 weeks), corresponding to clinical status severity.

In our case SAE had influence on HR and myocardium remodeling. It's known that resting HR is associated with markers of chronic low-grade inflammation. In 6518 healthy subjects from the the Danish general population were followed for 18 years underwent assessment of baseline HR, conventional cardiovascular risk factors, high-sensitivity C-reactive protein (hsCRP), and fibrinogen. RHR was associated with hsCRP and fibrinogen in uni- and multivariate models (p<0.0001). A 10 beats per minute increase in RHR was associated with increased cardiovascular and all-cause mortality in univariate models – HR (95%CI) (1.21 (1.14–1.29) and 1.15 (1.11–1.19); multivariate models adjusted for conventional risk factors – 1.16 (1.09–1.24) and 1.10 (1.06–1.14); multivariate models including hsCRP – 1.14 (1.07–1.22) and 1.09 (1.05–1.14); fibrinogen – 1.15 (1.07–1.22) and 1.09 (1.05–1.14); and both hsCRP and fibrinogen – 1.14 (1.07–1.22) and 1.09 (1.05–1.14) [13]. Furthermore, meta-analysis of 46 studies, involving 1 246 203 patients and 78 349 deaths for all-cause mortality, and 848 320 patients and 25 800 deaths for cardiovascular mortality. The relative risk with 10 beats/min increment of resting heart rate was 1.09 (95% CI 1.07–1.12) for all-cause mortality and 1.08 (95% CI 1.06–1.10) for cardiovascular mortality. Compared with the lowest category, patients with a resting heart rate of 60–80 beats/min had a relative risk of 1.12 (95% CI 1.07–1.17) for all-cause mortality and 1.08 (95% CI 0.99–1.17) for cardiovascular mortality, and those with a resting heart rate of greater than 80 beats/min had a relative risk of 1.45 (95% CI 1.34–1.57) for all-cause mortality and 1.33 (95% CI 1.19–1.47) for cardiovascular mortality [14].

4. Conclusion

STEMI is accomplished by endogenous intoxication. This phenomenon is not depended from essential AH. SAE has influence for resting HR and myocardium remodeling.

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