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Regular paper

Interindividual variability of atorvastatin treatment influence on the *MPO* gene expression in patients after acute myocardial infarction

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Myeloperoxidase (MPO) and C-reactive protein (CRP) may play critical roles in generation of oxidative stress and the development of the systemic inflammatory response. The aim of the study was to determine the effect of atorvastatin therapy on the *MPO* gene expression and its plasma level in relation to lipids level lowering and an anti-inflammatory response in patients after acute myocardial infarction. The research material was represented by 112 samples. Thirty-eight patients with first AMI receiving atorvastatin therapy (40 mg/day) and followed up for one month were involved in the study. The relative *MPO* gene expression in peripheral blood mononuclear cells (PBMCs) was examined using RT-qPCR in 38 patients before-, 38 patients after-therapy and in 36 patients as the control group. The plasma concentrations of MPO and serum concentrations of biochemical parameters were determined using commercially available diagnostic tests. After one month of atorvastatin therapy, in 60.5% patients a decrease of *MPO* gene expression, whereas in 39.5% patients an increase, was observed. The plasma MPO levels behaved in the same way as the *MPO* gene expression. However, the serum lipids and CRP concentrations were significantly lower after one month of atorvastatin therapy in both groups of patients — with decreased and increased *MPO* gene expression. Atorvastatin exhibited a different effect on *MPO* gene expression and its plasma level. Short-term atorvastatin therapy resulted in lipid lowering and anti-inflammatory activity in patients after AMI, independently of its effect on *MPO* gene expression. The molecular mechanisms of this phenomenon are not yet defined and require further research.

Key words: *MPO* gene expression, myeloperoxidase, C-reactive protein, atorvastatin, acute myocardial infarction

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INTRODUCTION

Acute coronary syndrome (ACS) is a predominant cause of human morbidity and mortality in developed countries. Inflammatory processes play a major role in all stages of the evolution of atherosclerotic plaque, from the early development of endothelial dysfunction, to the formation of the mature atheroma and its subsequent rupture (Nicholls *et al.*, 2005). Whereas the deposition and oxidation of lipids in atherosclerotic plaques are considered central events in plaque destabilization, maintaining the capping of the plaque by the extracellular matrix, plays a critical role in stabilizing the atherosclerotic lesions (Lau *et al.*, 2006). Myeloperoxidase (MPO) — enzyme released from activated neutrophils and monocytes during inflammation — is involved in the promotion of atherosclerosis, the destabilization of atherosclerotic plaque and the pathogenesis of ACS (Nicholls *et al.*, 2005; Tsimikas *et al.*, 2006; Ndrepepa *et al.*, 2011). MPO deposition has been shown in a murine model of acute myocardial infarction (AMI) to be increased near the sites of myocardial rupture (Vasilyev *et al.*, 2005). MPO is one of the important elements in the generation of oxidative stress and the pro-inflammatory stage progress (Zhang *et al.,* 2001). Systemic levels of MPO are significantly increased in subjects with angiographically documented cardiovascular disease (CVD), while high circulating MPO levels have been reported to be a risk factor for early adverse cardiovascular events in acute coronary syndromes (Andreou *et al.*, 2010). Patients, who are deficient in MPO, are less susceptible to CVD (Kumar *et al.*, 2005). MPO has also been listed as a candidate and potential biomarker of coronary atherosclerosis to predict future adverse clinical outcomes in subjects with ACS (Apple *et al.,* 2011). However, recent research has given conflicting results and the significance of MPO in the management of patients with coronary artery disease (CAD) is still disputable (Ndrepepa *et al.*, 2011; Chevrier *et al.*, 2006; Eggers *et al.,* 2010).

Statins, inhibitors of HMG-CoA reductase, have pleiotropic benefits independent of cholesterol levels, including anti-oxidant and anti-inflammatory effects. Statin-treated patients have significantly lower risk of CVD and myocardial infarction than patients using other lipid lowering agents (LLA), despite comparable reduction in cholesterol (Pedersen, 2004). Retrospective epidemiological studies found that patients treated with statins, but not other LLA, had reduced incidence of Alzheimer's disease (AD) or dementia. One feature common to CVD and AD is chronic inflammation with the infiltration of reactive monocyte/macrophages expressing MPO (Kumar *et al.*, 2005). One of the possible mechanisms of statins' action is their effect on MPO, which displays a diversity of the proatherogenic and pro-in-

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Abbreviations: ACS, acute coronary syndrome; AD, Alzheimer's disease; CRP, C-reactive protein; CVD, cardiovascular disease; LLA, lipid lowering agents; MPO, myeloperoxidase

flammatory properties including catalytic consumption of endothelium-derived nitric oxide, LDL oxidation, and functional inactivation of HDL (Boudjeltia *et al.*, 2004, Nicholls *et al.*, 2005). It has been established that treatment with atorvastatin for only one week can reduce the serum concentration of MPO and hsCRP in patients with ACS (Zhou *et al.*, 2006). Therefore, the aim of the present study was to determine the effect of atorvastatin therapy on the *MPO* gene expression in peripheral blood mononuclear cells (PBMCs) in relation to MPO plasma level. In addition, we explored the relationship between *MPO* gene expression and lipids level lowering and anti-inflammatory action of atorvastatin in patients after onset of myocardial infarction who had indications for the initiation of statin therapy.

MATERIALS AND METHODS

Subjects and study population. Thirty-eight consecutive patients (27 males, average age 59 (53–65) years, hospitalized for AMI were enrolled to the study (the baseline demographic is presented in Table 1)). The control group included 36, apparently healthy people (average age 57 (51–60) years, 9 males).

In 27 patients enrolled in the study ST-segment elevation MI (STEMI) was recognized. Eleven of the investigated patients underwent non ST-segment elevation MI (NSTEMI). All patients were referred to the catheterization laboratory for primary percutaneous coronary angioplasty (PTCA).

The inclusion criteria were: first episode of AMI, no history of dyslipideamia before enrollment in the study and age >18 years. Accordingly to the Third Universal Definition of Myocardial Infarction (The Writing Group *et al.*, 2012) the diagnosis of MI was confirmed by the detection of cardiac necrosis blood markers (troponin I) and the presence of at least one of the following: symptoms of ischaemia, new significant ST-segment–T wave changes, new left bundle branch block (LBBB), the development of pathological Q waves in the ECG or imaging evidence of a new loss of viable myocardium or new regional wall motion abnormalities. After echocardiographic assessment five cases of severe left ventricle dysfunction with LVEF <35% were observed. All the patients investigated received standard antiplatelet therapy (aspirin, clopidogrel). The GFR of each subject was estimated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula to assess the renal function.

The exclusion criteria consisted of: prior lipid-lowering therapy with statins and/or fibrates, history of any acute renal failure, hepatic failure, neoplasms, chronic inflammatory diseases, diabetes mellitus type 1, hereditary hipercholesterolaemia and pregnancy. Blood samples were collected during the first 24 hours of hospitalization in the Intensive Cardiological Care Unit before the first dose of statin. The patients fasted overnight and refrained from smoking for 12 hours. Thirty-eight patients with first AMI receiving atorvastatin therapy (40 mg per day) were followed up for a period of one month. All participants were fully informed of the aim of the study and formal consent was obtained from the patients before blood samples were collected. The presented trial complies with the ethical guidelines of the Declaration of Helsinki and the study protocol was approved by the local Ethical Committee.

Biochemical analyses. MPO was analyzed in sodium citrate plasma that had been stored frozen in aliquots at –20°C. MPO levels were measured using a chemiluminescent microparticle immunoassay (CMIA technology) for the quantitative determination of myeloperoxidase on the ARCHITECT *i*System according to manufacturer's protocol (Architect i2000 SR, Abbott Diagnostics, Abbott Park, IL). Serum lipoproteins (total cholesterol, triglycerides, and HDL cholesterol) and glucose levels, in samples that had been stored frozen in aliquost at –20°C, were determined by automated analyzer Cobas c501 (Roche Diagnostics GmBH, Mannheim, Germany). LDL cholesterol level was estimated by the Friedewald formula unless triglyceride levels were >300 mg/dL, in which case direct LDL cholesterol level determination was performed. The concentrations of high sensitive C-reactive protein (hsCRP) were measured using flex® reagents cartridge and Dimension Xpand instrument (Siemens HealthCare Diagnostics Ltd., Erlangen, Germany).

RNA isolation. Sodium citrate-blood was collected from patients at two time points: before and one month after atorvastatin treatment. Peripheral blood mononuclear cells (PBMCs), mainly comprising monocytes, T cells, B cells and natural killer (NK) cells, were purified using a BD Vacutainer® CPT™ Cell Preparation Tubes in accordance with the manufacturer's instructions (Becton, Dickinson and Co., Franklin Lakes, NJ, USA). Total RNA was isolated from PBMCs with the MagNA Pure Compact System (Roche Diagnostics GmbH, Germany) following the manufacturer's recommendations. The RNA quantity was determined by UV absorption (Nanodrop, LabTech International, UK). The quality of RNA samples was verified using Agilent 2100 Bioanalizer© and RNA 6000 Nano Kit (Agilent, Santa Clara, CA, USA). Samples with RNA integrity value of eight or above were considered suitable for analysis. RNA samples were stored at –80°C until further analysis.

Quantitative real-time RT-qPCR. The real-time reverse transcription-polymerase chain reaction (RT-qPCR) was used to quantify *MPO* gene expression levels. Reverse transcription was carried out using total RNA samples (200 ng) and the QuantiTect Reverse Transcription kit (Qiagen, Hilden Germany) according

Table 1. Baseline demographic in studied patients.

Number of patients, n	38
*Median age	59 (53–65) yrs
Male gender, n (%)	27 (71.1%)
STEMI, n (%)	27 (71.5%)
NSTEMI, n (%)	11 (28.9%)
Hypertension, n (%)	19 (50%)
Diabetes mellitus, n (%)	5 (13,2%)
Prediabetes, n (%) Impaired fasting glycaemia Impaired glucose tolerance	12 (31.6%) 8 (21.1%) 4 (10.5%)
Obesity **BMI >30, n (%)	8 (21.1%)
Overweight **BMI >25, n (%)	12 (31.6%)
Chronic Kidney Disease, n (%) Stage 3 (***eGFR < 60 ml/min/1,73m²) Stage 4 (***eGFR < 30 ml/min/1,73m²)	6 (15.8%) 5 (13.2%) 1 (2.6%)
Smoking, n (%)	16 (42.1%)
Family history of cardiovascular diseases, n (%)	4 (10.5%)

Data are presented as number (percentage) or *median (IQR, range from the 25th to the 75th percentile), **BMI, body mass index, ***eGFR, estimated glomerular filtration rate.

to the manufacturer's protocol. Primer sequences were as follow: *MPO* forward, 5' CACTGGCGTCAACTGCGAGA 3' and reverse 5' TGCTGGCGTCCACGAAGGAA 3'; *TUBB* forward, 5' CTTCAAGCGCATCTCGGAGC 3' and reverse 5' TGCGGTGGCATCCTGGTACT 3'. The specificity of the amplified product was demonstrated by melting curve analysis and agarose gel electrophoresis (data not shown). Each sample was run in triplicate in 96-well plates using LightCycler®480 and LightCycler®480 FastStart SYBR Green I Master (Roche Diagnostics GmbH, Germany). Quantification cycles (Cq) were calculated using the second derivative method (LightCycler®480 Software, Version 1.5 provided by Roche). The fold change of gene expression levels, corrected for the efficiency was analyzed using Relative Expression Software Tool (REST 2009) (Pfaffl *et al.*, 2002). Tubulin, beta class I (*TUBB*) was used as a normalization (housekeeping) gene since its expression did not significantly fluctuate between investigated groups in this study. All experiments (sample collection, preparation and storage, primer design) were performed according to the MIQE guidelines (Bustin *et al.*, 2009).

Statistical analysis. Statistical analysis was performed using the statistical software STATISTICA version 10 and p values < 0.05 were considered as statistically significant. Continuous variables were tested for normal distribution with the Shapiro-Wilk test. Results for normally distributed continuous variables are expressed as mean±standard deviation and mean values were compared with unpaired Student's t-test. Continuous variables with non-normal distribution are presented as the median value and the interquartile range (IQR, range from the 25th to the 75th percentile). Between-group comparisons of the distributions were assessed using the Wilcoxon rank-sum test. The correlation among continuous variables was assessed with Spearman rank correlation coefficient.

RESULTS

The median MPO plasma levels were significantly higher in all studied patients before therapy in relation the control group (152.5 (109.5–240.5) pmol/L *vs* 100.8 (82.1–125.2) pmol/L; $p = 0.0004$, respectively) (Fig. 1B). Likewise, the median MPO plasma levels were

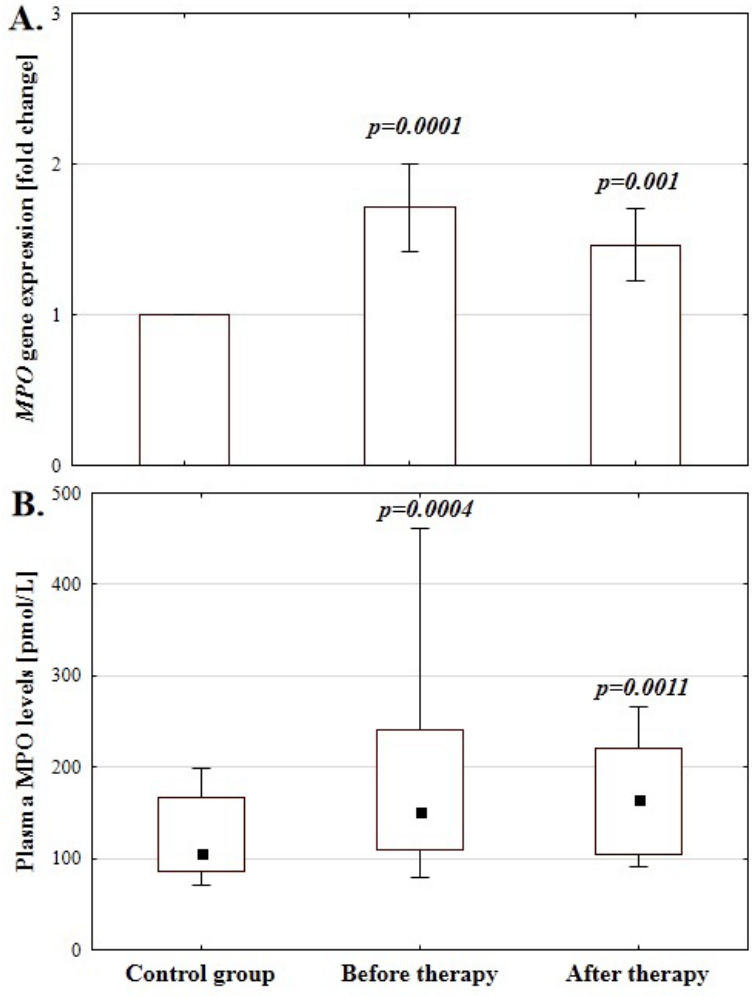

Figure 1. (A) *MPO* gene expression in PBMCs and (B) plasma MPO level in the control group versus studied patients (before and after atorvastatin therapy).
(**A**) mRNA expression levels for *MPO* gene were determined by RT-qPCR and normalized to reference gene *TUBB*. Data are presented as fold change relative to the expression in the control group±standard error. (**B**) Box-whisker plots of the MPO level before and after atorvastatin treatment are shown. Boxes encompass the 25th (Q1) to 75th (Q3) quartiles, the whiskers represent the 10–90% range of observations. Points within boxes represent median values.

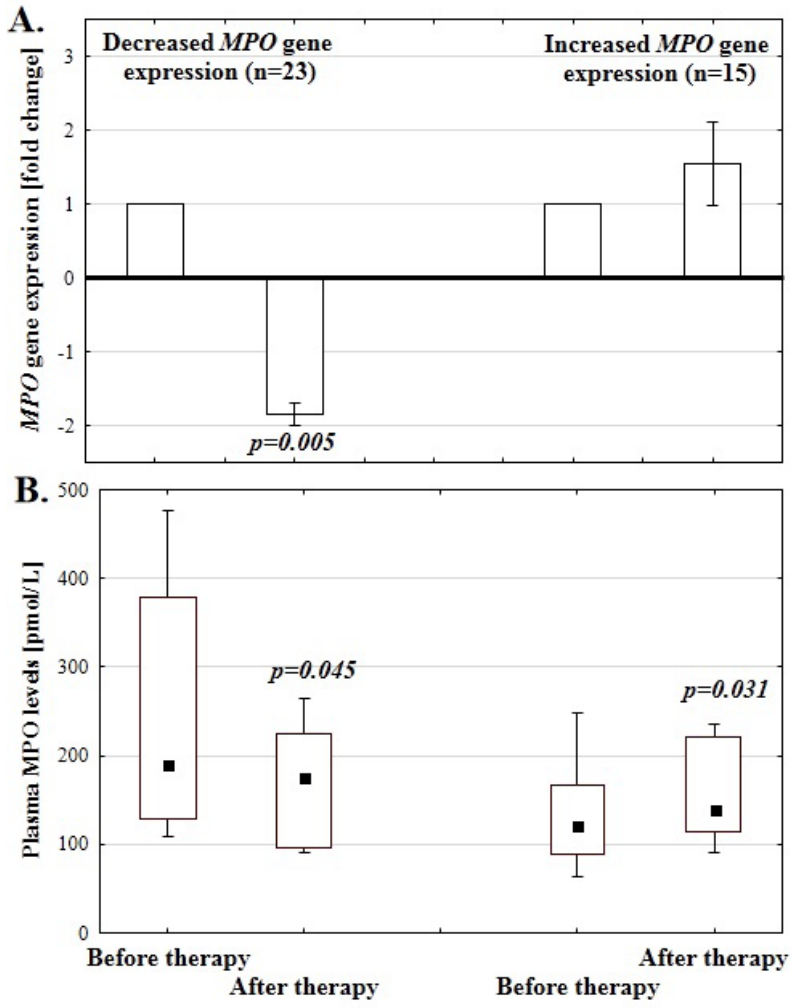

Figure 2. (A) *MPO* gene expression in PBMCs and (B) plasma MPO level before and after atorvastatin therapy in population with decreased- and with increased *MPO* gene expression.
(**A**) mRNA expression levels for *MPO* gene were determined by RT-qPCR and normalized to reference gene TUBB. Data are presented as fold change relative to expression in the group before therapy±standard error. p=0.005, after versus before atorvastatin therapy. (**B**) Box-whisker plots of MPO level before and after are shown. Boxes encompass the 25th (Q1) to 75th (Q3) quartiles, the whiskers represent the 10–90% range of observations. Points within boxes represent median values.

also significantly higher in all studied patients after the treatment in comparison with the healthy group (165.9 (104.5–220.5) pmol/L *vs* 100.8 (82.1–125.2) pmol/L; $p = 0.0011$, respectively) (Fig. 1B).

The *MPO* gene expression was significantly higher in all studied patients both before and after atorvastatin therapy in comparison to the control group (fold change 1.711; $p = 0.0001$ and fold change 1.461; $p = 0.001$, respectively) (Fig. 1A). In all studied patients a moderate correlation between the changes of plasma MPO levels (changes between the values after and before the therapy) and relative *MPO* gene expression ($r = 0.476$; $p < 0.05$) was observed.

The above mentioned results particularly proved that there is no relationship between *MPO* gene expression and its level in the plasma, which was surprising and probably caused by the ontogenetic variability of atorvastatin therapy response. Therefore, we distinguished two patient subgroups: with the decrease and the increase in *MPO* gene expression. The gene expression analysis revealed decreased *MPO* gene expression in 23 patients (60.5%) and increased *MPO* gene expression in 15 patients (39.5%) (Fig. 2A). After one month of atorvastatin therapy in patients with down-regulated *MPO* gene expression (n=23) (fold change –1.845; $p = 0.005$) (Fig. 2A) a significant reduction in MPO plasma levels (189.9 (128.6–378.7) pmol/L *vs* 176.0 (95.7–224.5) pmol/L; $p = 0.0447$) (Fig. 2B) was achieved. In contrast, in the subgroup of patients with up-regulation of the *MPO* gene expression observed (n=15) (fold change 1.545; $p > 0.05$) (Fig. 2A) the median MPO plasma level was also significantly higher after one month of atorvastatin therapy: 121.8 (88.1–165.0) pmol/L *vs* 139.0 (114.1–220.5) pmol/L; $p = 0.0309$) (Fig. 2B).

The lipid lowering effect of atorvastatin therapy is presented in Table 2. The decrease of total cholesterol and LDL cholesterol concentration was almost the same in both groups — with decreased and increased *MPO* gene expression, which may suggest that the lipid lowering and anti-inflammatory effect of atorvastatin is independent from its influence on *MPO* gene expression.

The median hsCRP serum levels were significantly higher in all studied patients (n=38) before therapy versus the healthy group (n=36) (12.3 (5.8–23.4)

Table 2. Lipid-lowering capabilities and anti-inflammatory action of atorvastatin therapy.

Parameter	Decreased *MPO* gene expression (n=23)				Increased *MPO* gene expression (n=15)			
	Before therapy (n=23)	After therapy (n=23)	Δ	*p*-value	Before therapy (n=15)	After therapy (n=15)	Δ	*p*-value
Total cholesterol [mmol/L]*	4.86±1.04	3.39±0.73	↓ 30.2%	$p<0.0001$	4.91±0.75	3.33±0.56	↓ 32.2%	$p<0.0001$
LDL-cholesterol [mmol/L]*	3.22±1.13	2.08±0.48	↓ 35.4%	$p<0.0002$	3.15±0.68	2.07±0.44	↓ 34.3%	$p<0.0001$
HDL-cholesterol [mmol/L]*	1.10±0.32	1.11±0.30	↑ 0.91%	$p=0.969$	1.25±0.29	1.21±0.27	↓ 3.2%	$p=0.563$
Triglicerides [mmol/L]*	1.61±1.14	1.40±0.85	↓ 13.0%	$p=0.455$	1.36±0.66	1.08±0.34	↓ 20.6%	$p=0.127$
hsCR*P* [mg/L]**	12.9 (6.8-36.2)	1.9 (1.34-5.1)	↓ 85.3%	$p<0.0001$	10.2 (1.94-18.8)	2.8 (1.52-7.24)	↓ 72.5%	$p=0.006$

Results are expressed as: *mean±standard deviation; **median (25–75 percentiles); Δ, means difference in the concentration between before and after atorvastatin therapy.

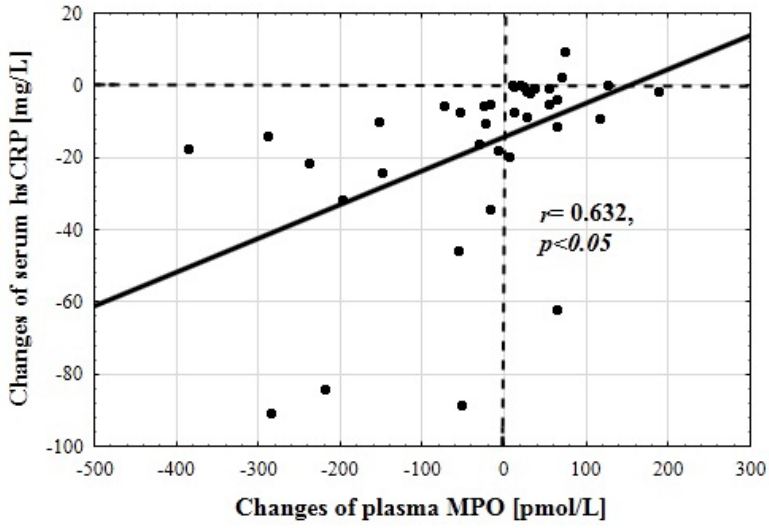

Figure 3. Correlation between the changes of serum hsCRP concentrations and changes of plasma MPO levels in all studied patients.
Spearman's rank strong correlation $r=0.632$, $p<0.05$.

mg/L vs 1.29 (0.98–2.00) mg/L; $p<0.0001$). Moreover, the median hsCRP serum levels measured one month after atorvastatin treatment were still significantly higher in studied patients in comparison to the control group (2.1 (1.4–6.3) mg/L *vs* 1.29 (0.98–2.00) mg/L; $p=0.0268$).

It is noteworthy that one month atorvastatin treatment resulted in the same effect on the hsCRP concentrations independently of the effect on the *MPO* gene expressions. In the group of patients with decreased *MPO* gene expressions, hsCRP levels were decreased: 12.9 (6.8–36.2) mg/L *vs* 1.9 (1.34–5.1) mg/L; $p<0.0001$ and in the group of patients with increased *MPO* gene expressions the hsCRP levels also decreased: 10.2 (1.94–18.8) mg/L *vs* 2.8 (1.52–7.24) mg/L; $p=0.006$ (Table 2).

In all studied patients a weak correlation between changes of serum hsCRP levels (changes between after and before the therapy) and relative *MPO* gene expression ($r=0.365$; $p<0.05$) was observed. In addition, statistical analysis demonstrated that there is a strong correlation between changes of serum hsCRP levels and changes of plasma MPO levels in studied patients ($r=0.632$; $p<0.05$) (Fig. 3).

DISCUSSION

There is increasing evidence to suggest that the benefits of statins are not limited to the effect on serum cholesterol (Davignon, 2004). The cholesterol independent effects of statins include the decrease in oxidative stress and inflammation (Pedersen, 2004; Greenwood *et al.*, 2007; Wang *et al.*, 2008). Peripheral blood mononuclear cells (PBMCs) play a key role in the expansion of inflammation and oxidative stress (Zhang *et al.,* 2001). We decided to use PBMCs to conduct the study because they can be obtained relatively easily from routinely collected blood samples, and represent the only site of active gene expression in blood. The PBMCs mainly comprise monocytes, T cells, B cells, and natural killer (NK) cells. The PBMCs contain different cell types that play important roles in the immune system monitoring and respond in an inflammatory manner. MPO is abundantly expressed not only in the granules of most leukocyte subspecies, including neutrophils, but also in monocytes (PBMCs population). MPO increases the oxidative potential of hydrogen peroxide by generating hydrochlorous acid through the peroxidation of chloride (Byun *et al.*, 1999). MPO is involved in low-density lipoprotein (LDL) oxidation, high density lipoprotein (HDL) modification leading to its functional impairment, nitric oxide breakdown, endothelial dysfunction and in post-MI remodeling. The role of MPO, particularly in the generation of dysfunctional HDL particles, seems to be important as the heart ischemia and its consequences can occur even in the presence of high levels of HDL cholesterol. Taken together all these data, it is of a great importance to reveal what is the effect of lipid lowering atorvastatin therapy, not only in the context of the HDL and LDL cholesterol concentration but also on the *MPO* gene expression as well as on the systemic level and/or on enzyme activity in patients undergoing the therapy.

Before the statin therapy (2–3 days after the onset of AMI), the *MPO* gene expression in PBMCs was significantly higher in patients than in control individuals with proven coronary artery disease (Fig. 1A). It has been

shown by Goldman *et al.* that MPO plasma levels remained elevated until 4h after the onset of symptoms and declined thereafter. After 24hours however, MPO levels increased again (Goldmann *et al.*, 2009). It has been indicated by Aminian *et al.* that coronary stenting is also associated with an acute and transient increase in plasma MPO levels in patients with stable angina but not in patients with acute myocardial infarction (Aminian *et al.*, 2009). Given these observations and our results, it may be suggested that PBMCs are still activated after successful coronary intervention in patients with AMI.

In the present study, we showed for the first time that atorvastatin caused a different effect on the *MPO* gene expression. Individual responsiveness to atorvastatin therapy is not uniform in all patients. After one month of atorvastatin therapy we observed a subgroup of patients (n=23) with significantly ($p=0.005$) decreased *MPO* gene expression as well as the enzyme concentration in the circulation (Fig. 2A and Fig. 2B). It is interesting that we were able to demonstrate numerous cases (15 patients) in which *MPO* gene expression (Fig. 2A) and plasma enzyme levels (Fig. 2B) were increased after one month therapy with atorvastatin. The different effect of atorvastatin therapy was independent from the anti-inflammatory action. In all studied patients significant decrease in serum concentration of hsCRP was stated (Table 2). It may therefore be suggested that inflammatory mediators are not co-responsible for *MPO* gene expression in PBMCs. In addition, we did not observe any differences between both groups in the cholesterol-lowering activity of atorvastatin (Table 2).

The different effect of atorvastatin is very important, as well as the unexpected observation that several studies have consistently demonstrated that statins down-regulate *MPO* gene expression and reduce serum MPO concentration (Kumar *et al.*, 2005; Zhou *et al.*, 2006). The molecular mechanism of ontogenetic variability of atorvastatin treatment remains unclear. One of the possible explanations of the mechanism of a different effect of atorvastatin on MPO are the differences in its affinity to the active site of HMG-CoA reductase. Andreou *et al.* suggested that the inhibiting effects of rosuvastatin on *MPO* gene expression are probably class effects for these agents and are based on the inhibition of mevalonate-dependent isoprenylation of small GPT-binding proteins (Andreou *et al.*, 2010). Rosuvastatin, however, has exhibited a more potent affinity for HMG-CoA reductase than other statins including atorvastatin (Olsson, 2001). Another possible mechanism responsible for this phenomenon is polymorphism in the promoter region of the *MPO* gene. Several genetic polymorphisms in the *MPO* gene were described (Wainstein *et al.*, 2010; Scharnagi *et al.*, 2014; Nikpoor *et al.*, 2001). Some studies suggest that *MPO* polymorphism in the promoter region (–463G/A) might be associated with coronary artery disease (Castellani *et al.*, 2006; Reynolds *et al.,* 2006; Yang *et al.*, 2013). However, this preliminary hypothesis still requires detailed studies. In the present study, a statistically moderate correlation was observed between *MPO* gene expression and changes of MPO plasma level ($r=0.476$; $p<0.05$). Thus, the determination of *MPO* mRNA expression by RT-qPCR reflects the changes of MPO plasma concentration, which should in turn allow the prediction of the patient`s reaction to the atorvastatin treatment. To our knowledge, little is known about the correlation between *MPO* gene expression in PBMCs and the changes of plasma MPO concentration in patients soon after the onset of AMI treated with atorvastatin. Our results seem to suggest that monitoring of *MPO* gene expression during statin therapy is predictive for cardiovascular outcomes. These data raise the possibility that the evaluation of *MPO* gene expression using RT-qPCR may serve as a very useful tool for studying the molecular mechanisms of pleiotropic atorvastatin action.

A limitation of the present study is the small number of participants. In addition, we did not analyze different doses of atorvastatin. We investigated only one typical dose of atorvastatin used for patients in secondary prevention after AMI. Our study did not show that the observed effects on *MPO* gene expression and MPO levels are dose-dependent. Recently it has been stated that different statins produce highly different changes in gene expression (Leszczynska *et al*, 2011). Therefore, our observations are limited only to atorvastatin. Further studies with a larger number of patients are needed to confirm our results and their clinical significance.

CONCLUSIONS

The one month atorvastatin treatment of studied patients exhibited a different effect on the *MPO* gene expression and on the MPO plasma level. Not in all patients does atorvastatin inhibit *MPO* gene expression. There is a small group of patients with increased *MPO* gene expression. Lipids level lowering as well as anti-inflammatory activity of atorvastatin is independent of the effect on *MPO* gene expression. It may be assumed that the determination of *MPO* gene expression and/or MPO plasma concentration may be a useful adjunct to the assessment of future cardiovascular events and of the potential benefit from atorvastatin therapy.

Conflict of interest

Authors declare no conflict of interest.

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