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OXIDANT STRESS AFTER CORONARY STENT IMPLEMENTATION

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Summary. *Literature data about oxidative stress in percutaneous coronary interventions are still controversial. The intensity of oxidative stress depends on the extent of ischemia, the degree of endothelial damage and, also on the possibility of antioxidant protection. The aim of this study was to determine the point at which the oxidative stress reaches its maximum height and the point of oxidative balance restoration after the stent implantation.The research included 22 patients with coronary artery disease (CAD) (aged 51 ± 4 years), who have undergone coronary angiography, with the indication for implantation of one stainless steel stent of the length of 12-18 mm. Diabetic patients were excluded. Blood samples for analysis were taken immediately before and after stent implantation as well as 6, 12, 24, and 72 hours after stent implantation. We have analyzed the parameters of free radical production – lipid peroxides (Lp) and xanthine oxidase - (XO) and catalase, as the enzyme of antioxidant defense. All parameters were determined in blood samples of 30 healthy persons at the same time. The results have shown that in patients with coronary artery disease there was a high level of oxidative stress before stent implantation compared to control group of healthy ones (CG) (XO: CG 3.92 ± 0.88 vs. CAD 17.6 ± 1.28, $p < 0.001$), MDA (malondialdehyde) in plasma of CG 8.29 ± 1.66 vs. CAD 10.39 ± 2.56 NS. There was no significant difference in catalase (CAT) activity between patient group before stent implantation and CG. The parameters of oxidative stress showed a slight increase immediately after the stent implantation, while the activity of catalase increased significantly. The values of prooxidant parameters normalized 72 hours after stent implementation. In patients with coronary heart disease, there is an intensive oxidative stress before stent implantation, which shows a slight temporary increase after stent implantation. It has no statistical significance. On the other hand, a significant increase of the catalase activity has been noticed after stent implantation, which indicates the activation of anti oxidant defence system. The values of oxidative stress parameters approach the values of those of the control group, 72 hours after stent implantation.*

Key words: *Oxidative stress, coronary stent*

Introduction

The percutaneous coronary intervention (PCI) is an invasive, therapeutic method with increasingly developing role in the field of treating coronary artery disease. In spite of the progressing technique of coronary stent implantation, under high pressure and using double anti aggregation therapy, some acute and postponed complications that are not related to the procedure performance skills, are possible. The frequency of coronary stent thrombosis (CST) in the modern era of stent implantation ranges from the lowest 0,4% to the high 2,8% in the group of patients with larger number of stents (1). The occurrence of restenosis has been significantly decreased by implanting stents coated with medicines (2), however, there is still a problem with stents made of stainless steel. The complication process could be caused by many factors and various mechanisms.

Inflating of a balloon through the coronary lesion and plaque rupture is a clinical model of plaque destabilization, and smaller or bigger damaging of the coronary endothel, which, at the same time represents an ischemia – reperfusion model. So, after PCI, an increase of myocardial damage marker can occur, which is insignificant in most elective procedures (3,4,5,6). PCI is considered to be a safe therapeutic technique, during which a moderate, transitory oxidative stress, which is not in correlation with myocardial damage, is induced. The oxidative stress has been considered to be possibly the result of vascular damage at the place of intervention (3). There are more and more evidences proving the significant role of redox process as vascular wall recovery mediator, but also as a factor which contributes to the appearance of restenosis. The results of the studies in which oxidative stress during PCI has been examined, are controversial. Some studies showed that lipid peroxidation during and after PCI remained unchanged (7,8), while some other ones proved the increased production of free radicals during percutaneous intervention (9,10).

Reactive oxygen species (ROS) have an important role in the control of cell function. They are intermedi-

ary metabolites in enzyme reactions and they control the ways of signal transduction. Endothelial cells and leucocytes can release ROS under certain stimulation. There is a strong relationship between concentration of ROS and the function of platelets which deserves further clinical examination of platelet hyperfunction significance under the conditions of oxidative stress (11). However, oxidative stress is not only the expression of increased ROS production, but also the result of balance between free radicals creation and the activity of antioxidant defense system.

The aim of our study was to show, through the analysis of prooxidant and antioxidant parameters, that in patients with stable angina pectoris and elective PCI, during implantation of stainless steel stent, an oxidative stress occurs.

Patients and Methods

Patients

The research included a group of 22 patients with stable angina pectoris to whom, an indication for performing percutaneous coronary intervention (PCI) and implantation of coronary stainless still stent was established, based on the previously made coronary angiography. The basic characteristics of the patients and the coronary disease risk factors are shown in Table 1.

Table 1. Basic characteristics of patients and coronary disease risk factors

	Stent Group	Control	
Age	51 ± 4	38 ± 3	p<0.01
Sex F/M	14/8	19/11	
Risk factors			
Diabetes mellitus	0/22	0/30	
Hypertensio arterialis	17/22	0/30	
Hiperlipoproteinemia	12/22	0/30	
SMOKERS	13/22	10/30	

The patients represented a homogeneous group with one vessel disease, where the length of lesion was 10-16 mm. The length of implanted stents was 12 to 18 mm, and it did not exceed the optimum length. The pressure of balloon inflation during stent implantation was 14 to 16 atm. Distribution and type of lesions in relation to the coronary artery is presented in Table 2.

All parameters were determined in blood samples of 30 healthy persons at the same time (KG) whose characteristics are shown in the Table 1.

Material used to perform percutaneous interventions: guiding catheter 6F, floppy coronary wires. All stents were placed by primo implantation.

All patients were under chronic therapy: Tablet Aspirin 100 mg/day, Tablet Clopidogrel 75 mg/day, longer than 7 days, and immediately before intervention and taking the first blood sample they received unfractionated heparin 70 units/kg or 7,000 to 10,000 units.

Table 2. Distribution and type of lesions relative to coronary artery

Coronary Lesion type	19 A; 3 B1; 0 B2 and C
Lesion length (mm)	10–16
Stent length (mm)	12–18
Inflation pressure (atm)	14–16
Inflation duration (sec)	12–16
Lesion location	LAD 10; ACX 3; ACD 9
Stenose size (%)	19 70-80% 3 90%

The blood sample for the analysis was taken from the periphery vein (v. cubitalis), in heparinized testtubes Terumo (standard quantity of heparine).

Sampling blood time: before and immediately after, as well as 6, 12, 24 and 72 hours after stent implantation. The blood was centrifugated with an aim to separate plasma, which was then frozen at –80°C.

Methods

The concentration of malondialdehyde (MDA) – product of lipid peroxidation and activities of xantine-oxidase (XO) and antioxidant enzyme – catalase (CAT) were determined in plasma and erythrocytes.

The activity of XO was measured by spectrophotometric method with minimum modification (12).

The product of lipid peroxidation reacts with thiobarbituric acid in 1% orthophosphoric acid, pH 2.0, by adding 1 μmol of ferrous sulphate. The absorbance was measured at 535 nm (13).

The activity of catalase in erythrocytes was determined according to Beutler method (1982), based on decomposition of H_2O_2, which was accompanied by direct decrease of absorbance to 230 nm (14).

Catalasa activity in plasma was measured by the method of Goth (15).

Statistical methods

Standard deviation and Student t test were used for data processing.

Results

The value of malondialdehyde (MDA) in plasma of the control group of tested patients was 8.29 μmol/L, while in plasma of coronary patients, before stent implantation it was 10.39 μmol/L. The values were higher in the group of coronary patients, but without statistically significant difference (NS). The value of malondialdehyde (MDA) in erythrocytes of coronary patients was 5.05 μmol/gHb, while in erythrocytes of the control group was 4.74 μmol/L (NS) (Fig. 1). After stent implantation and the initial drop of MDA value in plasma, there was an increase of concentration, 12 hours after stent implantation (initially 10.39 μmol/L in 12th hour 11.05) (Fig. 2).

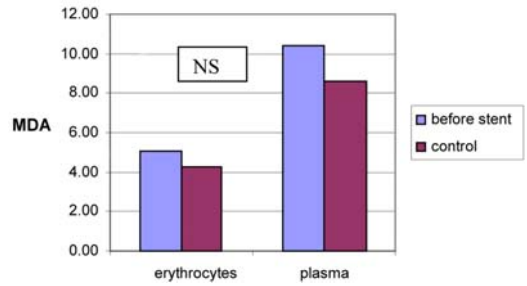

Fig. 1. Concentration of MDA in erythrocytes (μmol/gHb) and plasma (μmol/L)

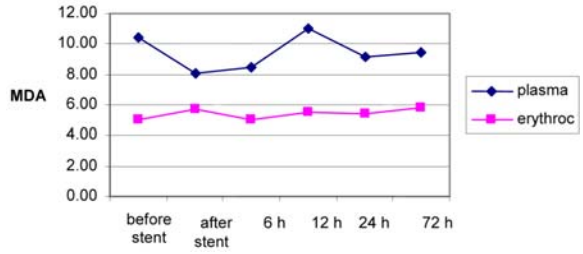

Fig. 2. Concentration of MDA in erythrocytes (μmol/gHb) and plasma in patients with stent (μmol/L)

The value of xantine oxidase (XO) in plasma of coronary patients before stent was significantly higher (17.16 U/L) compared to the values of XO in plasma of the control group (3.92 U/L) $p < 0.01$ (Fig. 3). The activity of XO approached the normal values 72 hours after stent implantation (it was 17.16 U/L before stent, and 5.41 U/L 72 hours later) (Fig. 4).

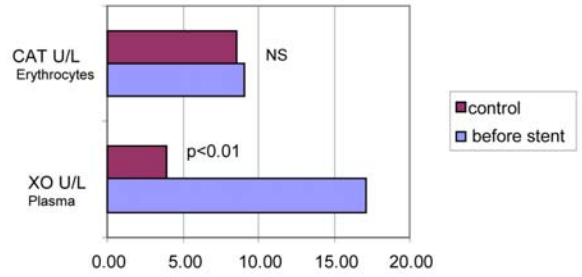

Fig. 3. Comparison of catalasa (CAT) and xanthine oxidase (XO) activities in control group vs before stent implementation

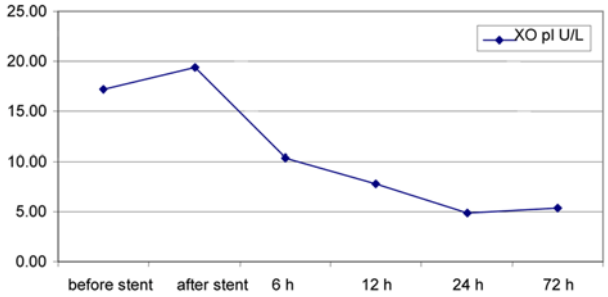

Fig. 4. Activity of xanthine oxidase (XO) in plasma of patients with stent

The activity of catalase (CAT), measured in erythrocytes of the control group was lower (8.58 U/L), compared to the values in coronary patients before stent implantation (9.1 U/L), but without statistically significant difference (Fig. 3). Plasma catalasa activity after stent implantation increased significantly (before stent it was 39.23 U/L, and 24 hours later it reached its maximum of 98.9 U/L) (Fig. 5).

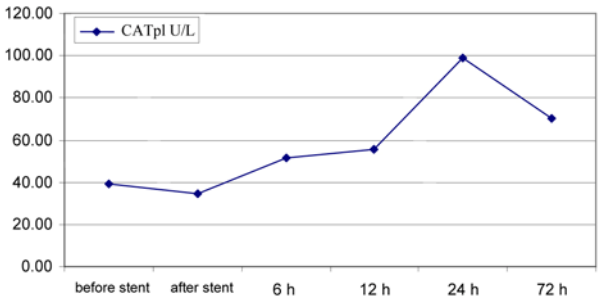

Fig. 5. Activity of catalase (CAT) in plasma of patients with stent

Discussion

The PCI process is a clinical model of the controlled ischemia–reperfusion syndrome, i.e. the controlled process of coronary plaque destabilization. Findings of the studies are controversial in whether the short episodes of ischemia during the elective procedure of PCI, i.e. certain level of coronary endothels injury, could cause detectable oxidative stress (16). The technology for the oxidative stress assessment and the cell damage in vivo, in patients with PCI (17), has not been specified so far. In a large number of studies, determination of the level of malonilaldehyde (MDA) as a product of phospholipids peroxidation, was mainly used. The activation of arachidonic acid metabolic pathway is also considered to be a marker of the cell membrane injury, induced by free oxygen radicals (18,19,20).

In our study, the level of malonilaldehyde in plasma of the coronary patients prepared for stent implantation is higher than the one in the control group, although the difference is not of statistical significance. The MDA concentration increase, which occurs 6 and 12 hours after stent implantation is in correlation with literature data (21) and it represents evidence that the procedure leads to plaque destabilization and release of free radicals from injured endothelial cells. Endothelial cells do not necessarily need to be the only source of free radicals, since it is known that activated neutrophiles also produce ROS and that their activation plays an important role in the mechanisms that lead to restenosis after PCI (22). It is possible that lipid peroxides, produced in response to ischemia/reperfusion, oxidize phospholipids in the walls of blood vessels, but also LDL and Lp in plasma, which were proved to release vasoactive substances that can cause vasoconstriction of microvasculature and the inability to reestablish the flow. The drop of the level of MDA 24 and 72 hours after the interven-

tion probably indicates restoring of the pro/anti-oxidant balance that starts already 12 hours after PCI, which is in correlation with the fact that regeneration of endothel starts 24 hours after injury (23).

Oxidative stress is a feature of endothel inflammatory response. Kawazaki and associates (24) proved that oxidative stress has a significant role in neointimal development after stent implantation. Several enzymes, which are also released during oxidative stress, have an important role in the genesis of oxidative stress: mitochondrial oxidase, xanthine oxidase, NAD(P)H oxidase, nitric oxide synthase (NOS), cytochrome P450, lipoxygenase and cyclooxygenase.

A significant source of the superoxide anion radical in the post-ischemic tissue is XO. It originates from xanthine dehydrogenase (XDH) in ischemic tissue. Circulating XO, while producing free radicals, causes the direct injury of vascular endothel, activates inflammatory cells that generate free radicals, spreading oxidative damage of vascular endothel. Depletion of intracellular ATP results in the increase of intracellular AMP, which is turned into hypoxanthine that serves as a substrate for XO. Endothelial cells are considered to be the main depots of XD and XO which, during ischemia and reperfusion, leak out of endothelial cells into circulation (25). In our study, we recorded a highly significant difference in the activity of xanthine oxidase in coronary patients related to the control values, which was another proof of oxidative stress existence in these patients, also before stent implantation. The more significant increase that occurs immediately after stent implantation, shows that oxidative stress becomes even more expressed after the intervention. This is supported by the results of McNally and associates (26), which indicate activation of XO mediated by kinases activated by oxidant stimuli during oxidative stress.

XO has a relatively long half-life that emphasizes its toxicity (27). For this reason a circulating XO can produce surplus of free radicals capable of causing massive endothelial and epithelial injuries of various tissues.

Antioxidant enzymes, superoxide dismutase and catalase and other "scavengers" of free radicals, normally present in tissues and extracellular fluids, show an increased activity during oxidative stress. As expected, contrary to the moving trend of oxidative stress parameter values, the activity of catalase which, even before stent implementation in these patients, was increased in relation to the control group, after the intervention it starts to grow, reaching the maximum of the activity 24 hours after stent implementation (Figure 5). The high growth of catalase indicates the strong activation of antioxidant defense system under these conditions. Since it is well known that H_2O_2 strongly contributes to platelet activation and aggregation in oxidative stress (28), this represents an important protective factor.

The production of free radicals shows rapid and transitory growth after PTCA in the acute myocardial infarction. A slight increase in the elective PCI in stable angina pectoris has been proved (29). Nevertheless, the published results show that elective PTCA, performed by inflation of the balloon in duration of 60s, is a safe procedure which does not cause peroxidative injury caused by reperfusion. The reason for such finding could be that the occlusion of the coronary blood vessel of 60s is not enough to reach an ischemic threshold, but it initiates the phenomenon of preconditioning (30). This is certainly the reason that in the majority of studies that analyzed the oxidative stress in elective PCI, as well as in our study, there is no significant increase of oxidative stress recorded. In our study, the length of the balloon inflation was 12-16 seconds.

However, the question is whether in these conditions there is no oxidative stress or it is the result of an increased influence of antioxidants which manage to maintain the pro/antioxidant balance. The achieved results can be an indirect proof of undetectable initiation of oxidative stress and utilization of antioxidants in restoring of pro/antioxidant balance, which is certainly going to be the subject of our further research.

Therefore, we consider that the follow-up of these, but also of other parameters of pro/antioxidant status, individually and continually in the mentioned time intervals during performing PCI, could be a predictive factor of impairment and possible early and late complications in these patients.

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References

1. Wenaeser P, Rey Ch, Eberly F, Togni M, Tuller D, Locher S, Remondino A, Seiler Ch, Hess O, Meier B, Windecker S. Stent thrombosis following bare-metal stent implantation: success of emeregency percutaneous coronary intervention and predictors of adverse outcome. EHJ 2005; 26: 1180-1187.
2. Morice MC, Serruys PW, Sousa JE, Fajadet J, Ban Hayashi E, Perin M, Colombo A, Schuler G, Barragan P, Falotico R. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. NEJM 2002; 346: 1773-1780.
3. Berg K, Wiseth R, Bjerve K,Brurok H, Gunnes S, Skarra S, Jynge P, Basu S.Oxidative stress and myocardial damage during elective percutaneous coronary interventions and coronary angiography. Free Radical Research 2004; 38 (5): 517-525
4. Kugelmass AD, Cohen DJ, Moscucci M, Piana RN, Senerchia C, Kuntz RE, Baim DS. Elevation ofthe creatine kinase myocardial isoform following otherwise successful directional coronary atherectomy and stenting. Am J Cardiol 1994; 74(8): 748-754.
5. Abdelmeguid AE, Topol EJ, Whitlow PL, Sapp SK, Ellis SG. Significance of mild transient release of creatine kinase-MB fraction after percutaneous coronary interventions. Circulation 1996; 94(7): 1528-1536.
6. Simoons ML, Van den Brand M, Lincoff M, Harrington R, Van der Wieken R, Vahanian A, Rutsch W, Kootstra J, Boersma E, Califf RM, Topol E. Minimal myocardial damage during coronary intervention is associated with impaired outcome. Eur Heart J 1999; 20: 1112-1119.

7. Roberts MJD, Young IS, Trouton TG, Trimble ER, Khan MM, Webb SW, et al. Transient release of lipid peroxides after coronary artery ballon angioplasty. Lancet 1990; 336: 143-5.
8. De Scheerder IK, van de Kraay AMM, Lamers JMJ, Koster JF, De Jong JW, Serruys PW. Myocardial malondialdehyde and uric acid release after short-lasting coronary occlusions during coronary angioplasty: potential mechanisms for free radical generation. Am J Cardiol 1991; 68: 392-5.
9. Paterson JR, Oldroyd KG, Rumley AG, Eteiba H, Rae AP, Hutton I, et al. Free radical activity during percutaneous transluminal coronary angioplasty. Biochem Soc Trans 1990; 18: 1183-1184.
10. Oostenbrug GS, Mensink RP, Bar FWHM, Hornstra G. Lipid peroxidation-associated oxidative stress during percutaneous transluminal coronary angioplasty in humans. Free Radic Biol Med 1997; 22: 129-36.
11. Iuliano L, Colavita A, Leo R, Pratico D, Violi F. Oxygen free radicals and platelet activation. Free Radic Biol Med 1997; 22(6): 999-1006
12. Kizaki H, Sakurada T. Simple micro-assay methods for enzymes of purine metabolism. J Lab Clin Med 1977; 89: 1135-44.
13. Andreeva IL, Kozhemyakin AL, Kishkun AA. A modified thiobarbituric acid test for measuring lipid peroxidation. Lab Del 1988; 11: 41-3.
14. Beutler E. Catalase; Manual of biochemical method. New York, Grune and Stratton 1982: 105-6.
15. Goth L. A simple method for determination of serum catalase activity and revision of reference range. Clin chem. Acta 1991; 196: 143-152.
16. Rigattieri S, Buffen A, Ramazzoti V, Santini S. Oxidative stress in ishemia-reperfuzion injuty assessment by three independent biochemical markers. Ital Heart J 2000; 1(1): 68-72.
17. Djordjevic V, Pavlovic D, Kocic G. Biohemija slobodnih radikala. Medicinski fakultet, Nis, 2000.
18. Di Pierro D, Tavazzi B, Lazzarino G, Giardina B. Malondialdehyde is a biochemical marker of peroxidative damage in the isolated reperfused rat heart. Mol Cell Biochem 1992; 116: 193-196.
19. Largilliere C, Melancon SB. Free malondialdehyde determination in human plasma by high-performance liquid chromatography. Anal Biochem 1988; 170: 123-126.
20. Lazzarino G, Di Pierro D, Tavazzi B, Cerroni L, Giardina B. Simultaneous separation of malondialdehyde, ascorbic acid, and adenine nucleotide derivatives from biological samples by ion-pairing high-performance liquid chromatography. Anal Biochem 1991; 197: 191-196.
21. Tsimikas S, Lau HK, Han K, Shortal B, Miller ER, Segev A, Curtiss LK Witzum JL, Strauss BH. Percutaneous Coronary InterventionResults in Acute Increases in Oxidized Phospholipids and Lipoprotein(a). Circulation 2004; 109: 3164-3170.
22. Inoue T, Kato T, Hikichi Y, Hashimoto S, Hirase T, Morooka T, Imoto Y, Takeda Y, Sendo F, Node K. Stent-induced neutrophil activation is associated with an oxidative burst in the inflammatory process, leading to neointimal thickening. Thromb Haemost 2006; 95: 43-48.
23. Lafont A, Durand E, Samuel JL, Besse B, Addad F, Lévy BI, Desnos M, Guérot C, Boulanger CM. Endothelial dysfunction and collagen accumulation: two independent factors for restenosis and constructive remodeling after experimental angioplasty. Circulation 1999; 100: 1109-1115.
24. Kawazaki R, Yamashita A, Nishihira K, Furukoji E, Hatakeyama K, Ishikawa T, Imamura T, Itabe H, Eto T, Asada Y. Different inflammatory response and oxidative stress in neointimal hyperplasia after balloon angioplasty and stent implantation in cholesterol-fed rabbits. Pathol Res Pract 2006; 202(6): 447-456.
25. Granger DN, Vowinkel T, Petnehazy T. Modulation of the Inflammatory Response in Cardiovascular Disease. Hypertension 2004; 43: 924-931.
26. McNally SJ, Davis ME, Giddens DP, Saha A, Hwang J, Dikalov S, Jo H, Harrison DG. Role of xanthine oxidoreductase and NAD(P)H oxidase in endothelial superoxide production in response to oscillatory shear stress. Am J Physiol Heart Circ Physiol 2003; 285: H2290-H2297.
27. Friedl HP, Till GO, Ryan US, Ward PA: Mediator-induced activation of xanthine oxidase in endothelial cells. FASEB J 1989; 3: 2512-2518
28. Practico D, Iuliano L, Pulcinelli FM, Bonavita MS, Gazzaniga PP, Violi F. Hydrogen peroxide triggers activation of human platelet selectively exposed to nonaggregating concentrations of arachidonic acid and collagen. J Lab Clin Med 1992; 119: 364-370.
29. Grisham MB, Granger DN, Lefer DJ. Modulation of leukocyte-endothelial interactions by reactive metabolites of oxygen and nitrogen: relevance to ischemic heart disease. Free Radic Biol Med. 1998; 25: 404-433.
30. Cedro K, Marczak E, Czerwosz L, Herbaczynska-Cedro K, Ruzyllo W. Elective coronary angioplasty with 60 s balloon inflation does not cause peroxidative injury. Eur J Clin Invest 2002; 32: 148-152.

OKSIDATIVNI STRES NAKON UGRADNJE KORONARNOG STENTA

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Kratak sadržaj: *Literaturni podaci o oksidativnom stresu u perkutanim koronarnim intervencijama su jos uvek kontroverzni. Stepen oksidativnog stresa zavisi od težine ishemije, intenziteta oštećenja endotela, ali i od mogućnosti antioksidativne zastite. Cilj našeg istrazivanja je bio da pokažemo kada je oksidativni stress najveći i kada se uspostavlja pro/antioksidativna ravnoteža nakon ugradnje koronarnog stenta. Ispitivanjem su obuhvaćena 22 bolesnika (starosti 51 ± 4 godine) kojima je postavljena indikacija, na osnovu prethodno uradjene koronarografije, za ugradnju jednog stenta od nerđajućeg čelika, dužine 12-18 mm. U grupi nije bilo dijabetičara. Krv za analizu je uzimana neposredno pre i nakon implantacije stenta, 6, 12, 24 i 72 časa od ugradnje stenta. Analizirani su parametri produkcije slobodnih radikala – lipidni peroksidi (Lp) i ksantin oksidaza (XO) i katalaza, kao enzim antioksidativne zaštite. Ujedno su isti parametri dobijeni iz krvi 30 zdravih osoba. Rezultati pokazuju da pre ugradnje stenta postoji*

visok oksidativni stress u koronarnih bolesnika (KB) u odnosu na kontrolnu grupu zdravih (KG) (KG : XO 3,92 ± 0,88 vs KB XO 17,6 ± 1,28, p < 0,001), MDA (malondialdehid) u plazmi KG 8,29 ± 1,66 vs KB 10,39 ± 2.56 NS. Ujedno postoji neznačajno viša aktivnost katalaze (KAT) pre ugradnje stenta vs KG. Neposredno nakon ugradnje stenta neznačajno su povećani parametri oksidativnog stresa, ali je zato značajno povišena aktivnost katalaze. Vrednosti prooksidativnih parametra se normalizuju 72 sata nakon implantacije stenta. U uslovima koronarne bolesti, pre ugradnje stenta, postoji intenzivni oksidativni stres. Nakon ugradnje stenta nastaje prolazno, blago povećanje oksidativnog stresa, koje statistički nije značajno. S druge strane, zapaženo je značajno povećanje aktivnosti katalaze nakon ugradnje stenta, što ukazuje na aktivaciju sistema antioksidativne zaštite. Vrednosti parametara oksidativnog stresa se približavaju vrednostima u kontrolnoj grupi 72 sata nakon ugradnje stenta.

Ključne reči: *oksidativni stres, koronarni stent*