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Serum peroxiredoxin-1 in patients undergoing carotid endarterectomy: A short report

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Abstract

Introduction: *Endarterectomy of the internal carotid artery (CEA) plays an important role in the prevention of cerebral ischemic stroke; however, this surgical procedure may cause neurological complications. The aim of this study was to evaluate changes in serum levels of the oxidative stress marker peroxiredoxin-1 (PRDX1) in patients undergoing CEA.*

Material and methods: *Twenty-four patients undergoing endarterectomy for critical stenosis of the internal carotid artery participated in the study. Blood for testing was collected before CEA and twice after surgery. PRDX1 was determined by ELISA.*

Results: *The timing of blood sampling did not affect PRDX1 levels ($p > 0.05$). There was no statistically significant difference in serum PRDX1 levels between male and female groups and depending on the age of the patients ($p > 0.05$).*

Conclusion: *PRDX1 cannot be considered as a marker of neurological complications after CEA.*

Key words: brain ischemia-reperfusion injury, carotid endarterectomy, peroxiredoxin-1

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Introduction

Stroke is the second leading cause of death worldwide and the leading cause of disability, with increasing prevalence in developing countries. An important cause of cerebral ischemic stroke is stenosis of the internal carotid artery. Secondary prevention of ischemic stroke includes carotid endarterectomy (CEA). The above surgical treatment can prevent cerebral ischemic stroke, but it also causes surgical complications [1–4].

The literature suggests that CEA may cause brain damage due to ischemia and reperfusion as well as postoperative hyperperfusion syndrome. The mechanism leading to cerebral hyperperfusion syndrome is unknown; it may be related to increased regional cerebral blood flow secondary to loss of cerebrovascular autoregulation. Cerebral damage due to ischemia and reperfusion has been observed in both experimental and clinical studies [5, 6].

Peroxiredoxins (PRDXs) are among the antioxidant enzymes involved in superoxide reduction to balance cellular levels of hydrogen peroxide (H_2O_2), which is essential for cell signaling and metabolism and acts as a regulator of redox signaling. In mammals, there

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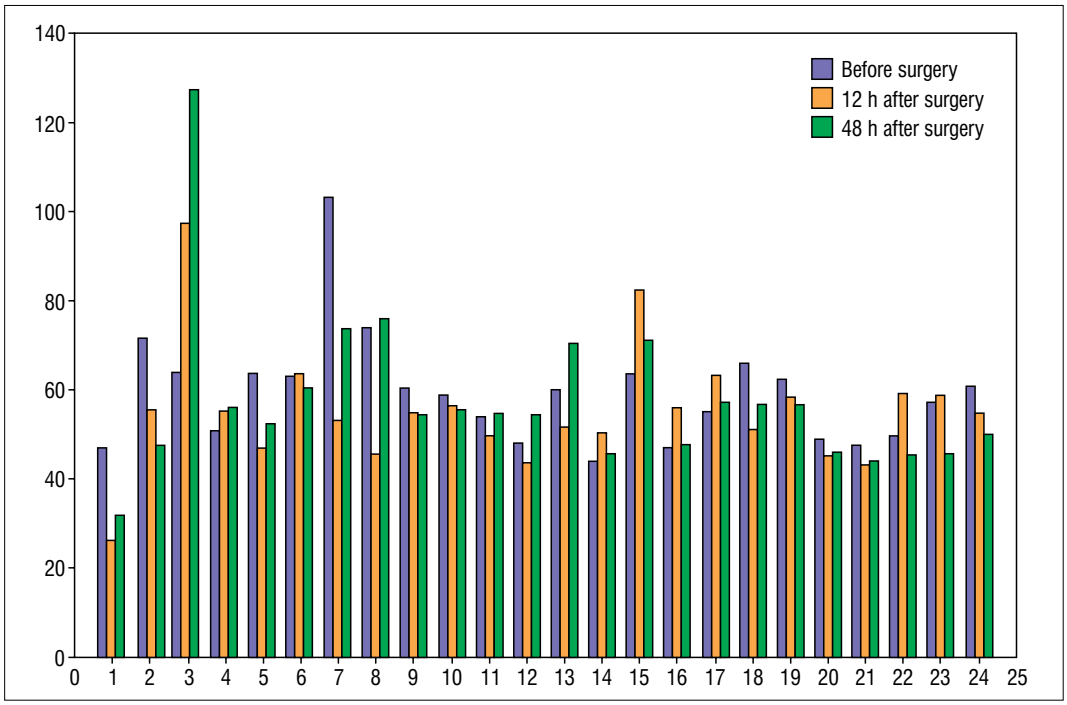

Figure 1. Serum PRDX1 [pg/mL] in patients

are six isoenzymes (PRDX1-6), classified as typical 2-Cys, atypical 2-Cys, or 1-Cys PRDXs. In addition to their superoxide scavenging activity, PRDXs are also involved in the regulation of various cell signaling pathways. Experimental studies indicate a protective role of PRDXs in various neurological diseases associated with oxidative stress and inflammation. There is also evidence suggesting a potential benefit of PRDXs in some human neurological diseases [7, 8]. PRDXs are released extracellularly from ischemic cells and initiate inflammation, leading to macrophage activation and a damaging cytokine response [9, 10].

The purpose of this study was to evaluate serum levels of PRDX1 in patients as a potential marker of CEA-induced neurological complications.

Material and methods

The study included patients hospitalized in the Department of Vascular Surgery and Angiology in Lublin. Patients were qualified for CEA because of critical stenosis of the internal carotid artery found on Doppler examination. Twenty-four patients (16 men, 8 women) participated in the study. The mean age of the patients was 71 years (55–88 years). Six patients had a history of ischemic stroke, while 4 patients had a history of transient cerebral ischemia.

Blood samples from the antecubital vein were collected: within 24 hours before CEA surgery [A], 12 hours after surgery [B], and 48 hours after surgery [C]. Serum PRDX1 levels were measured using a commercially available immunoassay Human PRDX1 (Peroxiredoxin-1) ELISA Kit; Wuhan Fine Biotech Co., Ltd., China).

For statistical analysis ANOVA test and Student's t-test were used. PRDX1 levels were determined in pg/mL. Values of $p < 0.05$ were taken as statistically significant.

The study was approved by the Bioethics Committee of the Medical University of Lublin.

Results

Serum PRDX1 levels in patients are presented in Figure 1.

Average PRDX1 level before CEA was 59.35 SD 12.45 pg/mL, 12 hours after surgery was 55.22 SD 13.44 pg/mL, and 48 hours after CEA was 57, 69 SD 18.06 pg/mL. ANOVA showed that the time of blood sample collection for testing did not affect PRDX1 levels ($p = 0.62$). However, there was a tendency for the level of the studied parameter to decrease 12 hours after surgery.

There was no statistically significant difference in serum PRDX1 levels between male and female groups and depending on the age of the patients ($p > 0.05$).

Discussion

A multicenter magnetic resonance imaging study reported 43.3% preoperative silent ischemic lesions and 9.2% new silent lesions after CEA [11]. Perioperative cerebral ischemic lesions on diffusion weighted imaging (DWI) after CEA are associated with a higher likelihood of recurrent cerebrovascular incidents. In patients undergoing CEA, symptom onset and elevated inflammatory markers are associated with a higher likelihood of lesions on perioperative DWI [12].

According to Shichita et al. [13], the onset of inflammatory process after ischemia is an important step in the progression of ischemia-reperfusion brain injury. The authors demonstrated that PRDXs family proteins released extracellularly from necrotic brain cells increase the expression of inflammatory cytokines through activation of Toll-like receptors 2 (TLR2) and TLR4, causing neuronal cell death, despite the fact that intracellular PRDXs exhibit neuroprotective effects. Intracellular release of PRDXs was observed 12 h after the onset of ischemic stroke, and neutralization of extracellular PRDXs by antibodies inhibited inflammatory cytokine expression and infarct volume growth. Brea et al. [14] found that PRDX1 expression was 10-fold stronger in ischemic stroke patients than in healthy subjects.

In the study conducted by Liu et al. [15], by using a mouse model of ischemia-reperfusion injury, the authors found that PRDX1 expression was up-regulated during ischemia-reperfusion injury in a time-dependent manner. Additionally, PRDX1-knockout mice showed reduced infarction area and alleviated neuropathological scores with decreased brain water contents. Furthermore, cell death and inflammatory response in mice with cerebral ischemia-reperfusion injury were markedly attenuated by PRDX1 knockout. The authors concluded that PRDX1 contributed to cerebral stroke by interacting with TLR4, providing an effective therapeutic approach for cerebral ischemia-reperfusion injury.

PRDX1 induces free radical scavenging. Based on their study, Tao et al. [16] conclude that nitrosative stress during ischemia activates E6AP E3 ubiquitin ligase, which ubiquitinates PRDX1 and subsequently exacerbates brain damage. Therefore, targeting the PRDX1 antioxidant defense pathway may represent a novel treatment strategy to protect the neurovascular system in stroke.

According to Richard et al. [17] accurately determining time-of-onset of cerebral infarction is important to clearly identify patients who could benefit from reperfusion therapies. The authors assessed the kinetics of PRDX1, a protein involved in oxidative stress during the acute phase of ischemia, and its ability to determine stroke onset in a population of patients with known onset of less than 24 hours and in a control group. PRDX1 levels were significantly higher in stroke patients compared to controls. PRDX1 levels were also higher in blood samples withdrawn before vs. after 3 hours following stroke onset, and before vs. after 6 hours. The authors suggest that PRDX1 levels could be the basis of a new method using biomarkers for determining cerebral infarction onset.

In our study, the change in serum PRDX1 levels could reflect the ischemia-reperfusion syndrome caused by CEA. However, this study showed that CEA had no significant effect on the serum PRDX1 levels of patients, which indicates that PRDX1 cannot be considered as a marker of neurological complications after CEA.

Conflict of interest

None.

References:

1. Campbell B, Khatri P. Stroke. The Lancet. 2020; 396(10244): 129–142, doi: 10.1016/s0140-6736(20)31179-x.
2. Campbell BCV, De Silva DA, Macleod MR, et al. Ischaemic stroke. Nat Rev Dis Primers. 2019; 5(1): 70, doi: 10.1038/s41572-019-0118-8, indexed in Pubmed: 31601801.
3. Orrapin S, Rerkasem K. Carotid endarterectomy for symptomatic carotid stenosis. Cochrane Database Syst Rev. 2017; 6: CD001081, doi: 10.1002/14651858.CD001081.pub3, indexed in Pubmed: 28590505.
4. Pasin L, Marrocco Trischitta MM, Landoni G, et al. Operative morbidity and mortality in octogenarians after carotid endarterectomy: a propensity score matching study. J Cardiovasc Surg (Torino). 2019; 60(6): 703–707, doi: 10.23736/S0021-9509.16.09488-X, indexed in Pubmed: 27625000.
5. Lieb M, Shah U, Hines GL. Cerebral hyperperfusion syndrome after carotid intervention: a review. Cardiol Rev. 2012; 20(2): 84–89, doi: 10.1097/CRD.0b013e318237eef8, indexed in Pubmed: 22183061.
6. Sundefeld Tardini DM, Bonetti Yoshida W. Brain injury due ischemia and reperfusion in carotid endarterectomy surgery. Rev Port Cir Cardiotorac Vasc. 2003; 10(3): 133–140.
7. Zhu H, Santo A, Li Y. The antioxidant enzyme peroxiredoxin and its protective role in neurological disorders. Exp Biol Med (Maywood). 2012; 237(2): 143–149, doi: 10.1258/ebm.2011.011152, indexed in Pubmed: 22302711.
8. Park MiH, Jo M, Kim YuRi, et al. Roles of peroxiredoxins in cancer, neurodegenerative diseases and inflammatory diseases. Pharmacol Ther. 2016; 163: 1–23, doi: 10.1016/j.pharmthera.2016.03.018, indexed in Pubmed: 27130805.
9. Garcia-Bonilla L, Iadecola C. Peroxiredoxin sets the brain on fire after stroke. Nat Med. 2012; 18(6): 858–859, doi: 10.1038/nm.2797, indexed in Pubmed: 22673994.
10. Kunze A, Zierath D, Tanzi P, et al. Peroxiredoxin 5 (PRX5) is correlated inversely to systemic markers of inflammation in acute stroke. Stroke. 2014; 45(2): 608–610, doi: 10.1161/STROKEAHA.113.003813, indexed in Pubmed: 24385276.

11. Pascot R, Parat B, Le Teurnier Y, et al. Predictive Factors of Silent Brain Infarcts after Asymptomatic Carotid Endarterectomy. Ann Vasc Surg. 2018; 51: 225–233, doi: 10.1016/j.avsg.2018.02.037, indexed in Pubmed: 29772320.
12. Rots ML, Meershoek AJA, Bonati LH, et al. Editor's Choice — Predictors of New Ischaemic Brain Lesions on Diffusion Weighted Imaging After Carotid Stenting and Endarterectomy: A Systematic Review. Eur J Vasc Endovasc Surg. 2019; 58(2): 163–174, doi: 10.1016/j.ejvs.2019.04.016, indexed in Pubmed: 31266681.
13. Shichita T, Hasegawa E, Kimura A, et al. Peroxiredoxin family proteins are key initiators of post-ischemic inflammation in the brain. Nat Med. 2012; 18(6): 911–917, doi: 10.1038/nm.2749, indexed in Pubmed: 22610280.
14. Brea D, Rodríguez-González R, Sobrino T, et al. Proteomic analysis shows differential protein expression in endothelial progenitor cells between healthy subjects and ischemic stroke patients. Neurol Res. 2011; 33(10): 1057–1063, doi: 10.1179/174313281lY.0000000038, indexed in Pubmed: 22196759.
15. Liu Q, Zhang Y. PRDX1 enhances cerebral ischemia-reperfusion injury through activation of TLR4-regulated inflammation and apoptosis. Biochem Biophys Res Commun. 2019; 519(3): 453–461, doi: 10.1016/j.bbrc.2019.08.077, indexed in Pubmed: 31526567.
16. Tao RR, Wang H, Hong LJ, et al. Nitrosative stress induces peroxiredoxin 1 ubiquitination during ischemic insult via E6AP activation in endothelial cells both in vitro and in vivo. Antioxid Redox Signal. 2014; 21(1): 1–16, doi: 10.1089/ars.2013.5381, indexed in Pubmed: 24295341.
17. Richard S, Lapierre V, Girerd N, et al. Diagnostic performance of peroxiredoxin 1 to determine time-of-onset of acute cerebral infarction. Sci Rep. 2016; 6: 38300, doi: 10.1038/srep38300, indexed in Pubmed: 27924073.