Austin Journal of Cardiovascular Disease and Atherosclerosis

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Austin Publishing Group

Research Article

Quantification of Hepcidin, Se, Zn, SOD and GPX in Chronic Kidney Disease Patients with Ischemic Stroke

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Received: May 01, 2017; **Accepted:** June 02, 2017; **Published:** June 09, 2017

Abstract

Objectives: Ischemic stroke in chronic kidney disease patients is usually caused by oxidative stress. Selenium, zinc, superoxide dismutase and glutathione peroxidase plays major role in anti oxidative defense system. Oxidative stress is combined with elevated free iron in organism; its level is regulates by peptide hepcidin. We searched for connection between hepcidin, selenium, zinc, SOD and GPX levels.

Methods: 13 patients with CKD and ischemic stroke were enrolled. We quantified iron, ferritin, and hepcidin, Se, Zn, SOD and GPX. Established results were compared to age and gender matched healthy controls.

Results: Patients with CKD and ischemic stroke showed significantly high serum hepcidin concentrations (205.1 ± 29.9 μg/L) compared to control group (20.4 ± 1.9 μg/L); P<0.001. Oxidative stress parameters were considerably decreased in CKD patient with ischemic stroke (Se: 304.7 ± 29.1 nmol/L; Zn: 9.8 ± 1.1 μmol/L; SOD: 32.1±8.7 μg/mL; and GPX: 7.4 ± 0.5 pg/mL) compared to controls (Se: 978.4 ± 41.1 nmol/L; Zn: 17.8 ± 1.7 μmol/L; SOD: 128.3 ± 10.9 μg/mL; and GPX: 40.8 ± 2.1 pg/mL); P<0.005.

Conclusion: Established results from our study showed essential correlation between hepcidin concentration and oxidative stress parameters in patients with CKD and ischemic stroke.

Keywords: Hepcidin; Chronic Kidney Disease; Ischemic Stroke; Selenium; Zinc; SOD; GPX

Introduction

Chronic kidney disease (CKD) is characterised by a cell metabolism changes, leading to oxidative stress. In the last years are presented more evidences of key role of free radicals in different cell damages. Oxidative stress takes major part in pathophysiology of generalized diseases, such as atherosclerosis, CKD, diabetes mellitus, malignancies [1]. Trace element selenium (Se) plays major role in anti oxidative defense system in human organism. Its function is achieved by proteins, in which selenium is included [2]. Se is a component of approximately 25 enzymes, including Glutathione Peroxidases (GPX), thioredoxin reductases and selenoprotein P, assuring anti oxidative activity against caused by oxidative radicals carcinogenesis. Zinc (Zn) is responsible for function of more than 300 active metal proteins. Zn acts in basic biochemical processes in human organism. Another antioxidant enzyme is Superoxide Dismutase (SOD). Deficiency of Se is connected to arterial damages and leads to increased vascular diseases [3]. Selenium may prevents ischemic neuronal impairment, thereby restricts ischemic cellular death [4]. Hepcidin might be a risk factor for atherosclerosis [5,6]. In patho-physiological process iron is retrieves from reticulo-endothelial depots, its free form increases and accumulates in tissues and cells. Hepcidin regulates iron transfer to blood stream from these cells [7]. Inflammatory cytokines are powerful stimulators for hepcidin secretion, and plays important role in functional iron deficiency in anemia of chronic diseases (ACD). Oxidative stress leads to neuronal structures damage and subsequently to cerebral ischemia. Free iron increases during ischemia and leads to oxidative brain injury.

Methods

13 patients with CKD and ischemic stroke were enrolled; average age 58.8 ± 5.3. They were diagnosed at University "Aleksandrovska" hospital at Clinic of Neurology, Clinic of Nephrology and Clinic of Dialysis treatment. We quantified iron, ferritin, and hepcidin, Se, Zn, SOD and GPX. Established results were compared to age and gender matched healthy controls. Biochemical parameters were analyzed on Dimension RxL MAX (Siemens Healthcare). CRP levels were measured by nephelometric method on BN ProSpec (Siemens Healthcare). Hepcidin, SOD and GPX were quantified by ELISA method. Obtained results were evaluated statistically by SPSS 13.0 (IBM). Correlation and significance were defined by Student's paired t-test and Parson's correlation.

Results

Table 1 represents established results from CKD patients with ischemic stroke and healthy controls.

Table 1 Analyzed parameters in CKD patients with ischemic stroke and healthy controls (presented as mean value ± SD). We determine significantly higher serum hepcidin levels in CKD patients with ischemic stroke (205.1 ± 29.9 μg/L) compared to controls (20.4 ± 1.9 μg/L); P<0.001. Oxidative stress parameters were considerably

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Citation: Petrova J, Manolov V, Hadjidekova S, Yonova D, Bogov B, Vasilev V, et al. Quantification of Hepcidin, Se, Zn, SOD and GPX in Chronic Kidney Disease Patients with Ischemic Stroke. Austin J Cardiovasc Dis Atherosclerosis. 2017; 4(1): 1032.

Table 1: Analyzed parameters in CKD patients with ischemic stroke and healthy controls (presented as mean value ± SD).

	CKD Patients With Ischemic Stroke		Healthy Controls	
Hepcidin (µg/L)	205.1	29.9	20.4	1.9
Se (nmol/L)	304.7	29.1	978.4	41.1
Zn (µmol/L)	9.8	1.1	17.8	1.7
SOD (µg/mL)	32.1	8.7	128.3	10.9
GPX (pg/mL)	7.4	0.5	40.8	2.1
Fe (µmol/L)	12.2	5.9	18.7	7.6
TIBC (µmol/L)	45	6.5	64.5	9.4
Ferritin (ng/mL)	536.3	87.4	89.2	17.1
Transferrin (g/L)	1.9	0.4	2.9	0.5
Creatinine (µmol/L)	716.1	182.3	73.1	7.7
CRP (mg/L)	11.5	4.1	1.6	0.4

CKD patients with ischemic stroke healthy controls.
Se – selenium; Zn – zinc; SOD – superoxide dismutase; GPX – glutathione peroxidase; Fe – iron; TIBC – total iron binding capacity; CRP – C-reactive protein

decreased in CKD patient with ischemic stroke compared to control group. Selenium concentrations were 304.7 ± 29.1 nmol/l to 978.4 ± 41.1 nmol/l; P<0.001. Zinc levels were 9.8 ± 1.1 µmol/l to 17.8 ± 1.7 µmol/l; P<0.005. Quantification of superoxide dismutase showed 32.1 ± 8.7 µg/ml in CKD cases, and 128.3 ± 10.9 µg/ml in controls; P<0.001. Glutathione peroxidase concentrations in CKD with ischemic stroke patients were 7.4 ± 0.5 pg/ml compared to 40.8 ± 2.1 pg/ml in healthy controls; P<0.001. Hepcidin concentrations correlated negatively to all oxidative stress assessment analyses (0.9<r<0.7, P<0.005).

Discussion

A chronic kidney disease (CKD) is characterized by cell metabolism changes, leading t oxidative stress, which is a key moderator of pathology of kidney injury. Free oxidative radicals damages different tissues and organs; trace and toxic elements enters and destroys cells. In CKD patients, in terminal stage, cadmium, chromium, copper, lead and vanadium levels are increased and selenium, zinc and magnesium are decreased compared to healthy persons. Some authors said there is no difference in selenium levels between CKD cases and healthy controls [8], in the opposites others finds lower levels [9]. Some researchers published reduction of selenium concentrations with disease progress [10]. It is considerably in terminal stages, when selenium concentration is much less than 50% (P < 0.0001), in comparison to the controls [11]. As a small peptide, hepcidin is eliminated through kidneys with endocytosis and proteolysis. Serum hepcidin concentrations might be increased in different conditions, which decrease hepcidin clearance [12]. Elevated circulated iron stimulates hepcidin secretion. Increased hepcidin, on the other hand, blocks iron in its storage sites, thus reduces iron overload. Low iron concentrations suppress hepcidin secretion and stimulate iron absorption through duodenal enterocytes and its exemption from iron tissue depots.

For the normal functioning of human organism it is essential to maintain iron in the reference values. Clinical significance have decreased and increased iron concentrations. Hepcidin, as iron homeostasis regulator plays a major role as diagnostic tool in differentiation between conditions with disturbed iron regulation. One of mechanism for hepcidin secretion regulation is inflammation through inflammatory cytokines [13]. Some authors show that chelators may decrease toxicity, caused by heart ischemia and reperfusion [14], as well as brain ischemia [15].

On the other side, low selenium concentrations leads to oxidative stress development, thus deepens neuronal brain injury. Our results show significant correlation between hepcidin, interleukin-6, and selenium and superoxide dismutase in patients with chronic kidney disease and ischemic stroke.

Conclusion

Quantification of superoxide dismutase, glutathione peroxidase, selenium, zinc and hepcidin in chronic kidney disease patients, on chronic dialysis with ischemic stroke is necessary for oxidative stress progress, which further worsens condition. Our results suggests important role of hepcidin in iron accumulation in CKD patients with cerebral ischemia.

Acknowledgement

This project is implemented with the financial support of Medical University - Sofia, “Grant 2013”, Contract № 10/2013; “Grant 2015”, Contract № 1-C/2015, “Grant 2016”, Contract № 4-C/2016; “Grant 2017”, Contract № Д-54/2017. We also kindly appreciate the support from “Marvena” (a “Siemens Healthcare” distributor in Bulgaria), especially to Mrs. Silviya Kirova and Mr. Velizar Dragoev.

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Austin J Cardiovasc Dis Atherosclerosis - Volume 4 Issue 1 - 2017
ISSN: 2472-3568 | www.austinpublishinggroup.com
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Citation: Petrova J, Manolov V, Hadjidekova S, Yonova D, Bogov B, Vasilev V, et al. Quantification of Hepcidin, Se, Zn, SOD and GPX in Chronic Kidney Disease Patients with Ischemic Stroke. Austin J Cardiovasc Dis Atherosclerosis. 2017; 4(1): 1032.