

Volume: 02 Issue: 02 | March-April 2021 ISSN: 2660-4159

www.cajmns.centralasianstudies.org/index.php

The influence of hypertension on the Pro-oxidant capacity and lipid peroxidation in oral fluid

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Received 2th February 2021,
 Accepted 27th February 2021,
 Online 04th March 2021

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ABSTRACT: On the basis of comparative studies of the performance of GENDER-AOS oral fluid in patients with normal blood pressure, pre-hypertension and clinically verified arterial hypertension the effect of hypertension on the increase in Pro-oxidant potential of oral liquid: a decrease in the activity of enzymes EPA – CT, SOD, MPO,GRIS AOA and the increase in the concentration of LPO products – OSH, DC,TC and MDA. Violations of the enzymatic and non - enzymatic links of the antioxidant protection of the oral fluid and the increase in the processes of POL in patients with hypertension determine the need for them to receive special additional dental care.

Key words: hypertension, enzymes, Oral fluid

Introduction.

Hypertension is a complex condition whose aetiology depends on several factors (smoking, diet, genetics, family history, pre-existing pathologies) and in most cases it is difficult to identify the underlying cause ("essential hypertension"). In addition to the complex aetiology of this disease, oxidative stress is an important factor in hypertensive disorders. There is still debate as to whether excessive production of lipoperoxidation products is a cause or consequence of hypertension, as in vitro and in vivo studies suggest that reactive oxygen species trigger the activation of certain molecular mechanisms, which in turn raise blood pressure levels.

Oral fluid is a multi-component mixture of biological fluids consisting of salivary gland secretion, blood plasma and serum and oral tissues. The salivary glands respond sensitively to pathological disorders and physiological shifts in the body by changing the composition and properties of the oral fluid. Saliva also has its own antioxidant properties related to the composition of its enzymatic (mainly peroxidase system) and non-enzymatic compounds (uric acid, glutathione, sialic

acid), which can be determined in saliva samples. Oral fluid analysis is an attractive tool for diagnosing and monitoring diseases and for predicting the progression of future diseases. As a clinical tool oral fluid has many advantages over serum, including ease of collection, storage and transport.

The study of oxidative biomarkers in oral fluid in many pathological processes has increased significantly over the last decade. Thus, given the fact that arterial hypertension is a chronic disease that involves various mechanisms such as oxidative stress, inflammation and endothelial dysfunction.

Purpose of the study: To assess the effect of different degrees of arterial hypertension on oral oxidative biomarker levels.

Materials and methods of research: The diagnosis of arterial hypertension was made when the systolic blood pressure was over 140 mmHg and the diastolic blood pressure was over 90 mmHg.

Salivary gland function was studied in 3 groups of patients:

- Group 1 consisted of 33 patients with normal BP (BP less than 120/80 mmHg who were not taking hypotensive medication);
- Group 2 consisted of 34 patients with borderline hypertension (systolic BP in the range of 120-139 or diastolic BP in the range of 80-89 mmHg on antihypertensive medication);
- Group 3 consisted of 35 patients with Stage I AH (systolic BP in the range 140-159 or diastolic BP in the range 90-99 mmHg on antihypertensive medication). To improve measurement accuracy BP was monitored twice. An automatic sphygmomanometer was used to eliminate differences between different measurements.

Participants in the present study were only hypertensive patients without systemic disease, patients with clinically diagnosed arterial hypertension taking medication for high BP (such as ketonal, valsacor, normodipine, enalapril). Patients taking diuretics and statins were excluded from the study because of their ability to cause xerostomia. The spitting method was used to collect unstimulated whole saliva. All saliva samples were collected at 25°C at 9-11 am. People were prohibited from eating, drinking, smoking or brushing their teeth for at least 90 minutes before sampling to reduce the effects of daily stress on saliva composition. Before sampling, participants were left sitting in a chair and asked to swallow all the saliva they had in their mouths. They were then asked not to swallow saliva for 5 minutes and to spit the collected saliva into sterilised cups provided by the researchers.

The activity of antioxidant system enzymes was studied in oral fluid samples: catalase (CT)-spectrophotometric method by reaction with molybdenum salts, superoxide dismutase (SOD)-by autooxidation of adrenaline by superoxide anion-radical in alkaline medium, Glutathione peroxidase (MPO) - by the oxidation rate of reduced glutathione in the presence of tret-butyl hydroperoxide, glutathione reductase (GR) activity - by spectrophotometric method by the NADPH oxidation rate. Total antioxidant activity was determined by the oxidation rate of reduced form of 2,6-dichlorophenolindophenol (2,6-DCPHF).

Concentration of primary products of lipoperoxidation - diene conjugates (DC), intermediate products - triene conjugates (TC) and final products - Schiff bases (SS) were determined in heptane-isopropanol fractions by relative values E232/220;E278/220 and E400/220, respectively, concentration of malonic dialdehyde (MDA) - by reaction with thiorbituric acid. Clinical parameters, oral fluid parameters were expressed as either percentages or mean values \pm standard deviation. Statistically significant differences were determined using Student's t-test. A value of <0.05 was considered significant. All analyses were performed using the NCSS 2000 statistical software package.

Research results. The concentrations of lipoperoxidation products and the activity of antioxidant defence enzymes in oral fluid in patients with different stages of hypertension are shown in the table and figure.

Table.

Performance of oral LPO-AOS processes in patients with different stages of hypertension.

Indicators	No hypertension Normal BP	Borderline hypertension BP 120-129/80/89	Arterial hypertension stage 1 BP 140-159/90-99
AOS enzymes			
Catalyses m cat/l	3,40±0,16	3,88±0,14	2,71±0,12
SOD	9,03±0,43	11,03±0,49	6,77±0,24
U.L.	24,17±1,17	30,42±1,62	18,42±0,90
MPO	18,01±0,07	20,15±1,02	15,32±0,67
Mk mol/min/l	2,11±0,09	2,51±0,11	1,67±0,75

DC r.unit	0,09±0,004	0,09±0,003	0,12±0,006
TCr.unit.	0,05±0,002	0,06±0,003	0,08±0,004
TC t.d.e.	1,80±0,08	2,02±0,081	2,45±0,11
MDA	0,35±0,01	0,41±0,017	0,47±0,021

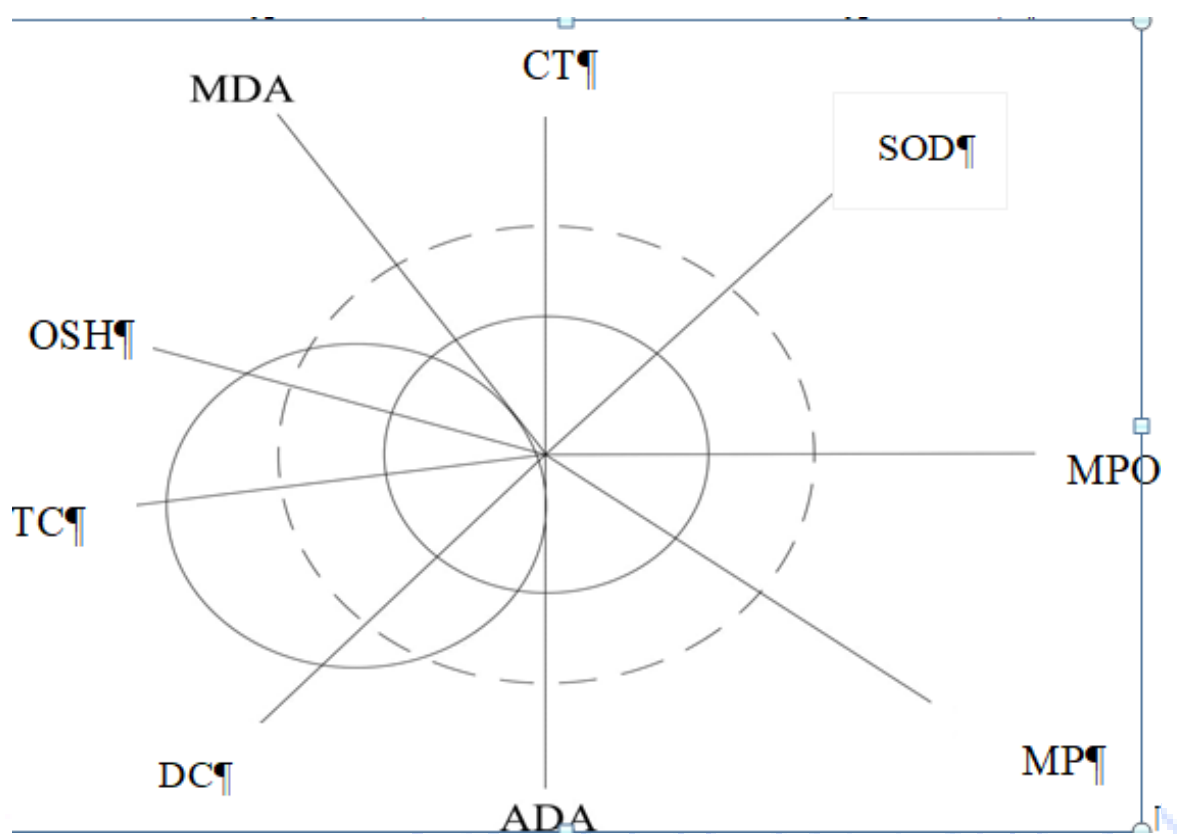
Products of lipid peroxidation

Note: P<0.05 relative to no hypertension; P<0.05 relative to borderline hypertension

As can be seen from the data presented in the table and figure, increasing concentrations of lipid peroxidation products in oral fluid in patients with various stages of hypertension are associated with its severity. Thus, the concentration of primary lipoperoxidation products, diene conjugates, was increased by 12.50% ($P \geq 0.05$) in patients with borderline hypertension compared with those examined without hypertension; lipoperoxidation intermediates - triene conjugates - by 20.00% ($P \leq 0.0\%$) and lipoperoxidation end products - Schiff bases - by 12.22% ($P \geq 0.05$); the corresponding dynamics in patients with hypertension was significantly more expressed - 50.00% ($P \leq 0.0\%$); 36.11% ($P \leq 0.0\%$) and 25.00% ($P \leq 0.0\%$).

Malonic dialdehyde is one of the most reliable markers of oxidative stress in clinical situations. Mean oral malonic dialdehyde concentrations were significantly higher in hypertensive patients compared to prehypertensive patients and healthy subjects. Thus, the increase in MDA concentration in patients with borderline hypertension was 17.14% ($P \geq 0.05$); and in patients with hypertension it was 34.29% ($P \leq 0.0\%$).

Fig. Lipid peroxidation - AOS processes in the oral fluid of patients with different stages of hypertension (in % relative to those without hypertension).



Catalase CT	Borderline HD	Hypertension
	114,18	79,71
SOD	122,15	75,47
MPO	125,86	76,21
MP	111,88	85,06
AOA	118,96	79,15
DC	112,50	150,0
TC	120,0	136,11
OSH	112,22	125,0
MDA	117,14	134,29

Fig. Oral fluid LPO-AOS indexes in patients with different stages of hypertension (in relation to non-hypertensive patients).

This significant and statistically significant increase in oral concentration of lipid peroxidation products in hypertensive patients is consistent with numerous studies that have found a significant increase in oxidative stress in biological fluids of patients with arterial hypertension and proving the pathogenetic role of oxidative stress in the pathogenesis of arterial hypertension.

Results:

For the present study demonstrated significant changes in the activity of antioxidant enzymes associated with different stages of hypertension.

Thus, in clinically verified borderline arterial hypertension there was an increase in the activity of the studied AOS enzymes, with catalase activity increasing by 14.18% ($P \geq 0.05$); SOD - by 22.15% ($P \leq 0.0\%$); MPO - by 25.86% ($P \leq 0.0\%$); MP - by 11.88% ($P \geq 0.05$); and AOA - by 18.96% ($P \leq 0.0\%$). In patients with advanced hypertension, there was a statistically significant decrease in the activity of antioxidant enzymes relative to healthy subjects, amounting to 20.29% ($P \leq 0.0\%$) for CT, 20.03% ($P \leq 0.0\%$) for SOD, 23.79% ($P \leq 0.0\%$) for MPO, 14.94% ($P \leq 0.0\%$) and 20.85% ($P \leq 0.0\%$) for AOA (Table, Figure).

We have found that arterial hypertension is associated with impaired antioxidant barrier and oxidative damage to proteins and lipids in the oral fluid. Oxidative stress is known to play a key role in the pathogenesis of hypertension. In arterial hypertension free oxygen radicals increase the expression of angiotensin II receptor, induce pro-inflammatory signaling pathways and activate genes responsible for angiogenesis and proliferation of endothelial cells. The same processes disrupt the relaxation phase of smooth muscle tissue within blood vessels and increase endothelial permeability to lipoproteins, which in oxidised form increase inflammation. It is well known that the assessment of oxidative stress levels cannot be based on a few markers alone. In our study we assessed the enzymatic and non-enzymatic antioxidant barrier, the oxidative-reductive status and oxidative damage to oral fluid proteins and lipids. Antioxidants are the first line of defence against oxidative stress. In our study we observed increased activity of antioxidant enzymes (CT, SOD, MPO, GR and AOA) of oral fluid in patients with prehypertension compared with control, indicating an adaptive response of the body to increased production of AOS. In hypertensive patients, the activity of oral antioxidant enzymes is significantly reduced, suggesting deficiency or depletion of adaptive resources that contribute to the progression of oral pathology. Total oxidative status is thought to reflect the content of oxidants in the biological system. Numerous studies on the problem have shown that the main source of AFC in hypertension is the overexpression of pro-oxidant enzymes generating significant amounts of superoxide radical anion (O_2^-) and hydrogen peroxide (H_2O_2). This is why patients with prehypertension show increased activity of SOD (O_2^- converting enzyme) and CT (H_2O_2 decomposing enzyme), reflecting an adaptive response corresponding to the relative stabilisation of pro-oxidant systems in the absence of marked clinical symptomatology and depletion of antioxidant enzyme activity in the presence of clinically verified hypertension. Despite an enhanced antioxidant barrier, in patients with borderline hypertension we found a statistically insignificant increase in lipid oxidative damage (MDA) and a statistically significant increase in concentrations of lipoperoxidation intermediates. Elevated levels of lipoperoxidation products, in turn, can penetrate through the damaged endothelium into the blood vessel walls and then be taken up by macrophages, leading to foam cell formation, which contributes significantly to the disruption of the blood lipid spectrum and the pathogenesis of hypertension. The same processes may contribute significantly to the activation of many signalling pathways in the pathogenesis of hypertension (production of pro-inflammatory cytokines, chemokines and adhesion molecules. However, further studies are needed to elucidate the role of oxidative stress in the maintenance of oral homeostasis. Thus, it is clear that patients with hypertension register oxidative stress in their oral fluid. The oral antioxidant barrier does not necessarily reflect central redox status. However, in patients with arterial hypertension the effect of hypertension on the risk of changes in relevant markers has been established, which proves a causal relationship between oral fluid oxidative stress and arterial hypertension and determines the importance of assessing oral fluid redox potential for the diagnosis of hypertension. In turn, oxidative stress initiated by hypertension may be an important factor in the development of oral pathology. The negative effect of oxidative stress on salivary gland function cannot also be excluded, since oxidative stress is a key pathological factor responsible for hyposalivation in many systemic diseases. Non-invasive analysis is particularly important for monitoring hypertension. Oxidative stress has now been

shown to play an important role in oral diseases and its association with various systemic diseases. Oxidative stress is an important pathogenetic mechanism in the development of hypertension, the development of which occurs with the involvement of chronic inflammation. Free radicals are detrimental to various organs of the body. This is due to lipid peroxidation and irreversible protein modification, which leads to apoptosis of cells or programmed cell death. In recent years, there has been an increase in oral diseases associated with oxidative stress. Oxidative stress in oral diseases is associated with other systemic diseases of the body, including cardiovascular disease, which includes hypertension.

Conclusions:

Thus, we have demonstrated an exacerbation of oral oxidative stress in hypertension. Further studies are needed for dentistry to assess the role of oxidative imbalances in the development of dental pathology in hypertensive patients:

- Hypertension is associated with abnormal enzymatic and non-enzymatic antioxidant protection of the oral fluid. Patients with hypertension should receive additional dental care;
- Oral redox balance may be a potential biomarker of hypertension, and its use in patients with arterial hypertension is possible as a potential marker for monitoring disease progression.

Reference List:

1. Ameena Ryhan Diajil, Lamia Ibrahim Sood, Rasha Abbas Azeez A Salivary α -Amylase Level in Relation to the Oral Health Parameters among Children in Baghdad City // Journal of Baghdad college of dentistry, 2016, Volume 28, Issue 2, pages 40-46
2. Akhmedov R.M., Mirkhojaev I.A., Khamdamov B.Z. Morphostructural changes in the liver in the elderly and old age // Conference proceedings. Journal of Problems of Biology and Medicine. - – 2016. - №3,1(90). - C. 18.56.
3. Azimov M. I., Shomurodov K.E. A technique for Cleft Palate Repair. Journal of research in health science. Vol. 1, No. 2, 2018, pp. 56-59.
4. Bekzhanova O.E., Rizaev E.A. Unity of systemic pathogenetic mechanisms of development of somatic pathology and periodontal diseases // Medical Journal of Uzbekistan. 2019. №3. C. 85-88.
5. Fotina I.A. Comparative analysis of biochemical indicators of blood serum and saliva in healthy and diabetic patients: Avtoref. d.m., Nizhny-Novgorod, 2012. - 28c.
6. Fotina I.A. Informative changes in biochemical parameters of oral fluid and blood serum in type II diabetes // Bulletin of new medical technologies. - 2011. - №4. - C. 184-186
7. González J, Valls N., Brito R., Rodrigo R. Essential hypertension and oxidative stress: New insights 2014 Jun 26;6(6):353-66. doi: 10.4330/wjc.v6.i6.353.
8. Kologrivova I. V., Koshelskaya O. A., Suslova T. E., Vinnitskaya I. V., Kravchenko E. S., Trubacheva O. A. Interrelation of inflammatory factors and metabolic parameters in obesity in patients with high and very high risk arterial hypertension // Russian Journal of Cardiology 2018; 23 (5): 27-33
9. Kumar J, Teoh SL, Das S and Mahaknaukrah P (2017) Oxidative Stress in Oral Diseases: Understanding Its Relation with Other Systemic Diseases. *Front. Physiol.* 8:693. doi: 10.3389/fphys.2017.00693
10. Kamalova M. I., Islamov Sh. E., Khaydarov N.K.// MORPHOLOGICAL CHANGES IN BRAIN VESSELS IN ISCHEMIC STROKE. Journal of Biomedicine and Practice 2020, vol. 6, issue 5, pp.280-284
11. Khamdamov B.Z. Indicators of immunocytocine status in purulent-necrotic lesions of the lower extremities in patients with diabetes mellitus.//American Journal of Medicine and Medical Sciences, 2020 10 (7) 473-478 DOI: 10.5923/j.ajmm.2020.- 1007.08

12. Madhloom B. N., Diajil A. R Oxidative Stress Status in Hypertensive Patients on Capoten Treatment International Journal of Science and Research (IJSR) ISSN (Online): 2319-7064 Volume 7 Issue 2, February 2018 . – P 442 -450.
13. Madhloom B. N., Diajil A. R.Oxidative stress status in hypertensive patients on amlodipine treatment // J Bagh College Dentistry. – 2020. - Vol. 32(1). – P.1 -9.
14. Pogodina A. V., Valyavskaya O. V., Kolesnikova L.R., Rychkova L.V., Kolesnikov S. I. Arterial hypertension and periodontitis: key aspects of comorbidity. Arterial hypertension. 2019;25(6):682-692. doi:10.18705/1607-419X-2019-25-6-682-692
15. Prasanthi B, Kannan N, Patil RR. Effect of diuretics on salivary flow, composition and oral health status: A clinico-biochemical study. Ann Med Health Sci Res 2014;4(4):549-53.
16. Sazonova OV, Myakisheva YV, Borodina LM, Ginzburg MM, Gavrushin MM, Gorbachev DA, Frolova OV Diagnostic informativeness of oral fluid analysis to assess metabolic status in obese patients // Science and Innovation in Medicine. - 2018. - 3(11). - C.21 - 24.
17. Skutnik-Radziszewska A., Maciejczyk M., Fejfer K., Krahel J., Flisiak I., Kołodziej U., Zalewska A. Salivary Antioxidants and Oxidative Stress in Psoriatic Patients: Can Salivary Total Oxidant Status and Oxidative Status Index Be a Plaque Psoriasis Biomarker? Oxid. Med. Cell. Longev. 2020;2020:9086024. doi: 10.1155/2020/9086024. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
18. Small H., Y., Migliarino S., Czesnikiewicz-Guzik M., Guzik T. J. // Hypertension: Focus on autoimmunity and oxidative stress Free Radical Biology and Medicine Volume 125, September 2018, Pages 104-115
19. Shomurodov K.E., Comparative assessment of the influence of different methods of palatoplasty on the growth and development of the upper jaw in children with congenital cleft palate. European Science Review. – Vienna. Prague. – 2018. - №5-6. – P.7-11
20. Vernerová A., Krčmová L.K., Melichar B., Švec F. Non-invasive determination of uric acid in human saliva in the diagnosis of serious disorders Clin Chem Lab Med. Received October 15, 2020; accepted November 12, 2020; published online November 30, 2020 <https://doi.org/10.1515/cclm-2020-1533>