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Research article

ENDOTHELIN-1 AS A RISK FACTOR CAUSING CARDIOVASCULAR PATHOLOGY IN YOUNG AND MIDDLE-AGED PEOPLE EMPLOYED UNDER HAZARDOUS WORKING CONDITIONS

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Our research goal was to reveal peculiarities related to changes in endothelin-1 contents in blood serum in young and middle-aged people exposed to occupational noise and industrial welding and silicon-containing aerosols with fibrogenic effects. Another goal was to establish a correlation between endothelin-1 contents and blood pressure, body mass, and dyslipidemia.

We examined workers employed at a metallurgic plant in Nizhniy Novgorod region. Endothelin-1 concentration in blood serum was determined with «Endothelin (1–21)», a reagent kit for ELISA produced by «Biomedica Medizinprodukte GmbH & Co KG» (Austria). We detected certain group differences in endothelin-1 contents in blood serum and frequency of its elevated concentrations between workers who had to work under different working conditions. We established a direct correlation between endothelin-1 and blood pressure, total cholesterol, and body mass index. Elevated endothelin-1 contents in people suffering from arterial hypertension can indicate a higher risk of complications this disease might have. People who have elevated endothelin-1 contents but normal blood pressure, total cholesterol within physiological standard and normal body mass index can be recommended to have regular medical check-ups focusing on functional state of their cardiovascular system; endothelin-1 in this case should be considered a risk factor that might cause cardiovascular pathology occurrence. An individual approach is required when assessing elevated endothelin-1 contents and probable use of this parameter as a risk factor that might cause cardiovascular pathology in young and middle-aged people employed under hazardous working conditions.

Key words: *adverse occupational factors, endothelin-1, blood pressure, total cholesterol, body mass, cardiovascular pathology, risk factor, biomarker.*

Over recent years, experts' attention has been concentrated on searching for biochemical markers that could indicate there was a cardiovascular pathology at an early stage in its development in young and middle-aged people. And it is especially vital when it comes down to men rather than women since signs of atherosclerotic diseases tend to appear

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earlier among them. Risk factors that may cause cardiovascular pathology are smoking, overweight, low physical activity, blood pressure, and hereditary predisposition [1]. A significant contribution is also made by adverse occupational factors [2, 3]. By now, there are several known biochemical parameters; analysis of changes in them together with examining functional and clinical parameters provides an insight into atherosclerotic process development and subsequent occurrence of cardiovascular pathology [4]. Such parameters as overall cholesterol and dextrose are to be determined during any periodical medical examination (according to the Order by the RF Ministry for Public Healthcare and Social Development issued on April 12, 2011 No. 302n[1]). Changes in these biomarkers together with EKG readings, body mass index (BMI), and blood pressure (BP) reflect only one side in pathogenesis of cardiovascular pathology, namely, a role probably played in this pathogenesis by metabolic disorders that contribute significantly into development of atherosclerosis and cardiovascular pathology[2]. However, pathogenetic mechanisms of cardiovascular pathology development are more complicated and it is a vital task to manage to reveal them at initial stages, especially among young people with their bodies still being highly adaptable to environmental factors [5]. Endothelin-1 (ET-1) is a marker that can be useful here since it is a marker of endothelial dysfunction that becomes apparent via changes in vascular tonus and damage to vessel walls making them thicker and thus resulting in vasoconstriction. All this plays a significant role in pathogenesis of atherosclerosis and arterial hypertension (AH) development [6, 7]. It was established that elevated overall peripheral vascular resistance (OPVR) was a significant pathogenetic component in AH occurrence; this resistance, in its turn, is closely connected with vascular endothelium condition and with excessive ET-1 formation in particular [8]. According to some authors, OPVR remains pathologically high among those young people who are prone to AH. Some research works revealed that 25 % people living in the USA aged 20 and older suffered from hypertension since their systolic blood pressure (SBP) was 120–139 mm Hg; and diastolic blood pressure (DBP), 80–89 mm Hg. A probability that essential hypertension would develop was 11 times higher among young people with such blood pressure than among those with optimal blood pressure (SBP being lower than 120 mm Hg and DBP lower than 80 mm Hg) [9]. A relation between ET-1 and AH is confirmed by many researchers [10, 11]; but relations between ET-1 and dyslipidemia and overweight require further investigation [12] and it provides an opportunity to consider ET-1 a risk factor that can cause cardiovascular pathology.

Workers employed at metallurgic and metal-processing productions are exposed to a set of adverse occupational factors [13, 14]. As a rule, they are young and middle-aged people who start their career at such enterprises at 23–25; it is extremely important to monitor their health, to provide timely prophylaxis for them in order to prevent work-related and occupationally induced pathologies since it will make their period of employment longer and result in longer life expectancy [15]. Issues related to examining endothelial dysfunction among young and middle-aged people and its relation with AH, dyslipidemia, and overweight among workers exposed to adverse occupational factors at their workplaces have not been studied in detail and require special attention by researchers and physicians.

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[1] On approving the list of adverse and (or) hazardous occupational factors and works which require obligatory preliminary and periodical medical examinations (checkups) and the Procedure for performing obligatory preliminary and periodical medical examinations (checkups) of workers who deal with hard labor and adverse and (or) hazardous working conditions at their workplaces: The Order by the RF Ministry for Pubic Healthcare and Social Development issued on April 12, 2011 No. 302n (last edited on May 18, 2020). *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_120902/ (January 29, 2021).

[2] Diagnostics and correction of lipid metabolism disorders for atherosclerosis prevention and treatment. Russian recommendations: the VI revisions by D.M. Aronov, G.G. Arabidze, N.M. Akhmedjanov, T.V. Balakhonova, O.L. Barbarash, S.A. Boitsov [et al.]. Moscow, 2017, 44 p.

Our research goal was to detect peculiarities related to changes in Endothelin-1 contents in blood serum among young and middle-aged workers exposed to occupational noise and welding and silicon-containing aerosols with predominantly fibrogenic effects and to reveal a relation between endothelin-1 contents and blood pressure, body weight, and dyslipidemia.

Data and methods. We examined 87 workers employed at a metallurgic plant in Nizhniy Novgorod region; they were all men aged from 25 to 51.Their working experience at this enterprise varied from 5 to 15 years. All these workers had a profound medical examination at an advisory polyclinic of Rospotrebnadzor's Scientific and Research Institute for Hygiene and Occupational Pathology. All the examined workers dealt with producing big-diameter metal pipes. They were divided into 2 groups depending on a type and essence of adverse occupational factors at their workplace; the first group (32 people aged 38.6 ± 8.3) was exposed to occupational noise (crane operators, pipe elector-welding mill operators, metal sorters, repairmen, and control unit operators); the second group (55 people aged 39.1 ± 9.5) were exposed to welding and silicon-containing aerosols with predominantly fibrogenic effects (pipe electro-welders, strop operators, metal cutters, milling machine operators, and rollers).

Working conditions were assessed according to the FZ-426 issued on December 28, 2013 "On special assessment of working conditions"[3]. According to this assessment, occupational noise at workplaces exceeded permissible levels (more than 80 dBA, and it even reached 83–85 dBA in some areas at production facilities). Aerosol contents in working area air exceeded maximum permissible concentrations and were within ranges that corresponded to working conditions belonging to 3.1 hazard category ("hazardous", the first degree).

The reference group (the third group) was made up of men (31 people aged 43.3 ± 9.6) who were not exposed to any adverse occupational factors at their workplaces; they were employed at an advertising agency and dealt with placing street advertising in the regional center and region. All three groups were comparable as per age, sex, and working experience ($p > 0.05$).

We excluded people with acute respiratory and inflammatory diseases, malignant neoplasms, type II pancreatic diabetes and exacerbation of chronic diseases from our research. All participants gave their voluntary informed consent to be examined and examination results to be published. Our research didn't infringe on rights of the examined people and didn't impose any threats for them in conformity with biomedical ethics requirements fixed by Helsinki Declaration issued by the World Medical Association (2000) and The Order by the RF Public Healthcare Ministry issued on June 19, 2003 No. 266[4].

Endothelin-1 concentration in blood serum was determined with "Endotelin (1-21)" reagent kit for ELISA tests produced by "Biomedica Medizinprodukte GmbH & Co KG" (Austria). A range of reference values for ET-1 concentrations in blood serum of healthy donors amounted to 1–3.5 pg/ml. Concentrations of cholesterol (CS), low density lipoproteins (LDLP-CS), high density lipoproteins (HDLP-CS), and triglycerides (TG) in blood serum were determined with "Thermo Fisher Scientific Oy" reagent kit (Finland) and "Konelab 20" biochemical analyzer produced by Thermo Fisher Scientific Oy" (Finland). CS, LDLP-CS, HDLP-CS and TG levels determined in the examined people were analyzed taking into account risks of cardiovascular pathology occurrence according to recommendations by experts from the Russian Society of Cardiology and the European Society of Cardiology / European Society of Hy-

[3] On special assessment of working conditions: The Federal Law No. 426 issued on December 28, 2013. *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_156555/ (January 29, 2021).

[4] On approving Rules for Clinical Practice in the Russian Federation: The Order by the RF Public Healthcare Ministry issued on June 19, 2003 No. 266 (Registered by the RF Ministry of Justice on June 20, 2003 No. 4808). *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_43346/ (January 29, 2021).

pertension (2018) [16]. Overweight and obesity were classified as per BMI in accordance with guidelines given by the WHO, 1997. BP levels were assessed according to "Clinical guidelines on diagnosing and treating arterial hypertension": optimal level for systolic BP was < 120 mm Hg; for diastolic BP, < 80 mm Hg; normal and elevated levels were 120–139 mm Hg and 80–89 mm Hg; AH, 140 mm Hg and higher than 90 mm Hg and above [17].

All the data were statistically processed with "Statisitca 6.1". We applied Shapiro – Wilk test to analyze whether parameters were distributed normally and dispersions were equal. All further statistical analysis was performed according to the results with non-parametric processing techniques. Data are given as *Med* ± *IQR* (25–75 %). We applied Kruskal – Wallis test to perform multiple comparison of the examined groups; to describe differences more precisely, we applied Mann – Whitney U-test that allowed assessing differences in parameters when a pair of group was compared; Bonferroni correction was used when *p* value were estimated. Differences between independent samplings were assessed as per a frequency of an examined parameter basing on Pearson's χ^2 test [18]. Critical significance of the results was taken at $p < 0.05$. When *p* varied from 0.05 and up to 0.1 inclusive, it was considered to be a trend.

Results and discussion. Table 1 contains data on ET-1 contents in blood serum and frequency of its occurrence in different concentrations in the examined groups.

Having compared ET-1 contents in three groups, we detected authentic differences between them (p = 0.013, H = 8.58, Kruskal – Wallis test). Pair analysis revealed statistically authentic differences in ET-1 contents in blood serum of workers who were exposed to occupational noise (the 1st group) and workers exposed to industrial aerosols (the 2nd group) against those who were not exposed to adverse factors at their workplaces (the 3rd group) (p_{1-3} = 0.003, Z = 2.9; p_{2-3} = 0.0008, Z = 2.6; Mann – Whitney U-test). ET-1 contents in blood serum of people from the 3rd group were 2 times lower than its contents in the first two groups. We didn't detect any differences in ET-1 contents between the 1st and the 2nd group (p_{1-2} = 0.831, Z = –0.2; Mann – Whitney U-test). Having analyzed frequency of different ET-1 contents, we revealed that elevated ET-1 contents in blood serum (higher than 3.5 pg/ml) were detected in more than 30.0 % of people in the 1st and the 2nd group against only 12.0 % in the 3rd group. And we should note that high ET-1 contents (more than 12 pg/l) were not detected at all in the 3rd group of workers whereas such high ET-1 contents were detected in 14.2 % and 12.0 % accordingly among workers form the 1st and the 2nd group.

We detected that normal and elevated BP prevailed in all three groups and one third of the examined people turned out to have AH (χ^2 = 12.42, p = 0.015). Differences were detected regarding frequency of optimal BP since it was most frequently detected among workers from the 2nd group (14.5 %) and least

Table 1

ET-1 concentrations (*Med* ± *IQR* (25–75 %)) and frequency of detecting different concentrations (%) in workers

Parameters	The 1st group (n = 32)	The 2nd group (n = 55)	The 3rd group (n = 31)
ET-1 concentration (pg/ml)	3.00 (2.36–7.20)	3.21 (2.57–6.78)	1.50 (1.04–1.80)
p	p_{1-2} = 0.831; p_{1-3} = 0.003; p_{2-3} = 0.0008		
ET-1 concentrations ranges (pg/ml)	Frequency of detecting ET-1 in different concentrations (%)		
3.50 and lower	64.2	69.0	88.0
3.51–12.0	21.6	19.0	12.0
Higher than 12.0	14.2	12.0	0

N o t e : *p* is validity of differences in ET-1 concentrations between workers' groups (Mann – Whitney U-test).

Table 2

Frequency of detecting different BP levels among workers, (%)

Parameter	The 1st group (n = 32)	The 2nd group (n = 55)	The 3rd group (n = 31)	χ^2 test	p
BP levels (mm Hg)	Frequency of different BP levels (%)				
Lower than 120 / 80	3.2	14.5	6.5	8.367	0.012
120–139 / 80–89	68.7	54.6	54.8	2.201	0.205
140 / 90 and higher	28.1	30.9	38.7	1.853	0.173

Table 3

ET-1 concentrations (*Med* ± *IQR* (25–75 %)) and frequency of its different concentrations detected in blood serum (%) depending on workers' BP

Parameters	BP (mm Hg)					
	Lower than 120 / 80 (n = 11)		120–139 / 80–89 (n = 69)		140 / 90 and higher (n = 38)	
ET-1 concentrations (pg/ml)	2.88 (2.18–3.6)		3.24 (2.64–6.6)		4.8 (3.02–15.21)	
p	p_{1-2} = 0.054; p_{1-3} = 0.021; p_{2-3} = 0.093					
Examined groups	Frequency of detecting different ET-1 concentrations (%)					
	Higher than 3.5 pg/ml	3.5 pg/ml and lower	Higher than 3.5 pg/ml	3.5 pg/ml and lower	Higher than 3.5 pg/ml	3.5 pg/ml and lower
1st (n = 32)	0	100.0	40.9	59.1	53.3	46.7
2nd (n = 55)	0	100.0	27.6	72.4	58.8	41.2
3rd (n = 31)	0	100.0	11.8	88.2	16.7	83.3

Note: p is validity of differences in ET-1 concentrations depending on BP (Mann – Whitney U-test).

frequently, among workers from the 1st group (3.2 %). These data are given in Table 2.

We examined a correlation between ET-1 concentration in blood serum and BP in the examined groups; the results are given in Table 3.

We didn't detect any statistically significant differences between the groups after comparing ET-1 concentrations in workers' groups distributed as per BP levels (p = 0.19, H = 3.29, Kruskal – Wallis test). Pair analysis revealed that in case BP was 140/90 mm Hg and higher, there was a trend (taking Bonferroni correction into account when p value was estimated) for growing ET-1 concentration in blood serum. ET-1 concentration in blood serum was the lowest among people with optimal BP and differed from ET-1 concentrations detected in people with higher BP levels (p_{1-2} = 0.054, Z = -0.14; p_{1-3} = 0.021, Z = -0.10, Mann – Whitney U-test).

We detected differences in frequency of elevated ET-1 contents in blood serum depending on BP levels in workers from different groups. Thus, there were no elevated ET-1 contents (higher than 3.5 pg/ml) among people with optimal BP in all three groups. Attention should be paid to people with normal and elevated BP since ET-1 contents were higher than reference values in 40.9 % examined people with such BP levels in the 1st group and in 27.6 % people in the 2nd group whereas elevated ET-1 contents were detected only in 11.8 % examined people with such BP from the 3rd group. A share of people with elevated ET-1 contents in blood serum grew by 2 times in the 2nd group (workers exposed to industrial aerosols) as BP levels increased, from 27.6 % to 58.8 % whereas ET-1 concentration grew by 12.4 % among those who were exposed only to occupational noise (the 1st group). The same trend was revealed in the reference group; however, an increase in frequency of detecting elevated ET-1 levels with a growth in BP was insignificant and amounted to 4.9 %. However, we should note that ET-1 contents were within the reference range in almost half of people with AH from the first two groups.

A share of people with AH who had normal ET-1 contents in their blood serum was the highest in the reference group and amounted to 83.3 %.

Our research revealed that almost half of the examined people in all three groups had dyslipidemia and were no differences in lipid profiles detected between the examined groups. A significant share of people (40.6–50.0 %) had elevated CS and LDLP-CS levels; almost one third had decreased HDLP-CS levels; elevated TG levels were detected in 13.7–18.7 % of the examined people. Having analyzed a correlation between ET-1 contents in blood serum and CS contents, we revealed that in case CS contents were more than 5.2 mmol/l, ET-1 concentration was authentically higher against the same parameter when CS contents were lower than 5.2 mmol/l ($p = 0.03$). Table 4 contains the results obtained via examining correlations between ET-1 concentrations in blood serum and CS concentrations in the examined groups.

Having analyzed relations between ET-1 and CS contents in three groups, we revealed certain trends for the parameters to differ. Thus, elevated CS levels in blood serum were accompanied with elevated ET-1 concentrations in more than half of workers exposed to permanent occupational noise (58.3 %) whereas in case CS levels were normal, elevated ET-1 contents were detected only in 20.0 % of the examined people. ET-1 contents in workers from this group was authentically higher in case CS was higher than 5.2 mmol/l against its values in case CS was lower than 5.2 mmol/l: 7.24 (2.88–12.6) against 2.64 (2.36–2.88) ($p = 0.012$). We didn't detect similar dependence among workers exposed to industrial aerosols and those who were not exposed to any adverse factors at their workplaces; and elevated ET-1 contents in blood serum with CS being higher than 5.2 mmol/l was detected in fewer people. We didn't detect any dependence between ET-1 contents in blood serum and TG, LDLP-CS and HDLP-CS concentrations.

Our analysis revealed two thirds of all the examined people had overweight or obesity and a greater number of people with obesity was detected among workers exposed to occupational noise than among those exposed to industrial aerosols or people with no exposure to adverse factors at their workplaces: 31.2 % against 14.0 % and 12.9 % accordingly. Table 5 contains data on a correlation between ET-1 contents and BMI of workers from three examined groups.

Having analyzed a correlation between ET-1 contents in blood serum and BMI, we revealed that in case BMI was 25 kg/m^2 and higher, ET-1 concentration was authentically higher than in people with BMI being lower than 25 kg/m^2 ($p = 0.03$). We revealed an ascending trend for ET-1 concentration almost in half of people with overweight and obesity who were exposed to adverse occupational factors at their workplaces and only in 17.1 % of workers who were not exposed to them. Elevated ET-1 concentration (higher than 3.5 pg/ml) was determined in a small number

Table 4

ET-1 concentrations (*Med* ± *IQR* (25–75 %)) and frequency of different concentrations (%) depending on CS levels among workers from the examined groups

Parameters	CS (mmol/l)			
	Lower than 5.2 (*n* = 58)		Higher than 5.2 (*n* = 60)	
ET-1 concentrations (pg/ml)	2.72 (1.84–3.44)		3.12 (2.24–7.8)	
p	*p* = 0.03			
Examined groups	Frequency of detecting different ET-1 concentrations (%)			
	Higher than 3.5 pg/ml	3.5 pg/ml and lower	Higher than 3.5 pg/ml	3.5 pg/ml and lower
1st (*n* = 32)	20.0	80.0	58.3	41.7
2nd (*n* = 55)	31.8	68.2	27.2	72.8
3rd (*n* = 31)	16.0	84.0	16.0	84.0

Note: *p* is validity of differences in ET-1 concentrations depending on CS levels as per Mann – Whitney U-test.

Table 5

ET-1 concentrations (*Med* ± *IQR* (25–75 %)) and frequency of detecting different concentrations (%) depending on workers' BMI

Parameters	BMI (kg/m^2)			
	below 25.0 (*n* = 40)		25.0 and above (*n* = 78)	
ET-1 concentrations (pg/ml)	2.64 (2.36–3.24)		3.24 (2.64–10.36)	
p	*p* = 0.03			
Examined groups	Frequency of detecting different ET-1 concentrations (%)			
	Higher than 3.5 pg/ml	3.5 pg/ml and lower	Higher than 3.5 pg/ml	3.5 pg/ml and lower
1st (*n* = 32)	24.5	75.5	42.1	57.9
2nd (*n* = 55)	14.2	85.8	54.1	45.9
3rd (*n* = 31)	16.6	83.4	17.1	82.9

Note: *p* is validity of differences in ET-1 concentrations depending on BMI as per Mann – Whitney U-test.

of workers with normal BMI in all three groups (24.5 %, 14.2 %, and 16.6 %). We should note that ET-1 contents were within the reference range in half of people from the 1st and 2nd group with overweight and obesity, and the highest share of people with ET-1 being 3.5 pg/ml and lower and overweight and obesity was detected in the 3rd group and amounted to 82.9 %.

Therefore, our research revealed that 50 % of workers exposed to adverse occupational factors at their workplaces had BP, CS, and BMI deviating from proper values. AH was detected in 20 % workers, one third of the examined people had elevated BP (according to JNC7 recommendations, these people can be considered pre-hypertensive) [19]. Optimal BP was detected only in 10.0 % of the examined people. Two thirds of workers had BMI equal to 25 kg/m^2 and higher. Half of the examined people had hypercholesterolemia.

The research results revealed a more apparent correlation between ET-1 concentrations in blood serum and BP, BMI, and CS contents among workers exposed to occupational noise. Thus, optimal BP was detected 4 times less frequently, and normal BP by 12 % more frequently among people with elevated ET-1 contents in blood serum who were exposed to occupational noise at their workplaces against those exposed to industrial aerosols. Elevated ET-1 levels together with CS contents being higher than 5.2 mmol/l were detected in more than half of workers exposed to occupational noise whereas ET-1 contents were higher than reference values only in 27.3 % of workers with such CS contents who were exposed to industrial aerosols. We should note that there were more people with obesity among workers exposed to occupational noise than among those exposed to industrial aerosols and workers without any exposure at their workplaces. Analysis of correlations between ET-1 contents in blood serum and BMI revealed that elevated ET-1 contents were detected 2 times more frequently even among workers with normal body weight who were exposed to occupational noise than among those exposed to industrial aerosols.

Special attention should be paid to workers with elevated ET-1 contents in blood serum and normal BP, CS, and BMI. Having analyzed such people, we revealed that elevated ET-1 contents were more frequently detected among those exposed to occupational noise. We can assume that endothelial dysfunction and ET-1 introduction into blood serum have occurred prior to AH development under exposure to occupational noise. On the other hand, ET-1 produces its effects on ET-B receptors in endothelial and smooth muscle cells thus stimulating formation of nitrogen oxide that helps resist vasoconstriction. There is a contribution by other factors that prevent vasoconstriction from developing such as prostacyclin and atrial natriuretic peptide that are produced by endothelium as a response to ET-1 release. In this case, elevated ET-1 levels in blood serum even if BP is normal and there is no dyslipidemia or obesity indicate that endothelium cells are activated and ET-1 has entered intracellular space and blood. That is, ET-1 as an endothelium dysfunction marker can be an independent risk factor of cardiovascular pathology. People with elevated ET-1 contents in blood serum and normal BP, CS, and BMI can be recommended to perform dynamic monitoring over their health with special attention paid to the cardiovascular system.

We should note that it is necessary to apply a personified approach when assessing elevated ET-1 contents and a probability to use it as a risk factor of cardiovascular pathology among young and middle-aged people working under adverse working conditions (especially under exposure to occupational noise). It is extremely vital given that personified activities aimed at reducing health risks are being actively developed at the moment [20, 21].

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References

1. Boitsov S.A., Pogosova N.V., Bubnova M.G., Drapkina O.M., Gavrilova N.E., Eganyan R.A., Kalinina A.M., Karamnova N.S. [et al.]. Cardiovascular prevention 2017. National guidelines. *Rossiiskii kardiologicheskii zhurnal*, 2018, vol. 23, no. 6, pp. 7–122 (in Russian).

2. Bukhtiyarov I.V., Izmerov N.F., Tikhonova G.I., Churanova A.N., Gorchakova T.Yu., Bryleva M.S., Krutko A.A. Work conditions as a risk factor mortality increase in able-bodied population. *Meditsina truda i promyshlennaya ekologiya*, 2017, no. 8, pp. 43–49 (in Russian).

3. Postnikova L.V., Pakseeva V.S., Matantseva M.E. Problem of expertise of professional suitability of workers of metallurgical production. *Meditsina truda i promyshlennaya ekologiya*, 2019, vol. 59, no. 9, pp. 723–724 (in Russian).

4. Cherepakhin D.I., Bazylev V.V., Evtyushkin I.A., Suchkov S.V., Bogopol'skaya O.M., Charchyan E.R., Belov Yu.V., Pal'tsev M.A. Modern markers in diagnostics of atherosclerosis. *Kardiologiya i serdechno-sosudistaya khirurgiya*, 2012, vol. 5, no. 3, pp. 26–29 (in Russian).

5. Zaitseva N.V., Zemlyanova M.A., Chashchin V.P., Gudkov A.B. Scientifiic principles of use of biomarkers in medico-ecological studies (review). *Ekologiya cheloveka*, 2019, no. 9, pp. 4–14 (in Russian).

6. Bohm F., Pernow J. The importance of endothelin-1 for vascular dysfunction in cardiovascular disease. *Cardiovasc Res*, 2007, vol. 76, no. 1, pp. 8–18. DOI: 10.1016/j.cardiores.2007.06.004

7. Jain A., Coffey C., Mehrotra V., Flammer J. Endothelin-1 traps as a potential therapeutic tool: from diabetes to beyond? *Drug Discov Today,* 2019, vol. 9, no. 24, pp. 1937–1942. DOI: 10.1016/j.drudis.2019.07.008

8. Barton M., Yanagisawa M. Endothelin: 30 Years from Discovery to Therapy. *Hypertension,* 2019, vol. 6, no. 74, pp. 1232–1265. DOI: 10.1161/HYPERTENSIONAHA.119.12105

9. Beck D.T., Casey D.P., Martin J.S., Emerson B.D., Braith R.W. Exercise training improves endothelial function in young prehypertensives. *Exp. Biol. Med. (Maywood),* 2013, vol. 4, no. 238, pp. 433–441. DOI: 10.1177/1535370213477600

10. Rautureau Y., Schiffrin E.L. Endothelin in hypertension: an update. *Current Opinion in Nephrology and Hypertension*, 2012, vol. 21, no. 2, pp. 128–136. DOI: 10.1097/MNH.0b013e32834f0092

11. Lin Y.J., Juan C.C., Kwok C.F., Hsu Y.P., Shih K.C., Chen C.C., Ho L.T. Endothelin-1 exacerbates development of hypertension and atherosclerosis in modest insulin resistant syndrome. *Biochem Biophys. Res. Commun.,* 2015, vol. 3, no. 460, pp. 497–503. DOI: 10.1016/j.bbrc.2015.03.017

12. Zaric B., Obradovic M., Trpkovic A., Banach M., Mikhailidis D.P., Isenovic E. Endothelial dysfunction in dyslipidaemia: Molecular mechanisms and clinical implications. *Curr. Med. Chem.*, 2019, vol. 27, no. 7, pp. 1021–1040. DOI: 10.2174/0929867326666190903112146

13. Bazarova E.L., Roslyi O.F., Osherov I.S., Roslaya N.A., Tartakovskaya L.Ya., Likhacheva E.I. The dynamics of the prevalence rate of general somatic diseases based on periodic medical examinations of metallurgical workers. *Gigiena i sanitariya*, 2017, vol. 96, no. 12, pp. 1167–1171 (in Russian).

14. Fokin V.A., Shlyapnikov D.M., Red'ko S.V. Risk assessment of occupational and occupationally conditioned diseases connection to noise when exceeding maximum permissible levels. *Meditsina truda i promyshlennaya ekologiya*, 2018, no. 10, pp. 17–19 (in Russian).

15. Popova A.Yu. Working conditions and occupational morbidity in the Russian Federation. *Meditsina truda i ekologiya cheloveka*, 2015, no. 3, pp. 7–13 (in Russian).

16. Kobalava Zh.D., Konradi A.O., Nedogoda S.V., Arutyunov G.P., Baranova E.I., Barbarash O.L., Villeval'de S.V., Galyavich A.S. [et al.]. Russian Society of Cardiology position paper on 2018 Guidelines of the European Society of Cardiology/European Society of Arterial Hypertension for the management of arterial hypertension. *Rossiiskii kardiologicheskii zhurnal*, 2018, no. 12, pp. 131–142 (in Russian).

17. Chazova I.E., Zhernakova Yu.V. Diagnosis and treatment of arterial hypertension. *Sistemnye gipertenzii*, 2019, vol. 16, no. 1, pp. 6–31 (in Russian).

18. Grzhibovskii A.M. Analysis of three and more independent groups of quantitative data. *Ekologiya cheloveka*, 2008, no. 3, pp. 50–58 (in Russian).

19. JNC 7 Express. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. U.S.A., U.S. Department of health and human services National Institutes of Health National Heart, Lung, and Blood Institute Publ., 2003, 1206 p.

20. Yang Y., Zhang E., Zhang J., Chen S., Yu G., Liu X., Peng C., Lavin M.F. [et al.]. Relationship between occupational noise exposure and the risk factors of cardiovascular disease in China: A meta-analysis. *Medicine (Baltimore)*, 2018, vol. 30, no. 97, pp. e11720. DOI: 10.1097/MD.0000000000011720

21. Health risk analysis in the strategy of state social and economical development. In: G.G. Onishchenko, N.V. Zaitseva eds. Perm': Izdatel'stvo Permskogo natsional'nogo issledovatel'skogo politekhnicheskogo universiteta Publ., 2014, 738 p. (in Russian).

Umnyagina I.A., Blinova T.V., Strakhova L.A., Troshin V.V., Ivanova Yu.V., Sorokina E.I. Endothelin-1 as a risk factor causing cardiovascular pathology in young and middle-aged people employed under hazardous working conditions. Health Risk Analysis, 2021, no. 2, pp. 105–113. DOI: 10.21668/health.risk/2021.2.10.eng

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