

The significance of soluble molecules of cellular adhesion, nitric oxide metabolites, and endothelin-1 and their associations as markers of progression of inflammation in COPD

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Abstract

© 2017, Nizhny Novgorod State Medical Academy. All rights reserved. The aim of the investigation was to assess the significance of the content of metabolites of the nitric oxide, sICAM-1 and sICAM-3 in blood serum and in exhaled breath condensate, the serum level of endothelin-1 as systemic and topical markers of inflammation in patients with COPD, and their correlations with the parameters of lung ventilation function. Materials and methods. 91 patients with COPD, aged from 46 to 67, and 21 healthy, non-smoking volunteers took part in the study. The material for investigation was blood serum and exhaled breath condensate. Results. The severity of progression of COPD was linked with an increase in the serum content of sCD50, sCD54, ET-1, as well as in the concentrations of metabolites of nitric oxide in blood and in exhaled breath condensate. For the patients with COPD we determined the associations between the function of pulmonary ventilation and the levels of ET-1, sICAM-1, sICAM-3 and the value of $\Sigma NO - 2 / NO - 3$. The resulting correlations between the concentration of soluble adhesion molecules, the values of nitrosative stress, and ET-1 level indicate that they are involved in the genesis of chronic inflammation in COPD patients.

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Keywords

Chronic obstructive pulmonary disease, COPD, Endothelin-1, ET-1, Exhaled breath condensate, Nitrosative stress, Soluble molecules of adhesion ICAM- 1 and ICAM-3

References

- [1] Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for diagnosis, management and prevention of chronic obstructive pulmonary disease. NHLBI/ WHO workshop report. Last updated 2013.
- [2] Novikov V.V., Evsegneeva I.V., Karaulov A.V., Baryshnikov A.Yu. Soluble forms of membrane antigens of immune system cells in social infections. *Rossiyskiy bioterapevticheskiy zhurnal* 2005; 4(2): 100-105.
- [3] Rothlein R., Mainolfi E.A., Czajkowski M., Marlin S.D. A form of circulating ICAM-1 in human serum. *J Immunol* 147(11): 3788-3793.
- [4] Bleijs D.A., Geijtenbeek T.B., Figdor C.G., van Kooyk Y. DC-SIGN and LFA-1: a battle for ligand. *Trends Immunol* 2001; 22(8): 457-463.

- [5] Kusterer K., Bojunga J., Enghofer M., Heidenthal E., Usadel K.H., Kolb H., Martin S. Soluble ICAM-1 reduces leukocyte adhesion to vascular endothelium in ischemiareperfusion injury in mice. *Am J Physiol* 1998; 275(2 Pt 1): G377-G380.
- [6] Ridker P.M., Hennekens C.H., Roitman-Johnson B., Stampfer M.J., Allen J. Plasma concentration of soluble intercellular adhesion molecule 1 and risks of future myocardial infarction in apparently healthy men. *Lancet* 1998; 351(9096): 88-92, [https://doi.org/10.1016/s0140-6736\(97\)09032-6](https://doi.org/10.1016/s0140-6736(97)09032-6).
- [7] Constans J., Conri C. Circulating markers of endothelial function in cardiovascular disease. *Clinica Chimica Acta* 2006; 368(1-2): 33-47, <https://doi.org/10.1016/j.cca.2005.12.030>.
- [8] Kwon Y.S., Chi S.Y., Shin H.J., Kim E.Y., Yoon B.K., Ban H.J., Oh I.J., Kim K.S., Kim Y.C., Lim S.C. Plasma C-reactive protein and endothelin-1 level in patients with chronic obstructive pulmonary disease and pulmonary hypertension. *J Korean Med Sci* 2010; 25(10): 1487-1491, <https://doi.org/10.3346/jkms.2010.25.10.1487>.
- [9] Wort S.J., Woods M., Warner T.D., Evans T.W., Mitchell J.A. Endogenously released endothelin-1 from human pulmonary artery smooth muscle promotes cellular proliferation. *Am J Respir Cell Mol Biol* 2001; 25(1): 104-110, <https://doi.org/10.1165/ajrcmb.25.1.4331>.
- [10] Santos S., Peinado V.I., Ramírez J., Melgosa T., Roca J., Rodriguez-Roisin R., Barberà J.A. Characterization of pulmonary vascular remodelling in smokers and patients with mild COPD. *Eur Respir J* 2002; 19(4): 632-638, <https://doi.org/10.1183/09031936.02.00245902>.
- [11] Wright J.L., Tai H., Churg A. Cigarette smoke induces persisting increases of vasoactive mediators in pulmonary arteries. *Am J Respir Cell Mol Biol* 2004; 31(5): 501-509, <https://doi.org/10.1165/rcmb.2004-0051oc>.
- [12] Dominguez-Avila N., Ruiz-Castañeda G., González- Ramírez J., Fernandez-Jaramillo N., Escoto J., Sánchez-Muñoz F., Marquez-Velasco R., Bojalil R., Espinosa- Cervantes R., Sánchez F. Over, and underexpression of endothelin 1 and TGF-beta family ligands and receptors in lung tissue of broilers with pulmonary hypertension. *Biomed Res Int* 2013; 2013: 190382, <https://doi.org/10.1155/2013/190382>.
- [13] Carratu P., Scoditti C., Maniscalco M., Seccia T.M., Di Gioia G., Gadaleta F., Cardone R.A., Dragonieri S., Pierucci P., Spanevello A., Resta O. Exhaled and arterial levels of endothelin-1 are increased and correlate with pulmonary systolic pressure in COPD with pulmonary hypertension. *BMC Pulm Med* 2008; 8(1): 20, <https://doi.org/10.1186/1471-2466-8-20>.
- [14] Roland M. Sputum and plasma endothelin-1 levels in exacerbations of chronic obstructive pulmonary disease. *Thorax* 2001; 56(1): 30-35, <https://doi.org/10.1136/thorax.56.1.30>.
- [15] Bourque S.L., Davidge S.T., Adams M.A. The interaction between endothelin-1 and nitric oxide in the vasculature: new perspectives. *Am J Physiol Regul Integr Comp Physiol* 2011; 300(6): R1288-R1295, <https://doi.org/10.1152/ajpregu.00397.2010>.
- [16] Nussler A.K., Billiar T.R. Inflammation, immunoregulation, and inducible nitric oxide synthase. *J Leukoc Biol* 1993; 54(2): 171-178.
- [17] Zweier J.L., Samouilov A., Kuppusamy P. Nonenzymatic nitric oxide synthesis in biological systems. *Biochim Biophys Acta* 1999; 1411(2-3): 250-262, [https://doi.org/10.1016/s0005-2728\(99\)00018-3](https://doi.org/10.1016/s0005-2728(99)00018-3).
- [18] Dejam A., Hunter C.J., Schechter A.N., Gladwin M.T. Emerging role of nitrite in human biology. *Blood Cells Mol Dis* 2004; 32(3): 423-429, <https://doi.org/10.1016/j.bcmd.2004.02.002>.
- [19] Eliseeva T.I., Kulpina Yu. S., Soodaeva S.K., Kubysheva N.I. Content of the nitrogen oxide metabolites in a condensate of exhaling air in children with a bronchial asthma control different level. *Sovremennye tehnologii v medicine* 2010; 4: 42-47.
- [20] Kubysheva N., Soodaeva S., Postnikova L., Novikov V., Maksimova A., Chuchalin A. Associations between indicators of nitrosative stress and levels of soluble HLA-I, CD95 molecules in patients with COPD. *COPD* 2014; 11(6): 639-644, <https://doi.org/10.3109/15412555.2014.898042>.
- [21] Lisitsa A.V., Soodaeva S.K., Klimanov I.A., Chuchalin A.G. Changes of oxidative stress parameters in patients with exacerbation of asthma under therapy with inhaled liposomal drugs. *Russian Pulmonology* 2010; 1: 74-79.
- [22] Mamaeva M.E., Alyasova A.V., Shumilova S.V., Kazatskaya Zh.A., Khazov M.V., Churkina N.N., Novikov V.V. Prognostic value of blood serum content of soluble CD50 and CD54 molecules in patients with uterine and cervical cancer. *Sovremennye tehnologii v medicine* 2015; 7(4): 141-146, <https://doi.org/10.17691/stm2015.7.4.19>.
- [23] Schmal H., Czermak B.J., Lentsch A.B., Bless N.M., Beck-Schimmer B., Friedl H.P., Ward P.A. Soluble ICAM-1 activates lung macrophages and enhances lung injury. *J Immunol* 1998; 161(7): 3685-3693.
- [24] Zhang X., Wang L., Zhang H., Guo D., Zhao J., Qiao Z., Qiao J. The effects of cigarette smoke extract on the endothelial production of soluble intercellular adhesion molecule-1 are mediated through macrophages, possibly by inducing TNF-alpha release. *Methods Find Exp Clin Pharmacol* 2002; 24(5): 261-265, <https://doi.org/10.1358/mf.2002.24.5.802302>.
- [25] Togo S., Holz O., Liu X., Sugiura H., Kamio K., Wang X., Kawasaki S., Ahn Y., Fredriksson K., Skold C.M., Mueller K.C., Branscheid D., Welker L., Watz H., Magnussen H., Rennard S.I. Lung fibroblast repair functions in patients with chronic obstructive pulmonary disease are altered by multiple mechanisms. *Am J Respir Crit Care Med* 2008; 178(3): 248-260, <https://doi.org/10.1164/rccm.200706-929oc>.

- [26] Leeuwenberg J.F., Smeets E.F., Neefjes J.J., Shaffer M.A., Cinek T., Jeunhomme T.M., Ahern T.J., Buurman W.A. E-selectin and intercellular adhesion molecule-1 are released by activated human endothelial cells in vitro. *Immunology* 1992; 77(4): 543-549.
- [27] Zandvoort A., van der Geld Y.M., Jonker M.R., Noordhoek J.A., Vos J.T., Wesseling J., Kauffman H.F., Timens W., Postma D.S. High ICAM-1 gene expression in pulmonary fibroblasts of COPD patients: a reflection of an enhanced immunological function. *Eur Respir J* 2006; 28(1): 113-122, <https://doi.org/10.1183/09031936.06.00116205>.
- [28] Madjdpour C., Jewell U.R., Kneller S., Ziegler U., Schwendener R., Booy C., Kläusli L., Pasch T., Schimmer R.C., Beck-Schimmer B. Decreased alveolar oxygen induces lung inflammation. *Am J Physiol Lung Cell Mol Physiol* 2003; 284(2): L360-L367, <https://doi.org/10.1152/ajplung.00158.2002>.
- [29] Barnett C.C. Jr., Moore E.E., Moore F.A., Carl V.S., Biffl W.L. Soluble ICAM-1 (sICAM-1) PROvokes PMN elastase release. *J Surg Res* 1996; 63(1): 6-10, <https://doi.org/10.1006/jsre.1996.0213>.
- [30] Spiropoulos K., Trakada G., Nikolaou E., Prodromakis E., Efremidis G., Pouli A., Koniavitou A. Endothelin-1 levels in the pathophysiology of chronic obstructive pulmonary disease and bronchial asthma. *Respir Med* 2003; 97(8): 983-989, [https://doi.org/10.1016/s0954-6111\(03\)00129-x](https://doi.org/10.1016/s0954-6111(03)00129-x).
- [31] Shi-Wen X., Denton C.P., Dashwood M.R., Holmes A.M., Bou-Gharios G., Pearson J.D., Black C.M., Abraham D.J. Fibroblast matrix gene expression and connective tissue remodeling: role of endothelin-1. *J Invest Dermatol* 2001; 116(3): 417-425, <https://doi.org/10.1046/j.1523-1747.2001.01256.x>.
- [32] Abraham D. Role of endothelin in lung fibrosis. *Eur Respir Rev* 2008; 17(109): 145-150, <https://doi.org/10.1183/09059180.00010907>.
- [33] Teder P., Noble P.W. A cytokine reborn? Endothelin-1 in pulmonary inflammation and fibrosis. *Am J Respir Cell Mol Biol* 2000; 23(1): 7-10, <https://doi.org/10.1165/ajrcmb.23.1.f192>.
- [34] Dinakar C., Malur A., Raychaudhuri B., Buhrow L.T., Melton A.L., Kavuru M.S., Thomassen M.J. Differential regulation of human blood monocyte and alveolar macrophage inflammatory cytokine production by nitric oxide. *Ann Allergy Asthma Immunol* 1999; 82(2): 217-222, [https://doi.org/10.1016/s1081-1206\(10\)62600-2](https://doi.org/10.1016/s1081-1206(10)62600-2).
- [35] Folkerts G., Kloek J., Muijsers R.B., Nijkamp F.P. Reactive nitrogen and oxygen species in airway inflammation. *Eur J Pharmacol* 2001; 429(1-3): 251-262, [https://doi.org/10.1016/s0014-2999\(01\)01324-3](https://doi.org/10.1016/s0014-2999(01)01324-3).
- [36] Krishna M.T., Chauhan A.J., Frew A.J., Holgate S.T. Toxicological mechanisms underlying oxidant pollutant-induced airway injury. *Rev Environ Health* 1998; 13(1-2): 59-71.
- [37] Morrison D., Rahman I., Lannan S., MacNee W. Epithelial permeability, inflammation, and oxidant stress in the air spaces of smokers. *Am J Respir Crit Care Med* 1999; 159(2): 473-479, <https://doi.org/10.1164/ajrccm.159.2.9804080>.
- [38] Clini E., Bianchi L., Pagani M., Ambrosino N. Endogenous nitric oxide in patients with stable COPD: correlates with severity of disease. *Thorax* 1998; 53(10): 881-883, <https://doi.org/10.1136/thx.53.10.881>.
- [39] Franciosi L.G., Page C.P., Celli B.R., Cazzola M., Walker M.J., Danhof M., Rabe K.F., Della Pasqua O.E. Markers of disease severity in chronic obstructive pulmonary disease. *Pulm Pharmacol Ther* 2006; 19(3): 189-199.
- [40] Woska J.R. Molecular comparison of soluble intercellular adhesion Molecule (sICAM)-1 and sICAM-3 binding to lymphocyte function-associated antigen-1. *J Biol Chem* 1998; 273(8): 4725-4733, <https://doi.org/10.1074/jbc.273.8.4725>.