DOI: 10.22055/IVJ.2022.345026.2473

Immunotoxicity study of crude oil gaseous pollutants in development of the rat embryonic and neonates' development

Hassan Salehvand[1], Mohammad Khosravi[2*], Kaveh Khazaeil[3], Mohammad Reza Tabandeh[4] and Zahra Basir[3]

[1] PhD Student of Anatomy and Embryology, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran

[2] Associate Professor, Department of Pathobiology, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran

[3] Associate Professor, Department of Basic Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran.

[4] Associate Professor, Department of Basic Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran

Received: 30.05.2022 Accepted: 04.07.2022

Abstract

Environmental pollution, especially oil and gas pollutants, has devastating effects on maternal and fetal health. In this study, the direct effects of petroleum gases on the development and function of the immune system during prenatal and neonatal periods in rats were investigated. Pregnant rats (N=36) were divided into two groups: one exposed to pollutants and one serving as the control group. The group of pollutants was exposed to oil vapors in the vivarium compartment for 5 hours per day starting from the first day of pregnancy. Fetal spleen samples were taken on day 20 of embryonic life to investigate the expression of tumor necrosis factor alpha (TNF-α), interferon beta-1 (IFN-β1), alpha lymphotoxin (LT-α), and Transforming Growth Factor-β1 (TGF-β1) genes. The total serum immunoglobulins and antibody titer to sheep red blood cells were evaluated when the neonates were 45 days old. Innate immune responses were investigated in terms of serum bactericidal, lysozyme, myeloperoxidase, anti-protease, and complement activity. The expression of the mentioned genes in newborns was also evaluated at the ages of 15 and 30 days compared to the control group. The results indicated a significant decrease in the activity of lysozyme, complement, and myeloperoxidase, as well as a non-significant reduction in the serum bactericidal activity and humoral immune response of the pollutant group compared to the control group. The expression levels of LT-α and IFN-β1 were reduced, while the expressions of TNF-α, IL-1, and IL-10 were elevated in the embryos exposed to pollutants. An age-related increase in TNF-α and TGF-β1 was observed in the offspring of the pollutant group. In conclusion, petroleum vapors have been shown to have a destructive and significant effect on the innate, humoral, and cellular immune responses of fetuses and neonates. The mechanisms involved in these destructive effects can be investigated in future studies.

Key words: Crude oil pollutants, Immunotoxics, Fetus, Neonate, Development

* **Corresponding Author**: Mohammad Khosravi, Associate Professor, Department of Pathobiology, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran
E-mail: m.khosravi@scu.ac.ir

Refrences

Al-Dasooqi, N., Bowen, J. M., Gibson, R. J., Logan, R. M., Stringer, A. M., & Keefe, D. M. (2011). Selection of housekeeping genes for gene expression studies in a rat model of irinotecan-induced mucositis. *Chemotherapy, 57*(1), 43-53.

Allan, L. L., Mann, K. K., Matulka, R. A., Ryu, H. Y., Schlezinger, J. J., & Sherr, D. H. (2003). Bone marrow stromal-B cell interactions in polycyclic aromatic hydrocarbon-induced pro/pre-B cell apoptosis. *Toxicological Sciences, 76*(2), 357-365.

Altshuler, A. E., Penn, A.H., Yang, J. A., Kim, G. R., Schmid-Schönbein G. W. (2012). Protease activity increases in plasma, peritoneal fluid, and vital organs after hemorrhagic shock in rats. *PLoS One. 7*(3):e32672.

Bluhm, K., Seiler, T. B., Anders, N., Klankermayer, J., Schaeffer, A., & Hollert, H. (2016). Acute embryo toxicity and teratogenicity of three potential biofuels also used as flavor or solvent. *Science of the total environment*, 566, 786-795.

Boule, L. A., Burke, C. G., Fenton, B. M., Thevenet-Morrison, K., Jusko, T. A., Lawrence, B. P. (2015). Developmental activation of the AHR increases effector CD4+ T cells and exacerbates symptoms in autoimmune disease-prone Gnaq+/− mice. *Toxicological Sciences, 148*(2), 555-566

Boulé, L. A., Chapman, T. J., Hillman, S. E., Kassotis, C. D., O'Dell, C., Robert, J., Lawrence, B. P. (2018). Developmental exposure to a mixture of 23 chemicals associated with unconventional oil and gas operations alters the immune system of mice. *Toxicological Sciences, 163*(2), 639-654.

Boverhof, D. R., Ladics, G., Luebke, B., Botham, J., Corsini, E., Evans, E., Yang, Y. (2014). Approaches and considerations for the assessment of immunotoxicity for environmental chemicals: a workshop summary. Regulatory *Toxicology and Pharmacology, 68*(1), 96-107.

Cerrizuela, S., Vega-Lopez, G. A., & Aybar, M. J. (2020). The role of teratogens in neural crest development. *Birth Defects Research, 112*(8), 584-632.

Chapman, T. J., & Georas, S. N. (2014). Regulatory tone and mucosal immunity in asthma. *International immunopharmacology, 23*(1), 330-336.

Cho, J. Y. (2008). Suppressive effect of hydroquinone, a benzene metabolite, on in vitro inflammatory responses mediated by macrophages, monocytes, and lymphocytes. *Mediators of inflammation*, 2008.

Dezateux, C., Lum, S., Hoo, A. F., Hawdon, J., Costeloe, K., & Stocks, J. (2004). Low birth weight for gestation and airway function in infancy: exploring the fetal origins hypothesis. *Thorax*, *59*(1), 60-66.

Dezateux, C., Stocks, J., Dundas, I., & Fletcher, M. E. (1999). Impaired airway function and wheezing in infancy: the influence of maternal smoking and a genetic predisposition to asthma. *American journal of respiratory and critical care medicine, 159*(2), 403-410.

Dietert, R. R. (2009). Developmental immunotoxicology: focus on health risks. *Chemical research in toxicology, 22*(1), 17-23.

Dietert, R. R. (2014). Developmental immunotoxicity, perinatal programming, and noncommunicable diseases: focus on human studies. Advances in medicine, 2014.

Esser, C. (Ed.). (2016). Environmental influences on the immune system (pp. 1-17). Vienna, Austria: Springer.

Hahad, O., Lelieveld, J., Birklein, F., Lieb, K., Daiber, A., & Münzel, T. (2020). Ambient air pollution increases the risk of cerebrovascular and neuropsychiatric disorders through induction of inflammation and oxidative stress. *International journal of molecular sciences, 21*(12), 4306.

Hanson, M. L., Holásková, I., Elliott, M., Brundage, K. M., Schafer, R., & Barnett, J. B. (2012). Prenatal cadmium exposure alters postnatal immune cell development and function. *Toxicology and Applied Pharmacology, 261*(2), 196-203.

Hubert, F. X., Voisine, C., Louvet, C., Heslan, M., & Josien, R. (2004). Rat plasmacytoid dendritic cells are an abundant subset of MHC class II+ CD4+ CD11b− OX62− and type I IFN-producing cells that exhibit selective expression of Toll-like receptors 7 and 9 and strong responsiveness to CpG. *The Journal of Immunology, 172*(12), 7485-7494.

Inglis, J. E., Radziwon, K. A., Maniero, G. D. (2008). The serum complement system: a simplified laboratory exercise to measure the activity of an important component of the immune system. *Advances in Physiology Education*, *32*(4), 317-312

Johnson, N. M., Hoffmann, A. R., Behlen, J. C., Lau, C., Pendleton, D., Harvey, N., Zhang, R. (2021). Air pollution and children's health—a review of adverse effects associated with prenatal exposure from fine to ultrafine particulate matter. *Environmental health and preventive medicine, 26*(1), 1-29.

Kawabata, T. T., White Jr, K. L. (1990). Effects of naphthalene and naphthalene metabolites on the in vitro humoral immune response. *Journal of Toxicology and Environmental Health, Part A Current Issues, 30*(1), 53-67.

Kirkeleit, J., Riise, T., Bratveit, M., & Moen, B. E. (2008). Increased risk of acute myelogenous leukemia and multiple myeloma in a historical cohort of upstream petroleum workers exposed to crude oil. *Cancer Causes & Control, 19*(1), 13-23.

Kirkeleit, J., Ulvestad, E., Riise, T., Bråtveit, M., Moen, B. E. (2006). Acute suppression of serum IgM and IgA in tank workers exposed to benzene. *Scandinavian Journal of Immunology, 64*(6), 690-698.

Laffon, B., Aguilera, F., Ríos-Vazquez, J., García-Lestón, J., Fuchs, D., Valdiglesias, V., Pasaro, E. (2013). Endocrine and immunological parameters in individuals involved in Prestige spill cleanup tasks seven years after the exposure. *Environment international*, 59, 103-111.

Langenau, D. M., Traver, D., Ferrando, A. A., Kutok, J. L., Aster, J. C., Kanki, J. P., ... & Look, A. T. (2003). Myc-induced T cell leukemia in transgenic zebrafish. *Science, 299*(5608), 887-890.

McLoone, P., Dyussupov, O., Nurtlessov, Z., Kenessariyev, U., & Kenessary, D. (2021). The effect of exposure to crude oil on the immune system. Health implications for people living near oil exploration activities. *International Journal of Environmental Health Research, 31*(7), 762-787.

MacDonald, G. Z., Hogan, N. S., Köllner, B., Thorpe, K. L., Phalen, L. J., Wagner, B. D., & Van Den Heuvel, M. R. (2013). Immunotoxic effects of oil sands-derived naphthenic acids to rainbow trout. *Aquatic toxicology, 126*, 95-103.

Maione, M., Mocca, E., Eisfeld, K., Kazepov, Y., & Fuzzi, S. (2021). Public perception of air pollution sources across Europe. *Ambio, 50*(6), 1150-1158.

Malle, E., Furtmüller, P. G., Sattler, W., & Obinger, C. (2007). Myeloperoxidase: a target for new drug development? *British Journal of Pharmacology, 152*(6), 838-854.

Markey, B., Leonard, F., Archambault, M., Cullinane, A., & Maguire, D. (2013). *Clinical veterinary microbiology e-book*. Elsevier Health Sciences.

McLoone, P., Dyussupov, O., Nurtlessov, Z., Kenessariyev, U., & Kenessary, D. (2021). The effect of exposure to crude oil on the immune system. Health implications for people living near oil exploration activities. *International Journal of Environmental Health Research, 31*(7), 762-787.

McMullin, T., Bamber, A., Flores, J., Vigil, D., & Van Dyke, M. (2017). Assessment of Potential Public Health Effects from Oil and Gas Operations in Colorado. Colorado Department of Public Health and Environment. http://accdan. org/assets/FULL_REPORT-CDPHE_Study. pdf.

McMullin, T., Bamber, A., Flores, J., Vigil, D., & Van Dyke, M. (2017). Assessment of Potential Public Health Effects from Oil and Gas Operations in Colorado. Colorado Department of Public Health and Environment. http://accdan. org/assets/FULL_REPORT-CDPHE_Study. pdf.

Nakagawa, M., Karim, M. R., Izawa, T., Kuwamura, M., & Yamate, J. (2021). Immunophenotypical characterization of M1/M2 macrophages and lymphocytes in cisplatin-induced rat progressive renal fibrosis. *Cells, 10*(2), 257.

Nel, A. E., Diaz-Sanchez, D., Ng, D., Hiura, T., & Saxon, A. (1998). Enhancement of allergic inflammation by the interaction between diesel exhaust particles and the immune system. *Journal of Allergy and Clinical Immunology, 102*(4), 539-554.

Ng, S. P., Silverstone, A. E., Lai, Z. W., & Zelikoff, J. T. (2006). Effects of prenatal exposure to cigarette smoke on offspring tumor susceptibility and associated immune mechanisms. *Toxicological Sciences, 89*(1), 135-144.

Novosad, J., Fiala, Z., Borska, L., & Krejsek, J. (2002). Immunosuppressive effect of polycyclic aromatic hydrocarbons by induction of apoptosis. Acta Medica (Hradec Kralove), 45(4).

O'Bryan, M. K., Gerdprasert, O., Nikolic-Paterson, D. J., Meinhardt, A., Muir, J. A., Foulds, L. M., & Hedger, M. P. (2005). Cytokine profiles in the testes of rats treated with lipopolysaccharide reveal localized suppression of inflammatory responses. American Journal of Physiology-Regulatory, *Integrative and Comparative Physiology, 288*(6), R1744-R1755.

Oertelt-Prigione, S. (2012). The influence of sex and gender on the immune response. *Autoimmunity Reviews, 11*(6-7), A479-A485.

Perrichon, P., Donald, C. E., Sørhus, E., Harboe, T., & Meier, S. (2021). Differential developmental toxicity of crude oil in early life stages of Atlantic halibut (Hippoglossus hippoglossus). *Science of the Total Environment*, 770, 145349.

Peters, L. E., MacKinnon, M., Van Meer, T., van den Heuvel, M. R., & Dixon, D. G. (2007). Effects of oil sands process-affected waters and naphthenic acids on yellow perch (Perca flavescens) and Japanese medaka (Orizias latipes) embryonic development. *Chemosphere, 67*(11), 2177-2183.

Pompermayer E, De La Corte FD, Rubin MI. Zinc sulphate turbidity as a screening test of passive transfer of immunity in newborn foals. *Acta Scientiae Veterinariae.* 2019;47(1).

Puett, R. C., Yanosky, J. D., Mittleman, M. A., Montresor-Lopez, J., Bell, R. A., Crume, T. L., Liese, A. D. (2019). Inflammation and acute traffic-related air pollution exposures among a cohort of youth with type 1 diabetes. *Environment international*, 132, 105064.

Rasne, A., Sonwane, V., Somani, R., & Kumthekar, P. (2018). Evaluation of immunomodulatory activity of protocatechuic acid. *J Res Notes*, 1, 1007.

Reynaud, S., & Deschaux, P. (2006). The effects of polycyclic aromatic hydrocarbons on the immune system of fish: a review. *Aquatic toxicology, 77*(2), 229-238.

Robertson, S. A., Chin, P. Y., Femia, J. G., & Brown, H. M. (2018). Embryotoxic cytokines—Potential roles in embryo loss and fetal programming. *Journal of Reproductive Immunology*, 125, 80-88.

Robinson, S. N., Shah, R., Wong, B. A., Wong, V. A., & Farris, G. M. (1997). Immunotexicological effects of benzene inhalation in male Sprague-Dawley rats. *Toxicology*, *119*(3), 227-237.

Rondelli, C. M., Larsen, M. C., N'jai, A., Czuprynski, C. J., & Jefcoate, C. R. (2016). PAHs target hematopoietic linages in bone marrow through Cyp1b1 primarily in mesenchymal stromal cells but not AhR: A reconstituted in vitro model. Stem Cells International, *2016*.

Saidana, D., Mahjoub, M. A., Boussaada, O., Chriaa, J., Chéraif, I., Daami, M., Helal, A. N. (2008). Chemical composition and antimicrobial activity of volatile compounds of Tamarix boveana (Tamaricaceae). *Microbiological Research, 163*(4), 445-455.

Salaberria, A. M., Labidi, J., & Fernandes, S. C. (2014). Chitin nanocrystals and nanofibers as nano-sized fillers into thermoplastic starch-based biocomposites processed by melt-mixing. *Chemical Engineering Journal*, 256, 356-364.

Salaberria, I., Brakstad, O. G., Olsen, A. J., Nordtug, T., & Hansen, B. H. (2014). Endocrine and AhR-CYP1A pathway responses to the water-soluble fraction of oil in zebrafish (Danio rerio Hamilton). *Journal of Toxicology and Environmental Health, Part A, 77*(9-11), 506-515.

Smits, J. E., Hersikorn, B. D., Young, R. F., & Fedorak, P. M. (2012). Physiological effects and tissue residues from exposure of leopard frogs to commercial naphthenic acids. *Science of the total environment*, *437*, 36-41.

Sun, H., He, X., Tao, X., Hou, T., Chen, M., He, M., & Liao, H. (2020). The CD200/CD200R signaling pathway contributes to spontaneous functional recovery by enhancing synaptic plasticity after stroke. *Journal of Neuroinflammation, 17*(1), 1-15.

van Grevenynghe, J., Bernard, M., Langouet, S., Le Berre, C., Fest, T., & Fardel, O. (2005). Human CD34-positive hematopoietic stem cells constitute targets for carcinogenic polycyclic aromatic hydrocarbons. *Journal of Pharmacology and Experimental Therapeutics, 314*(2), 693-702.

Veraldi, A., Costantini, A. S., Bolejack, V., Miligi, L., Vineis, P., & van Loveren, H. (2006). Immunotoxic effects of chemicals: A matrix for occupational and environmental epidemiological studies. *American Journal of Industrial Medicine, 49*(12), 1046-1055.

World Health Organization. (2005). Effects of air pollution on children's health and development: a review of the evidence.

Wu, B. (2019). Introductory chapter: new theory and technology in early clinical embryogenesis. In Embryology-theory and practice. IntechOpen.

Yamane, H., & Paul, W. E. (2013). Early signaling events that underlie fate decisions of naive CD 4+ T cells toward distinct T-helper cell subsets. *Immunological Reviews, 252*(1), 12-23.