The Effects of Inorganic Mercury Intoxication on Atherosclerosis in Rats

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***Abstract*—** Today many populations are exposed to multiple species of mercury. The reports indicate that inorganic mercury may have intoxication effect on heart. This study was exerted to determine the effect of inorganic mercury intoxication on atherosclerosis in rats. In this laboratory experimental study , rats were exposed to 5mg/kg, 10mg/kg, 15mg/kg and 20 mg/kg of mercury. After 28 days, tissues samples placed on lam and checked with microscope. The data was analyzed using ANOVA. Our data show that measure of atherosclerosis increased significantly when exposed to 15 mg/kg and 20 mg/kg of inorganic mercury ($P<0.01$). Other doses of inorganic mercury had no significant effect on intoxication in atherosclerosis in rats. Our findings show that high dose of inorganic mercury has intoxication effects on atherosclerosis in rats.

***Index Terms*—** Inorganic mercury, intoxication, atherosclerosis**.**

I. INTRODUCTION

Many population are exposed to multiple species of mercury **[**1**]** Inorganic mercury compounds exist in two oxidative states (mercurous, Hg^{+}; mercuric, Hg^{++}), which are generally in solid states as mercurous or mercuric salts and mercury compounds with chlorine, sulfur, or oxygen **[**2**].** The known intoxications are mainly occupational (mining, agriculture, incineration) or related to the use of dental amalgams or the consumption of contaminated fish and shellfish **[**3**].** Human toxicity varies with the form of mercury, the dose and the rate of exposure. The target organ for inhaled mercury vapor is primarily the brain. Mercurous and mercuric salts chiefly damage the gut lining and kidney, while methyl mercury is widely distributed throughout the body. Toxicity varies with dosage: large acute exposures to elemental mercury vapor induce severe pneumonitis, which in extreme cases can be fatal. Low-grade chronic exposure to elemental or other forms of mercury induces subtler symptoms and clinical findings, as discussed hereinafter **[**4**].**

Atherosclerosis is hypercholesterolemia, as excess cholesterol initiates foam cell formation in the arterial wall. Subsequently, inflammatory processes including recruitment of innate and adaptive immune cells contribute to further development of the plaque, which may eventually lead to plaque rupture and/or vessel occlusion **[**5**]** Most of the damage occurs when plaques become fragile and rupture. Plaques that rupture cause the formation of blood clots that can block blood flow or break off and travel to another part of the body. In either of these cases, if a clot blocks a blood vessel that feeds the heart, it causes a heart attack. If it blocks a blood vessel that feeds the brain, it causes a stroke. If blood supply to the arms or legs is reduced or blocked, it can cause difficulty walking and eventually gangrene. Atherothrombotic stroke is the most common stroke. It occurs when a blood clot forms on a atherosclerotic plaque within a blood vessel in the brain and blocks blood flow to that part of the brain **[**6**].**

Studies show that Human exposure to mercury has a very long history. Several thousand years ago in China, an inorganic mercury compound (mercury sulfide) was used to prepare red dye pigment vermilion, which is a brilliant red ore, namely cinnabar. Inorganic mercury compounds have also been used in medical applications since ancient Egypt. **[**7**]** On the other hand researches show that some doses of inorganic mercury have intoxication effect on heart diseases **[**8]-[14**].** This study was exerted to determine the effect of inorganic mercury intoxication on atherosclerosis in rats.

II. MATERIAL AND METHODS

In this laboratory experimental study, white male rats was prepared from Pasteur research complex and different doses of mercury (5mg/kg, 10mg/kg, 15mg/kg and 20mg/kg) were used in our study.

Briefly, the procedure was continued and carried out in the following steps:

Mercury was injected to rats until 28 days. After this 28days period, that rats were anesthetized with chloroform and blood samples were taken by syringe 10ml from the right atrium animal's heart and samples transferred to container. After washing samples, heart and aorta were placed in 10% formalin in samples container and then samples are cut for molding and were placed within liquid paraffin and after samples molding, samples are ready for tissues cutting. After removal of the samples, they are cut by microtome devices and placed into hot water and after this stage, samples placed on lam and coloring by eosin _ Haematoxylin color and checked our tissue with microscope.

Statistical significance was evaluated b one-way analysis variance (ANOVA) using SPSS 16 . Differences with $P<0.01$ were considered significant.

III. RESULTS

Figure I shows the atherosclerosis in response to different doses of inorganic mercury. Our finding show that atherosclerosis increases significantly in animals receiving 10

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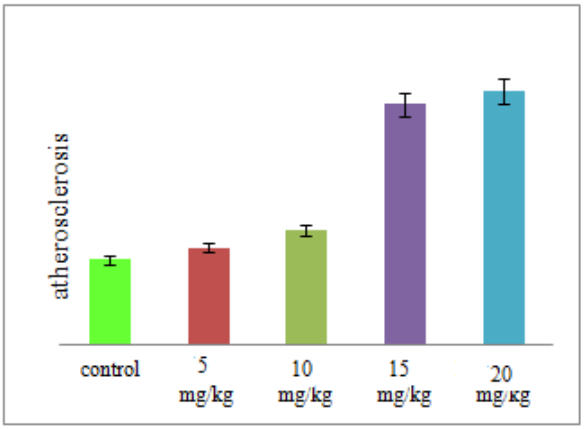
mg/kg (P<0.05), 15 or 20 mg/kg (P<0.01) of mercury compared with control group.



FigI. Atherosclerosis in animal receiving 5mg/kg , 10mg/kg , 15 mg/kg and 20mg/kg of mercury.

IV. Discussion

We have shown that high dose of inorganic mercury intoxication has increasing effect on atherosclerosis. In line with our finding there are also other records indicating that inorganic mercury may have atherosclerosis effects. Studies also suggest that Patients with Minamata disease and hair mercury levels above 100 µg per gram did not have a higher rate of death from heart disease than controls, nor did they have a higher degree of arteriosclerosis **[**15-16**].** However , it has been shown that Guallar et al. (Nov. 28 issue) report that a toenail mercury level as low as 0.11 to 0.66 µg per gram (estimated hair level, 0.34 to 2.03 µg per gram) was directly associated with a doubling of the risk of myocardial infarction **[**12**].**

The cardiovascular effects of cadmium have been observed in in vitro studies and in experimental animal models **[**17-18**].**

Mercury-induced oxidative damage has been observed both in vivo and in vitro, including myocardial tissues. The mechanisms by which mercury exerts its cardiovascular effects are not fully understood. However, exposure to mercury can lead to oxidative stress induction **[**19**].** The combination of high mercury and low selenium was not associated with higher CVD risk **[**20**]** Toxic effects of mercury also induce a number of stress proteins which include heat shock proteins and glucose-regulated proteins that have also been implicated in cardiovascular pathophysiology **[**21**].**

V. CONCLUSION

We have shown that high dose of inorganic mercury has intoxication effect on atherosclerosis in rats.

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REFRENCES

[1] Ishitobi H, Stern S, Thurston SW, Zareba G, Langdon M, Gelein R, et al. Organic and inorganic mercury in neonatal rat brain after prenatal exposure to methylmercury and mercury vapor. Environ Health Perspect. 2010 Feb;118(2):248

[2] Jung-Duck Park and Wei Zheng. Human Exposure and Health Effects of Inorganic and Elemental Mercury. J Prev Med Public Health. 2012 Nov; 45(6): 344–352. http://dx.doi.org/10.3961/jpmph.2012.45.6.344

[3] Dias D, Bessa J, Guimarães S, Soares ME, Bastos Mde L, Teixeira HM. Inorganic mercury intoxication: A case report. Forensic Sci Int. 2016 Feb;259:e20-4. http://dx.doi.org/10.1016/j.forsciint.2015.12.021

[4] Bernhoft RA. Mercury toxicity and treatment: a review of the literature. J Environ Public Health. 2012;2012:460508 http://dx.doi.org/10.1155/2012/460508

[5] van Dam AD, Bekkering S, Crasborn M, van Beek L, van den Berg SM, Vrieling F. BCG lowers plasma cholesterol levels and delays atherosclerotic lesion progression in mice. 2016 May 19;251:6-14

[6] Excerpted and adapted from "When Risk Factors Unite," appearing in the Stroke Connection Magazine January/February 2005 (Last science update April 2014) .

[7] Jung-Duck Park , Wei Zheng. Human Exposure and Health Effects of Inorganic and Elemental Mercury. J Prev Med Public Health. 2012 Nov; 45(6): 344–352. http://dx.doi.org/10.3961/jpmph.2012.45.6.344

[8] Mostafalou S, Abdollahi M. Environmental pollution by mercury and related health concerns: renotice of a silent threat. Arh Hig Rada Toksikol. 2013;64(1):179-81. http://dx.doi.org/10.2478/10004-1254-64-2013-2325

[9] Carpenter DO. Health effects of persistent organic pollutants: the challenge for the Pacific Basin and for the world. Rev Environ Health. 2011;26(1):61-9. http://dx.doi.org/10.1515/reveh.2011.009

[10] T. Sarafian and M. A. Verity, "Oxidative mechanisms underlying methyl mercury neurotoxicity," International Journal of Developmental Neuroscience, vol. 9, no. 2, pp. 147–153, 1991. http://dx.doi.org/10.1016/0736-5748(91)90005-7

[11] Rhee HM, Choi BH. Hemodynamic and electrophysiological effects of mercury in intact anesthetized rabbits and in isolated perfused hearts. Experimental and Molecular Pathology. 1989;50(3):281–290. http://dx.doi.org/10.1016/0014-4800(89)90038-5

[12] Guallar E, Sanz-Gallardo MI, Van'T Veer P, et al. Mercury, fish oils, and the risk of myocardial infarction. The New England Journal of Medicine. 2002;347(22):1747–1754 http://dx.doi.org/10.1056/NEJMoa020157

[13] Minoia C, Ronchi A, Pigatto P, Guzzi G. Effects of mercury on the endocrine system. Crit Rev Toxicol. 2009;39(6):538. http://dx.doi.org/10.1080/10408440903057029

[14] Dolbec J, Mergler D, Larribe F, Roulet M, Lebel J, Lucotte M. equential analysis of hair mercury levels in relation to fish diet of an Amazonian population, Brazil. Sci Total Environ. 2001 Apr 23;271(1-3):87-97. http://dx.doi.org/10.1016/S0048-9697(00)00835-4

[15] Tamashiro H, Akagi H, Arakaki M, Futatsuka M, Roht LH.Causes of death in Minamata disease: analysis of death certificates.Int Arch Occup Environ Health 1984;54:135-46. http://dx.doi.org/10.1007/BF00378516

[16] Oyanagi K, Furuta A, Ohama E, Ikuta F. Does methylmercuryintoxication induce arteriosclerosis in humans? A pathological investigationof 22 autopsy cases in Niigata, Japan. Acta Neuropathol(Berl) 1992;83:217-27. http://dx.doi.org/10.1007/BF00296782

[17] S. Sarkar, P. Yadav, R. Trivedi, A. K. Bansal, and D. Bhatnagar,"Cadmium-induced lipid peroxidation and the status of theantioxidant system in rat tissues," Journal of Trace Elements inMedicine and Biology, vol. 9, no. 3, pp. 144–149, 1995.

[18] S. Satarug, M. Nishijo, J. M. Lasker, R. J. Edwards, and M. R. Moore, "Kidney dysfunction and hypertension: role for cadmium, p450 and heme oxygenases?" Tohoku Journal of Experimental Medicine, vol. 208, no. 3, pp. 179–202, 2006. http://dx.doi.org/10.1620/tjem.208.179

[19] M. Yonaha, M. Saito, and M. Sagai, "Stimulation of lipid peroxidation by methyl mercury in rats," Life Sciences, vol. 32, no. 13, pp. 1507–1514, 1983. http://dx.doi.org/10.1016/0024-3205(83)90917-7

[20] K. Yoshizawa, E. B. Rimm, J. S. Morris et al., "Mercury and the risk of coronary heart disease in men," The New England Journal of Medicine, vol. 347, no. 22, pp. 1755–1760, 2002. http://dx.doi.org/10.1056/NEJMoa021437

[21] J. L. Rojko, and R. J. Marler, "Mercury induces regional and cell-specific stress protein expression in rat kidney," Toxicological Sciences, vol. 53, no. 2, pp. 447–457, 2000. http://dx.doi.org/10.1093/toxsci/53.2.447