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Review Article

MERCURY TOXICITY AND ITS MANAGEMENT

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ABSTRACT

Mercury is an element that has been known for at least 4000 years (Chang 1985). It is a metal that is liquid at room temperatures and is widely used in our modern society. Today, the unique chemical and physical properties of mercury are widely used in industry, agriculture, medicine, mining, dentistry and other areas of everyday life. Some of these are used in the manufacture or processing of felt, fireworks, batteries, blackening brass, photography pigments for rubber and plastics, wine colouring and medicine. Medical compounds comprised of 75 % of the list and included antibacterial, antiseptic, topical anaesthetic, immunosuppressant, anti-infective and fungicide, diuretic, cathartic and preservative agents. There are two goals to treatment. First, get rid of the mercury, second, control symptoms so you can be comfortable and productive during the prolonged period when mercury is removed and healing takes place. In order to control the symptoms it is necessary to identify the metabolic defects mercury is causing for you.

Keywords: mercury hazards, minamata disease, DMSA.

INTRODUCTION

Mercury is an element that has been known for at least 4000 years (Chang 1985). It is a metal that is liquid at room temperatures and is widely used in our modern society. Its medical aspects are well understood, yet it is highly reviled by the general public for its misunderstood and / or misrepresented toxic properties. Mercury is a naturally occurring element with 30,000 to 150,000 tons being released into the atmosphere by the degassing of the earth's crust and the oceans. Another 2,000 to 3,000 tons are released from human activities, primarily burning household and the industrial waste and especially from burning fossil fuels, such as coal.[1-3] Mercury is the 80th element in the periodic chart. Its synonyms are quick silver and hydrodynium (Water metal) hence its symbol Hg (Sunderman 1988). It is silver white metal with a mirror like surface when it is liquid and has an atomic weight of 200.6, specific gravity; 13.55, melts at: 38.8^{o}C and boils at 356.7^{o}C. It is rather a poor conductor of heat compared to other metals and a fair conductor of electricity. As a vapour, it is odorless and colorless and has a high vapour pressure. Pure mercury does not tarnish when exposed to air at ambient temperature. It forms an alloy, a process called amalgamation with most metals other than iron. Mercury occurs naturally and is found throughout the environment. It is in air, water and food that we consume. The average atmospheric mercury level is 1.5 µg / m^3. The daily consumption of mercury from air, food and water is 10.20 µg and this is on a low fish diet. Today, the unique chemical and physical properties of mercury are widely used in industry, agriculture, medicine, mining, dentistry and other areas of everyday life. The research on carcinogenesis of mercury and its compounds has indicated to positive results in humans but teratogenesis of organic mercury compounds has been observed in numerous systems.

Compounds of Mercury

Inorganic Mercury[4,5]

Highly toxic and poisoning usually results due to accidental or intentional ingestion. Mercury chloride (HgC / 2): listed as 'Violent poison' in the Merck's index (1996). It is caustic in nature. When ingested lining of GI tract is lost. Patient exhibits severe pain, nausea, vomiting and diarrhea. Cardiovascular collapse may occur with in several hours after exposure.

Organic Compounds

They are short and long chain alkyl and aryl compounds. Of the alkyl compounds, methyl and ethyl are the most common and very toxic. These compounds are absorbed 90 % into the gut and have biological half life of 70-90 days. These forms of mercury get into the food chain and finally are consumed by humans. Episodic methyl mercury poisoning has occurred to large groups of people where fish and / or shellfish are a major part of their diet. Industrial discharge of mercury in the waterway is converted into methyl mercury and during chronic consumption, degenerative neurological disorders are found in the populations.

Elemental Mercury

It has little or no toxic effect when swallowed. Some bizarre forms of elemental mercury poisoning can occur when the mercury is injected S.C., I.M., or I.V. Some of these are the result of suicidal attempts or mistaken effort to build muscle mass.

Mercury Vapor

Significant toxicity can occur when vapors of mercury are inhaled. 80 % of mercury vapour inhaled or inspired is absorbed in the lungs and the toxic exposure is generally cumulative. Acute toxicity can occur but is infrequent. Large dose of mercury vapour can cause acute pneumitis, renal failure, seizures and neurological dysfunction. Chronic

exposure to mercury vapors can cause neurological impairment which manifests as mild to moderate central nervous system dysfunction with irritability, memory loss, insomnia, renal failure, anorexia and tremors[6-8].

Absorption, Transportation and Excretion in the Body

Absorption of Mercury[9]

Skin	Lungs	Gastrointestinal Tract
Elemental -	80 %	0.01 %
Inorganic -	80 %	7 %
Organic -	-	95–98

Mercury Exposure in Dental Practice

Various means of exposure to mercury

- Storage of mercury
- Preparation and placement of amalgam restoration.
- Polishing silver amalgam restoration
- Removal of amalgam filling.
- Storage of waste silver amalgam.

Exposure of mercury may be either in the form of vapour or particulate amalgam dust (Hg^{2+}).

Methods to Detect Mercury Vapor Release

1. Mercury thermometer.
2. Jerome mercury vapours detectives.
3. Gold film mercury vapour detectives
4. Twin cell photo acoustic mercury detector
5. Atomic absorption mercury detector.
6. Scanning electron microscopy (SEM) and energy dispensive, x-ray analysis (EDXA) of sectioned teeth with amalgams.
7. Perkins Elmer flow infection mercury system.

Mercury Exposure Hazards and Risk Assessment

It is seen that, most mercury released into the mouth is swallowed and passes into gastrointestinal tract. This mercury is oxidized to less toxic mercury ion (Hg^{+2}) and about 5-10 % is absorbed.

- Mercury vapor from dental amalgam restoration results in absorption of 1 μg / day in lungs.
- Amount of mercury swallowed - > 1 μg/day is absorbed by GIT.
- Threshold for absorption of mercury vapor by lungs: 20 μg / day.
- Threshold for GIT absorption: 400 μg / day

Mercury Deposits Maybe Found In

1. Spinal ganglion: neurons and satellite cells.
2. Anterior pituitary: Secretary Cells.
3. Adrenal medulla : Chromatin cells and macrophages
4. Pancreas: Islets of langherans.
5. Liver: Hepatocytes and Kupffer cells.
6. Kidney: Proximal tubular cells.
7. Lungs: Macrophages.
8. Lymph glands: Macrophages and reticular cells.

Kidney is the main organ to accumulate inorganic mercury and it is principally due to its ability to complex with metallothione and selenium. Studies have shown that mercury may pass from mother to fetus in blood and may be found in amniotic fluid and milk. Its level depends mainly on the amount of fish in the diet of mother rather than amalgam fillings.

Mercury Toxicity

Acute mercury vapor poisoning is a rare but fatal toxicological emergency. People are exposed to mercury in daily life by the way of foods, vaccines, antiseptics, ointments, amalgam or occupation[10]. Only under very rare circumstances have the symptoms of mercury toxicity been observed in human beings (industrial pollution in Minamata Bay, inadvertent contaminated grain consumption in New Mexico and Iraq). The Minamata Bay incident in Japan in 1952 is the most in famous. A local chemical plant (Chisso Corporation) disposed of its methyl mercury waste into the nearby bay, contaminating the shellfish and causing toxic levels of mercury of the fish eaten by the local population. By the time the source was identified, 52 individuals had died and 202 others were stricken by mercury poisoning. Since this time, mercury poisoning of this kind is known as Minamata disease. The symptoms of mercury poisoning identified during this incident were

1. Ataxic gait
2. Convulsions
3. Numbness in mouth and limbs
4. Constriction in visual field.
5. Difficulty in speaking.

Harmful effects of mercury from the dental amalgam could be in the form of

1. Toxicity.
2. Hypersensitivity

Mercury has been found to be a causative agent of various sorts of disorders, including alterations of motor function and neuroendocrine secretion at very low exposure levels of inorganic Hg[11], Nephrological (Kidney injury from mercury is known to cause dose-related tubular dysfunction and idiosyncratic nephrotic syndrome)[12], An immunological effect has also been observed in studies on clinically asymptomatic workers with low level exposure[13], cardiac, motor, reproductive and even genetic. Recently heavy metal mediated toxicity has been linked to diseases like Alzeihemer's, Parkinson's, Autism, Lupus, Amyotrophic lateral sclerosis, etc. Besides this, it poses danger to wildlife[14]. Some of the "Disease" a modern physician might mistakenly misdiagnose chronic mercury poisoning are addison's disease, allergies, alzheimer's disease, ankylosing spondylitis, anorexia nervosa, anxiety, asthma, attention deficit hyperactivity disorder, auto immune disease, bipolar disorder, borderline personality disorder, bulimia, candidiasis, crohn's disease etc. Quantitative diagnostic procedures are done to decide whether the problems are due to mercury poisoning or not.

Mercury Management

Like all other materials in the world, mercury has the potential to be hazardous if not managed properly. Acute inhalation of metallic or inorganic mercury vapours mainly induces pulmonary diseases, whereas chronic inhalation rather induces neurological or renal disorders[15]. It is very important that the alloying reaction of mercury with silver, tin go to completion to ensure that mercury does not diffuse into the oral environment. Once the reaction is complete, only extremely small amount of minute levels of mercury can be released and those are far below the current health standard. The important perspective is that mercury enters the body everyday no matter what restorative fillings. Materials are present in the mouth. As long as the toxic levels are low,

there is no threat for mercury toxicity. Historically, a major source although rare, mercury contamination in dental office was accidental spillage of quantities of liquid mercury. Mercury was commonly purchased in bottles containing approximate 1 pound. This was then transferred to individual capsules for mixing. Mishandling at any stage could result in mercury splashing on the bench or floor, causing it to be widely scatted as small droplets. Fortunately, the current use of precapsulated amalgam has eliminated more opportunities for a major spill, but care must be maintained to avoid hazards to routine use of amalgam. Careful reviews of amalgam handling characteristics reveals that the critical times are when metallic mercury exists in liquid or vapor form, rather than bound air a set amalgam. In the dental office, the sources of mercury exposure related to amalgam include

1. Amalgam raw materials being stored for use (usually precapsulated packages).
2. Mixed but unhardened amalgam during trituration, insertion and intra oral hardening.
3. Amalgam scrap that has insufficient alloy to completely consume the mercury present.
4. Amalgam undergoing finishing and polishing operation
5. Amalgam restoration being removed.

It is difficult, if not impossible to totally contain liquid or gaseous mercury because it is very mobile, has high diffusion rate and penetrates through extremely fine spaces. Even in packages that include plastic blister wrapping and layers of cardboard, Hg vapor leakage is possible, because Hg containing products should not be stored open, but rather in closets or the offices. Storages location should be near a vent that exhausts air out of the building.
Before use: Stored in a plastic container with threaded cover
After use: Stored in a fixes solution containing Ag with binds with mercury.

Treatment

The physician must be able to recognize the clinical manifestations of mercury intoxication and understand the importance of biological markers in making a definitive diagnosis of mercury poisoning. In a desire to treat the patient complaining of symptoms similar to some that can be caused by mercury, a growing number of physicians, particularly those in alternative medicine fields, result to chelation to "rid" the body of the mercury, believed to be the cause of the ailments. And although the use of chelation is increasing, controlled studies showing that this procedure actually improves outcome are lacking. If chelation therapy is considered to be indicated, the attending physician should communicate the risks of chelation to the patient before beginning treatment with metal-chelating drugs[16]. There are two goals to treatment. First, get rid of the mercury, second, control symptoms so you can be comfortable and productive during the prolonged period when mercury is removed and healing takes place. In order to control the symptoms it is necessary to identify the metabolic defects mercury is causing for you. Either 2,3-dimercaptosuccinic acid (DMSA), 2,3-dimercaptopropanol (BAL), 2,3-Dimercapto-1-propanesulfonic acid, Dimaval (DMPS) or N-acetyl-D, L-penicillamine (NAP) can be used in the treatment of mercury poisioning.[17] Meso-2,3-dimercaptosuccinic acid (DMSA) is a sulfhydryl-containing, water-soluble, non-toxic, orally-administered metal chelator which has been in use as an antidote to heavy metal toxicity since the 1950s. More recent clinical use and research substantiates this compound's efficacy and safety and establishes it as the premier metal chelation compound, based on oral dosing, urinary excretion and its safety characteristics compared to other chelating substances[18]. Using a proper protocol, e.g. DMSA every 3-4 h on alternate weeks; 2-6 months to feel better; then DMSA + L.A. every 3-4 days every week or two to clear the brain and internal organs, 2-6 months to feel better. Continue supplements and diet control with continuing DMSA + LA chelation while healing takes place. Moderately poisoned patient is feeling depressed, tired and icky. 6-11 months of DMSA + LA treatment. It cures immediately, if taken right supplements and medicines, but chelation is required to get rid of the mercury.

- In case of chronic fatigue, fibromyelgia, environmental sensitivities, severe allergies or asthma, emotional disturbances, 14-25 months of DMSA-LA required.
- In case of multiple chemical sensitivities, chronic fatigue syndrome, serious emotional disturbances – seriously poisoned - > 20-36 months of DMSA + LA.
- To reduce the chances of future problems, neurological disease, or premature aging and to remove more mercury from the brain, chelate with DMSA + LA for 6 months to a year.

DMSA was able to increase the excretion of mercury to a greater extent than NAP. Acute Hg intoxication can be managed with BAL as first choice chelator, whereas the less toxic 2,3-dimercaptosuccinic acid (DMSA) and 2,3-dimercaptopropane-1-sulfonic acid (DMPS) should be reserved for cases of less severe inorganic Hg or methyl-Hg acute intoxication. Such agents, recommended only for the treatment of acute Hg poisoning, should not be used for patients suffering from neurological diseases in which environmental Hg exposure is hypothesised[19].

CONCLUSION

An important part of program for handling toxic materials in periodic monitoring is of actual exposure levels. Biological determination can be performed on personnel using Hg to measure Hg levels in blood and urine. The risk of mercury exposure to such personnel cannot be ignored, but close adherence to simple hygiene procedures helps ensure a safe working environment. As mercury can give rise to allergic and immunotoxic reactions which may be genetically regulated, in the absence of adequate dose-response studies for immunologically sensitive individuals, it has not been possible to set a level for mercury in blood or urine below which mercury related symptoms will not occur. The most significant contribution to mercury assimilation from dental amalgam is via vapour phase. The patients encounter with Hg vapour during insertion of restoration is brief and the total amount of mercury vapour released during function is far below the "no effect" level. The most reliable estimates suggest that Hg from dental amalgam does not contribute a significant amount to the total exposure of patient. However in continuity to use amalgam, dentist must observe strict Hg and amalgam hygiene procedures so that the health of dental workers is not put at risk. It is also necessary to safety dispose mercury. It must be prevented from reaching the sewage system so as to avoid environmental contamination.

REFERENCES

1. Dodes JE. The amalgam controversy, JADA 2001; 132: 348–356. PMid:11258092
2. Pacyna EG, Pacyna JM, Steenhuisen F and Wison S. Global anthropogenic mercury emission inventory for 2000. Atmospheric environment 2006; 40: 4048–4063. http://dx.doi.org/10.1016/j.atmosenv.2006.03.041
3. Wong CC, Duzgoren Aydin NS, Aydin A and Wong MH. Sources and trends of environmental mercury emissions in Asia. Science of the Total Environment 2006; 368: 649–662. http://dx.doi.org/10.1016/j.scitotenv.2005.11.024 PMid:16405972
4. Theodore M Roberson, Harald O Heymann, Edward J Swift. Sturdevent's Art and Science of Operative Dentistry, Fifth edition; p. 162-169.
5. Vimal Sikri. Textbook of Operative Dentistry, Isted; p. 237-239.
6. James S Woods, Michael D Martin, Brian G Leroux, Timothy A De Rouen, Jorge G Leitão, Mario F Bernardo, Henrique S Luis. The Contribution of Dental Amalgam to Urinary Mercury Excretion in Children, Environ Health Perspect 2007; 115(10): 1527-1531.
7. Echeverria D, Aposnian HV, Woods JS, Heyer NJ, Aposhian MM, Bittner AC, *et al*. Neurobehavioral effects from exposure to dental amalgam: new distinctions between recent exposure and Hg body burden. FASEB J 1998; 12: 971-980. PMid:9707169
8. Preben Hörsted Bindslev. Amalgam toxicity—environmental and occupational Hazards, Journal of Dentistry 2004; 32(5): 359–365. http://dx.doi.org/10.1016/j.jdent.2004.02.002 PMid:15193783
9. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Mercury. US Department of Health and Human Services: Public Health Service. www.atsdr.cdc.gov/toxprofiles/tp46.pdf; 1999.
10. Oz SG, Tozlu M, Yalcin SS, Sozen T, Guven GS. Mercury vapor inhalation and poisoning of a family. Inhal Toxicol 2012; 24(10): 652-8. http://dx.doi.org/10.3109/08958378.2012.708677
11. Lucchini R, Cortesi I, Facco P, Benedetti L, Camerino D, Carta P, Urbano ML, Zaccheo A, Alessio L. Neurotoxic effect of exposure to low doses of mercury. Med Lav 2002; 93(3): 202-14. PMid:12197270
12. Miller S, Pallan S, Gangji AS, Lukic D, Clase CM. Mercury-associated nephrotic syndrome: a case report andsystematic review of the literature. Am J Kidney Dis 2013; 62(1): 135-8. http://dx.doi.org/10.1053/j.ajkd.2013.02.372
13. Zahir F, Rizwi SJ, Haq SK, Khan RH. Low dose mercury toxicity and human health. Environment toxicology pharmacology 2005; 20(2): 351 -60. http://dx.doi.org/10.1016/j.etap.2005.03.007
14. Kazantzis G. Mercury exposure and early effects: an overview. Med Lav 2002; 93(3): 139-47. PMid:12197264
15. Bensefa Colas L, Andujar P, Descatha A. Mercury poisoning. Rev Med Interne 2011; 32(7): 416-24. http://dx.doi.org/10.1016/j.revmed.2009.08.024
16. Risher JF, Amler SN. Mercury exposure: evaluation and intervention the inappropriate use of chelating agents in the diagnosis and treatment of putative mercury poisoning. Neurotoxicology 2005; 26(4): 691-9. http://dx.doi.org/10.1016/j.neuro.2005.05.004 PMid:16009427
17. Bluhm RE, Bobbitt RG, Welch LW, Wood AJ, Bonfiglio JF, Sarzen C, Health AJ, Branch RA. Elemental mercury vapour toxicity, treatment and prognosis after acute, intensive exposure in chloralkali plant workers. Part I: History, neuropsychological findings and chelator effects. Hum Exp Toxicol 1992; 11(3): 201-10. http://dx.doi.org/10.1177/096032719201100308 PMid:1352115
18. Miller AL. Dimercaptosuccinic acid (DMSA), a non-toxic, water-soluble treatment for heavy metal toxicity. Altern Med Rev 1998; 3(3): 199-207. PMid:9630737
19. Boscolo M, Antonucci S, Volpe AR, Carmignani M, Di Gioacchino M. Acute mercury intoxication and use of chelating agents. J Biol Regul Homeost Agents 2009; 23(4): 217-23. PMid:20003760

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